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THE METABOLIC AND HORMONAL RESPONSE TO CATARACT SURGERY: A COMPARISON BETWEEN GENERAL AND LOCAL ANAESTHESIA

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Abstract

This thesis compares the endocrine and metabolic response to cataract extraction in patients receiving either general or local anaesthesia.

Under general anaesthesia, plasma cortisol concentrations increase more than two–fold during cataract surgery, with smaller changes in circulating glucose and catecholamine concentrations. Both retrobulbar and peribulbar anaesthesia completely abolish these changes. Retrobulbar blockade also improves cardiovascular stability, as measured by changes in heart rate and mean arterial pressure. When retrobulbar blockade is combined with general anaesthesia, changes in circulating cortisol and glucose concentrations are prevented during surgery, but there is a marked increase in cortisol concentration during the immediate postoperative period.

Similar increases in cortisol concentration are seen in non–insulin–dependent diabetic (NIDDM) patients receiving general anaesthesia. The glycaemic response is greater in NIDDM than in non–diabetic patients, and there is a failure of insulin secretion postoperatively in the diabetic patients receiving general anaesthesia. Retrobulbar blockade maintains hormonal and metabolic stability, which is important in these patients, in whom cataracts are a common complication.

The results of a postoperative questionnaire on 231 patients following cataract surgery under either general or local anaesthesia show the acceptability of both techniques. There is significantly less nausea and sore throat in the local anaesthetic patients, but more bruising of the eye. There is no difference in the severity of postoperative pain, but local anaesthetic patients drank and ate much earlier following their operations.

The results provide evidence of the benefits of local anaesthesia for cataract surgery in the elderly patient. Both peribulbar and retrobulbar blockade prevent the metabolic and hormonal changes seen when surgery is performed under general anaesthesia and provide better cardiovascular stability. The findings are particularly important to the diabetic patient.

Acknowledgements

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Abbreviations used in this thesis:

ANOVA	Analysis of variance
βOH	Beta-hydroxybutyrate
CBV	Choroidal blood volume
CO_2	Carbon Dioxide
CT	Computerised tomography
CVP	Central venous pressure
EGTA	Ethyleneglycol-bis-(β aminoethyl)-N,N,N',N'-tetraacetic acid
Fig	Figure
GA	General Anaesthesia
HPLC	High pressure liquid chromatography
h	Hours
INR	International normalised ratio
IOP	Intraocular pressure
IV	Intravenous
kg	Kilogram
kPa	KiloPascals
LA	Local Anaesthesia
NEFA	Non-esterified fatty acids
NIDDM	Non-insulin-dependent diabetes mellitus
ns	Not significant
OCR	Oculocardiac reflex
PB	Peribulbar blockade
RB	Retrobulbar blockade
SEM	Standard error of the mean
min	Minutes
WHO	World Health Organisation
yr	Years

Chapter One

Anaesthesia for cataract surgery

Cataracts can be congenital, senile, associated with metabolic disorders or traumatic in origin. They are associated with dystrophia myotonica, inborn errors of metabolism, chromosomal abnormalities, diabetes mellitus and steroid therapy. The senile variety are the most common, with 46% of people over 75 years of age having cataracts (Kahn et al, 1977). Surgical management of cataracts has changed over the last few years. Hodgkins and colleagues (1992) conducted a survey of surgical practice by consultant ophthalmologists in England and Wales. They obtained an 86% response rate, and showed that the most common technique in cataract surgery is non–automated extracapsular extraction, routinely undertaken by 53% of consultants. 93% performed some variant of extracapsular surgery and 99% of surgeons routinely implanted an intraocular lens. This contrasts with 1985, when only 34% of consultants regularly performed extracapsular extraction, and less than 50% implanted an intraocular lens (Wong and Steele, 1985).

Anaesthesia can contribute to the success or failure of ophthalmic surgery. The requirements for such surgery are anaesthesia, akinesia and hypotonia, that is to say, the surgeon requires a still, soft eye. Movement of the eye unexpectedly during a delicate part of surgery can lead to blindness. In one study, 30% of eye injury claims associated with anaesthesia were due to patient movement during ophthalmic surgery, leading to blindness in all cases (Gild et al, 1992). This occurred under both general and local anaesthesia. Intraocular pressure (IOP) needs to be controlled before, during and after the procedure for a successful outcome. An understanding of eye anatomy and physiology, and the effects of anaesthesia on IOP, is important when making anaesthetic decisions for eye surgery.

History

Anaesthesia for cataract surgery has evolved over the past century. The discovery of cocaine as a local anaesthetic by Koller in 1884, led to the use of topical anaesthesia for eye surgery. In the same year, Knapp described the technique of retrobulbar anaesthesia (Knapp, 1884), but it was not until 50 years later, with the introduction of better local anaesthetic agents, that it became generally accepted. Local anaesthesia, whether topical or by retrobulbar blockade, was the anaesthetic method of choice because of the eye's accessibility and the disastrous effects of coughing under general anaesthesia.

As general anaesthesia evolved, the physiology of the eye was understood and new anaesthetic agents and techniques became available, general anaesthesia became more popular. With general anaesthesia, a still eye can be provided relatively easily and IOP can be controlled. However, the patients are often elderly and may have associated medical diseases, such as hypertension, heart disease, respiratory problems or diabetes.

General anaesthesia became the method of choice, partly fuelled by the patients' expectations of being asleep for their operation. However, in recent years, local anaesthesia has seen a revival with more operations performed under retrobulbar or peribulbar blockade. Regional anaesthesia is suitable for a wide variety of eye operations, including cataract extraction, trabeculectomy, vitrectomy and strabismus repair. Cataract surgery is by far the most common ophthalmic operation done under local anaesthesia. Almost all cataract surgery is performed under local anaesthesia in the United States and India, while in the United Kingdom, 50% is still performed under general anaesthesia (College News, 1992).

However, the pattern is changing (Wong, 1993).

Anatomy

The wall of the eyeball is made up of three coats (Fig 1.1). The outer fibrous coat is an extension of the dural sheath of the optic nerve, and consists of the sclera posteriorly and the cornea anteriorly. The middle coat is continuous with the arachnoid and pia mater. This is the vascular layer, and consists of the choroid, the ciliary body and the iris. The inner coat, the retina, is an expansion of the neuronal tissue of the optic nerve. The body of the eyeball is filled with vitreous humour, the lens and the aqueous humour.

Intraocular pressure

Normal intraocular pressure (IOP) is 1.3–2.6 kPa (10–20 mmHg) (MacRae, 1990) and is maintained by a balance between the production and drainage of aqueous humour. Aqueous is formed partly as an ultrafiltrate and partly as a secretion from the ciliary plexus. It passes into the anterior chamber, where it is drained into the canal of Schlemm and the episcleral veins. If the outflow is obstructed, such as in glaucoma, the eyeball, surrounded by its inelastic sclera, is unable to expand, and the pressure increases.

Other important influences on IOP are changes in choroidal blood volume (CBV), systemic arterial and central venous pressures, CO_2 tensions, and extraocular muscle tone. Sudden increases in systemic arterial blood pressure cause a transient swelling of CBV, and thus a brief rise in IOP, but IOP is more affected by changes in central venous pressure (CVP) (Murphy, 1985). Coughing, straining, emesis and the Valsalva manoeuvre all significantly increase CVP and thus increase IOP. Coughing can increase IOP to 30–40 mmHg. CBV, and thus IOP, also increases in response to respiratory acidosis, hypercarbia and hypoxia. Thus allowing the patient to hypoventilate during anaesthesia will cause an increase in IOP. Carefully maintained anaesthesia with mild hyperventilation and a gentle head–up tilt produces optimum venous and ocular pressures.

Most anaesthetic agents reduce IOP by relaxing extraocular muscle tone, depressing the central nervous system, improving the flow of aqueous humour and lowering venous and arterial blood pressure. Halothane, enflurane and isoflurane have all been shown to reduce IOP to a similar degree (Runciman et al, 1978; Ausinsch et al, 1975; Earnshaw, 1984). However, suxamethonium and ketamine may increase IOP. The effect of ketamine varies. Recent data suggest that IOP is not affected when ketamine is given after a diazepam premedication (Cunningham and Barry, 1986). Suxamethonium causes a transient but significant increase in IOP of 10–20 mmHg lasting 4–6 min (Donlon, 1994). This is not due solely to the muscle fasciculations caused by suxamethonium, since sectioning the recti eye muscles does not prevent the rise in IOP (Donlon, 1994). The increase in IOP with suxamethonium may depend on timing and dose, on a direct effect of suxamethonium on CBV or aqueous formation, or on the special tonic response of the extraocular muscles because of their unique morphological structure (the Felderstruktur) (Cunningham and Barry, 1986).

Laryngoscopy and endotracheal intubation are the anaesthetic interventions most likely to increase IOP and can cause a rise of 10–20 mmHg (Murphy, 1985; Cunningham and Barry, 1986). This may be related to sympathetic cardiovascular responses to intubation, and various pretreatments have been tried to overcome this response. These include the use of intravenous lignocaine and alfentanyl (Badrinath, Braverman and Ivankovich, 1988), oral clonidine (Ghignone et al, 1988), intravenous dexmedetomidine (Jaakola et al, 1992) and intranasal nitroglycerine (Mahajan, 1988).

Akinesia

Akinesia, or lack of movement of the eye, can be easily obtained with general anaesthesia (GA), but can also be produced under local anaesthesia (LA). The globe is moved by four rectus muscles (superior, medial, inferior and lateral) and two oblique muscles (superior and inferior). Together the four rectus muscles produce a cone with the point at the orbital apex and the base at the equator of the globe. (Fig 1.2) Within this cone, lie the optic nerve, artery, vein and the ciliary ganglion. Local anaesthetic solution is deposited inside the cone for retrobulbar blockade, and outside it for peribulbar blockade. Computed tomography (CT) scanning following these LA blocks has demonstrated that the anaesthetic solution can spread freely between the inside and outside of the cone, wherever it is deposited (Ropo et al, 1991).

The orbicularis muscle also needs to be immobilised or the patient may squeeze the eyelids, which interferes with surgery and increases IOP. This muscle is supplied by the facial nerve and akinesia can be achieved by blocking the facial nerve at its terminal branches (described by van Lint in 1914), superior branches (Atkinson block) (Atkinson, 1953) or proximal trunk (O'Brien or Nadbath block) (Nadbath and Rehman, 1963). Facial nerve block can be painful. It is unnecessary with peribulbar blockade, where the larger volumes of LA used, combined with orbital decompression devices, lead to effective spread from the orbit through the orbital septum to provide eyelid akinesia. It has also been shown that a 3 ml retrobulbar injection of LA gives adequate orbicularis akinesia in 88% of patients (Martin, Baker and Muenzler, 1986). However, younger patients present more of a challenge in achieving total akinesia than the elderly because denser connective tissues hinder access of anaesthetic agents to the oculomotor nerves (Morsman and Holden, 1992).

The oculocardiac reflex

Traction on the extraocular muscles, or pressure on the globe, can induce cardiac arrhythmias, most commonly sinus bradycardia, and even asystole can occur. The afferent fibres of this oculocardiac reflex (OCR) run in the short and long ciliary nerves to the ciliary ganglion, then via the ophthalmic division of the trigeminal nerve to the gasserian ganglion in the floor of the 4th ventricle (Donlon, 1994). The efferent fibres run in the vagus. The OCR is seen most commonly in operations performed under GA, usually in strabismus or retinal detachment surgery, where considerable traction can be applied to the globe. The afferent pathway can be blocked by regional anaesthesia, and the combination of regional techniques with GA has been used to prevent the reflex (Jedeikin and Hoffman, 1977). However, pressure on the globe can also initiate the OCR, thus rapid distension of the tissues by local anaesthetic solutions or haemorrhage, or application of pressure to the globe too soon after the block, may induce dysrrhythmias (Wong, 1993). LA blocks cannot be relied upon to protect against the reflex, and sinus arrest has occurred with traction under both retrobulbar (Smith, Douglas and Petruscak, 1972) and peribulbar (Batterbury et al, 1992) blockade.

Local anaesthetic blocks

Retrobulbar or intracone block (Fig 7.4) as described by Knapp (1884), has been used successfully for many years to provide analgesia for ophthalmic surgery. A small volume of local anaesthetic solution (3 ml) is placed intraconally in mid–

orbit. Care is taken to avoid the orbital contents, which include the optic nerve and ophthalmic artery.

Peribulbar or pericone block was described by Davis and Mandel (1986), and has become the technique of choice in recent years. Local anaesthetic solution is injected outside the cone (Fig 7.5), avoiding the intraconal structures, and thus carrying a lower risk of serious complications. Hamilton, Gimbel and Strunin (1988) have shown that safe, comfortable and effective analgesia and akinesia can be obtained with this technique. There are many variations of the peribulbar technique, with injections placed in one or more sites, commonly in the inferotemporal and the superonasal quadrants; or with a single injection just medial to the caruncle (Brahma et al, 1994).

Reports of rare, but serious, complications of intraconal anaesthesia have prompted the concept of non–akinetic methods of regional anaesthesia for cataract extraction surgery. **Subconjunctival injection** has been described (Petersen and Yanoff, 1991), where a small volume of local anaesthetic is injected near the superior limbus, mainly for anterior segment surgery. **Sub–Tenon's block** (Tsuneoka et al, 1993) produces better iris and anterior segment anaesthesia than subconjunctival injection. Here, the local anaesthetic solution is injected into sub–Tenon's space within Tenon's capsule. The degree of abolition of extraocular muscle movement is proportional to the volume and depth of the injectate. Recently there has been a reintroduction of **topical corneoconjunctival anaesthesia** for cataract extraction (Harr, 1991). The iris and the ciliary muscle retain their sensitivity, especially in the young and anxious patient (Grabow, 1993). Patients with dense or trauma–induced cataracts, those with small pupils which fail to dilate and those with macular degeneration, are best managed with other forms of anaesthesia.

Two excellent reviews on regional anaesthesia for ophthalmic surgery have been published recently (Wong, 1993; Hamilton, 1995). They highlight the discussions which have taken place, not only over which block to perform, but over the best manner in which to perform it, the equipment and the local anaesthetic solutions to use, whether or not to use sedation, and the role of the anaesthetist.

Eye position

It is generally agreed that the best position for the eye during retrobulbar block is in the primary gaze position. Traditional teaching required the patient to look "up and in" during needle placement. This has now been shown, using computerized tomography in cadavers (Unsold, Stanley and DeGroot, 1981) and magnetic resonance imaging in a normal subject (Liu, Youl and Moseley, 1992), to displace the optic nerve downward and outward and to bring it closer to a needle passed intraconally. With the globe in the primary gaze position, the optic nerve remains mobile and away from the needle.

Needles

Discussion has also taken place over the type of needle used for eye blocks. Sharp, fine–gauge needles are less painful for the patient, but may not show any appreciable change in resistance should the globe or optic nerve be penetrated. Blunt, or short–bevelled needles may show some resistance, and thus it is believed that they may reduce the risk of these complications. However globe penetration and optic nerve injury can still occur (Duker et al, 1991; Pautler et al, 1986; Joseph et al, 1991). Although Hay and colleagues (1991) showed no difference in the severity of injury and visual outcome between the use of sharp or blunt needles, Grizzard and colleagues (1991) reported that, unless there were multiple exit wounds, visual acuity was better preserved where the globe had been perforated with a sharp needle. It has also been shown, on rat sciatic nerves, that short bevelled needles do more damage than long bevelled needles (Rice and McMahon, 1992).

Needle length is also important, as optic nerve perforation and brainstem anaesthesia are usually associated with needles of 35mm or longer. Curved needles have been designed to try to reduce the risks of retrobulbar injections (Straus, 1988). However there is doubt about their effectiveness (Grizzard et al, 1991). All needles used should be orientated tangentially, with the bevel opening towards the globe (Hamilton, 1995).

Pressure reduction

Intraocular pressure is increased after local anaesthetic injections, and many different devices have been designed to reduce this. These include the Honan balloon (Jay et al, 1985), the Storz Autopressor (Ropo et al, 1990) and the Nerf ball (Drews, 1982). Injection of 4ml of retrobulbar LA has been shown to increase IOP by an average of 6.2 mmHg (range 1–17 mmHg) (Palay and Stulting, 1990). The Honan balloon decreased this to below baseline levels within 2.5 min. Continuous application caused a further gradual decrease in IOP of 0.35 mmHg/min over the next 10 minutes.

Local anaesthetic solutions

Any of the LA agents may be used for ocular anaesthesia, the commonest being a mixture of lignocaine and bupivacaine (Hamilton, Gimbel and Strunin, 1988; Fry and Henderson, 1990). Lignocaine is used for its fast onset, bupivacaine for its prolonged duration of action. Adrenaline can be added to increase the extent of the block and prolong its duration, and a concentration of 1:200,000 is devoid of systemic effects (Sarvela, Nikki and Paloheimo, 1993). However in blinded studies, adrenaline does not appear to improve the quality, or effectiveness, of the block (Morsman and Holden, 1992). It has been shown to decrease ophthalmic artery pressure by 50%, and so should probably not be used in patients with a compromised circulation (Hoven, 1978).

Hyaluronidase hydrolyses the C_1–C_4 bonds between glucosamine and glucuronic acid in ground substance, thus promoting the diffusion of the anaesthetic through the tissues (Wong, 1993). It has been shown to promote spread within the orbit, speeding the onset of the block and enhancing akinesia. 7.5 IU/ml is a sufficient concentration (Morsman and Holden, 1992; Sarvela and Nikki, 1992).

Painless local injections

Various measures have been suggested to reduce discomfort for the patient during the performance of the LA block. Local anaesthetic drops can be introduced into the eye initially to anaesthetize the conjunctiva; the injection is subsequently made through the conjunctiva rather than transcutaneously (Hamilton, 1995). A solution made up by adding 1.5 ml of any full–strength local anaesthetic to 15 ml of balanced salt solution produces a virtually pain–free injection, and 1ml of this solution is injected first (Farley, Hustead and Becker, 1994). The full strength LA solution, warmed to body temperature (Bloom, Scheie and Yanoff, 1984), can then follow painlessly.

Role of anaesthetists

It has been argued that retrobulbar anaesthesia should be performed by ophthalmologists (Lichter, 1991) because of their knowledge of the anatomy and physiology of the orbit and the reported higher incidence of globe perforations when the block was performed by anaesthetists or nurse anaesthetists (Grizzard et al, 1991). However, there are also reports of anaesthetists performing large numbers of blocks with very few complications (Hamilton, Gimbel and Strunin, 1988; Kimble et al, 1987). The anaesthetist can play an important role in the perioperative care of these elderly patients who may have systemic disorders which need stabilisation. Indeed, the Report of the Joint Working Party on Anaesthesia in Ophthalmic Surgery (1993) recommends that the best practice is for the anaesthetist to be responsible for advising on the use of LA or GA in a particular patient, prescribing sedation if necessary, giving the LA block, providing intravenous access and supervising postoperative recovery. The report emphasises that the surgeon cannot be expected to monitor the patient's condition while performing the operation, and recommends that an anaesthetist should be present to monitor the patient and to provide resuscitation should it be required.

Sedation

Sedation is defined as the use of a drug, or drugs, which produces a state of depression of the central nervous system, while maintaining verbal contact. Loss of consciousness is a state of anaesthesia with all its attendant risks, and should not occur. Sedation may lead to airway problems, decreases in oxygen saturation, restlessness or sudden arousal. It cannot take the place of an inadequate block providing poor analgesia. Many of the reported complications of retrobulbar and peribulbar blockade, such as respiratory depression (Wittpen et al, 1986), brainstem anaesthesia (Javitt et al, 1987) and cardiopulmonary arrest (Rosenblatt, May and Barsoumian, 1980), have occurred in patients who have been sedated. Thus sedation requires careful management and constant monitoring by an anaesthetist. In the survey of Hodgkins and colleagues (1992) of consultant ophthalmologists in the United Kingdom, 45% of surgeons said they preferred their patients to be sedated while performing surgery under LA. The sedation used is most frequently given by the oral route (26%) but intravenous sedation is used routinely by 11%, increasing to 21% among those surgeons using LA "frequently" (more than 75% of cases).

However, Rubin (1990) suggested that patients generally tolerate the procedure very well and not more than 1% should require minimal sedation. This is backed up by the experience of Strunin and Lewis (1991) in Alberta, Canada, who found the incidence of complications reduced dramatically when the use of sedative drugs was stopped. Operating on an awake, cooperative patient is the safest scenario.

General anaesthesia

There have been several changes in general anaesthesic practice over recent years which have allowed general anaesthesia to remain a popular choice for many patients, particularly in the United Kingdom. The introduction of the laryngeal mask, providing the anaesthetist with control of the airway without the need for intubation, has decreased the arterial pressure changes associated with laryngoscopy and intubation (Moffat and Cullen, 1995) and allowed smoother inductions with less likelihood of an increase in IOP. The use of the laryngeal mask is also associated with less coughing and breath–holding at the end of the operation (Holden et al, 1991; Denny and Gadelrab, 1993), which also favours a lower IOP (Myint et al, 1995).

The introduction of new anaesthetic agents has allowed a more rapid return to consciousness, providing an extra margin of safety in this elderly group of patients. Propofol is an induction agent providing a smooth induction and a rapid, pleasant recovery profile. Newer inhalational agents, such as isoflurane, desflurane and sevoflurane, also allow rapid recovery. The new muscle relaxant, mivacurium, reverses easily at the end of the operation without the need for neostigmine. Alternatively, the patient can be allowed to breathe spontaneously on a laryngeal mask allowing a smooth recovery and a faster theatre turn–round time.

Day care

Day case surgery is increasingly widespread in Great Britain, and its cost effectiveness and popularity with patients are well established (Ogg and Obey, 1987). More cataract surgery is conducted on a day stay basis, reducing waiting lists and costs. Most of this surgery is performed under LA (Watts and Pearce, 1988), but with the newer anaesthetic agents and techniques, GA is also possible. Both Moffat and Cullen (1995) and Strong and colleagues (1992) have shown that GA is feasible for day case cataract surgery, providing strict admission criteria are followed. Moffat and Cullen (1995) used two different GA techniques and showed that all their patients were deemed fit for discharge 2h after surgery.

In conclusion, both GA and LA are widely used for cataract surgery, the choice commonly being dictated by surgeon and/or patient preference. Chapter Three will review the studies which have been done to compare and contrast the effects of these two techniques on different aspects of eye surgery.

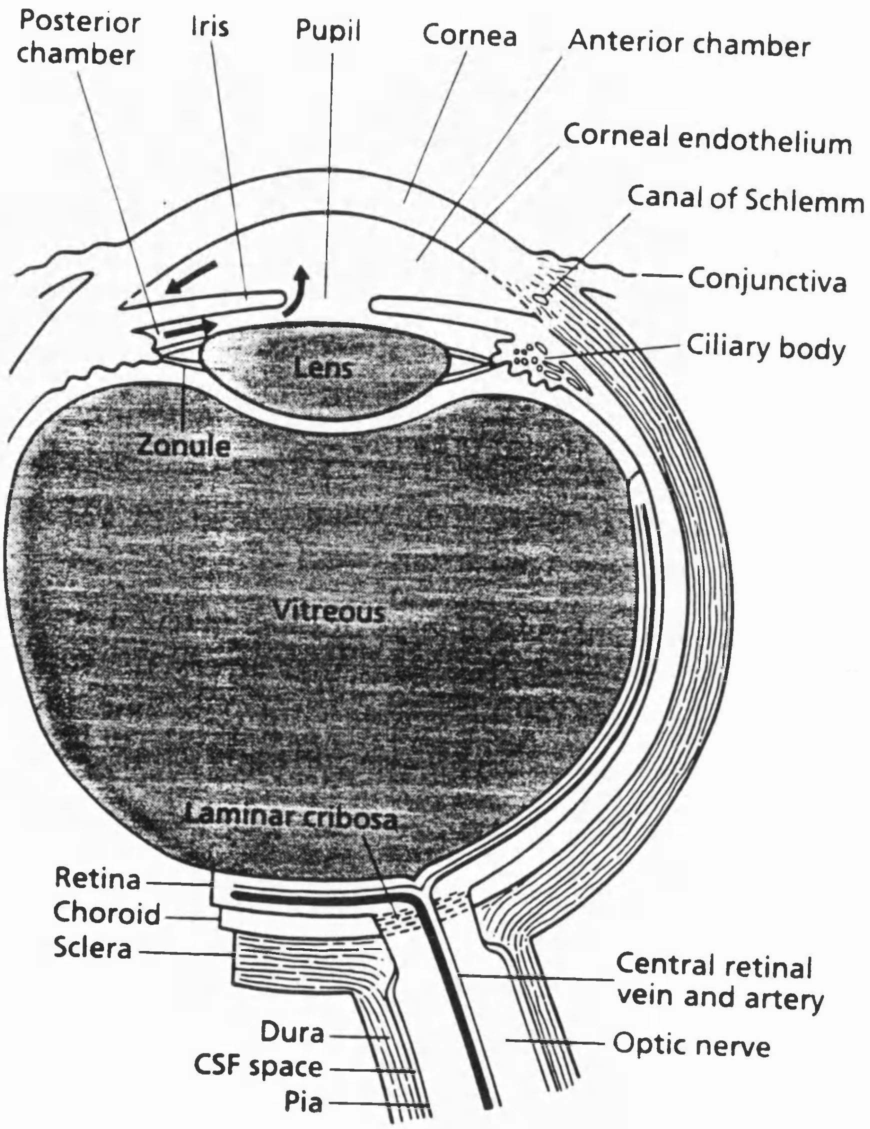
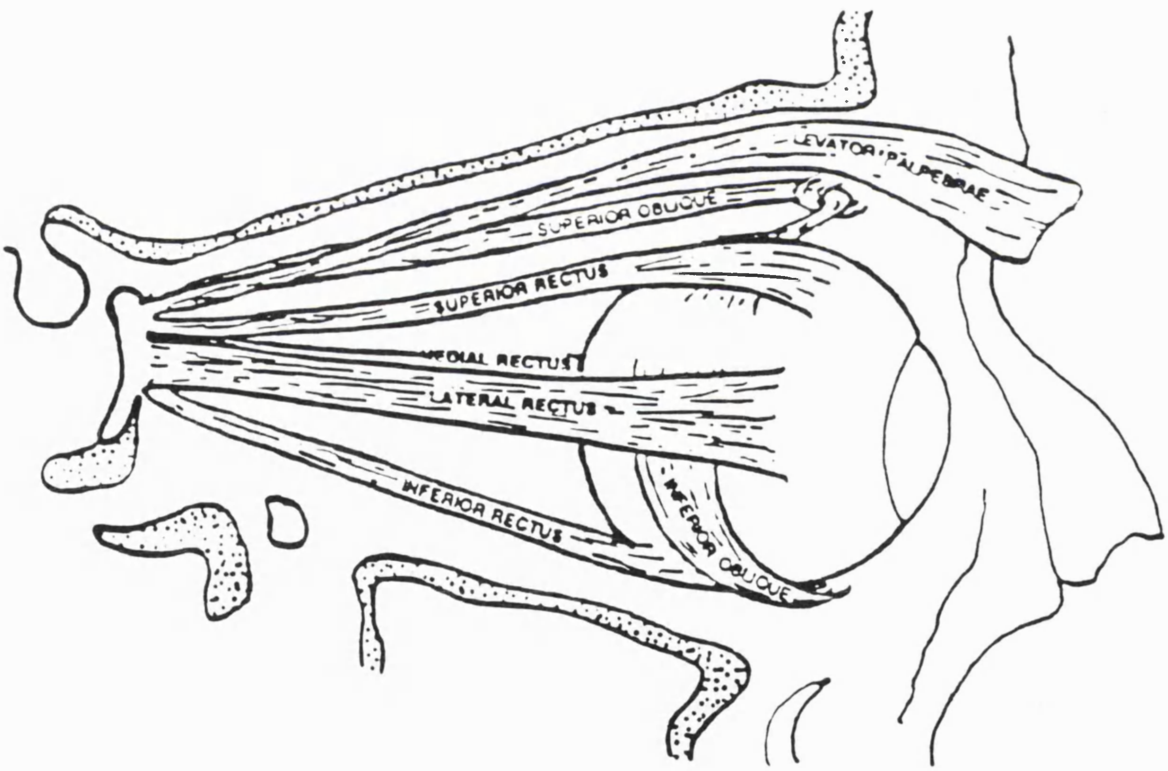


Fig 1.1 *Cross section of the eye*

(from Anaesthesia Volume 1, 1990: edited by Nimmo WS & Smith G; P533: Blackwell Scientific Publications)

Fig 1.2 *Diagram to show the muscle cone of the eye*

(Wong, 1993)



Chapter Two

The endocrine and metabolic response to surgery

The endocrine and metabolic changes which occur with surgery or trauma, commonly known as the "stress response", result in substrate mobilisation, a negative nitrogen balance, potassium loss and sodium and water retention. Surgery is associated with an increase in pituitary hormone secretion, with increased circulating concentrations of adrenocorticotrophic hormone (ACTH), β endorphin, growth hormone (GH), prolactin and arginine vasopressin (AVP). Stimulation of the sympathetic nervous system causes an increase in circulating adrenaline and noradrenaline concentrations. The increased secretion of ACTH causes a corresponding increase in plasma cortisol concentrations, and aldosterone and renin values are also elevated. Coinciding with this increase in catabolic hormone secretion, there is suppression of the anabolic hormones, testosterone and insulin.

These hormonal changes are responsible for the substrate mobilisation which occurs. Catecholamine secretion leads to hyperglycaemia; the increase in blood glucose is roughly proportional to the severity of the surgical trauma. Suppression of insulin and the increase in cortisol concentrations also play a part. Postoperatively, insulin secretion increases, but is ineffective (insulin resistance) and the hyperglycaemia is maintained. The increase in blood glucose is due to a rise in production, first by glycogenolysis, then gluconeogenesis in the liver and kidney, together with a decreased rate of utilisation by the peripheral tissues.

Mobilisation of fatty acids and glycerol from adipose tissue is also under the control of catecholamines, β–adrenergic stimulation causing lipolysis, and of insulin, which is lipogenic. Thus an increase in non–esterified fatty acids (NEFA), commonly used to assess fat metabolism, might be expected during surgery. However, there is usually little change in NEFA values, although extradural anaesthesia for pelvic surgery has been shown to be associated with a reduction in plasma NEFA and glycerol as a result of sympathetic blockade (Kehlet et al, 1979; Cooper et al, 1979).

Protein breakdown is a major part of the body's response to surgical trauma, as quantified by an increase in the urinary excretion of nitrogen. Patients can lose 0.5kg of lean tissue per day (Johnston, 1964). The amino acids released from muscle, particularly glutamine and alanine, are used for essential protein synthesis and gluconeogenesis in the liver, ensuring the maintainance of the supply of glucose. The proteins synthesised are the acute–phase proteins such as C–reactive protein, proteins of the complement series, fibrinogen, α_1–antitrypsin, serum amyloid A and caeruloplasmin, and are produced at the expense of the oncotically active protein, albumin. The factors responsible for this protein loss are not fully understood. The catabolic hormones appear to have only a minor role, but the lack of, and later resistance to, circulating insulin is probably important, and the cytokines are now thought to be important mediators.

These hormonal changes and the ensuing metabolic effects have been described in detail by Traynor and Hall (1981) and reviewed recently by Desborough and Hall (1993).

Initiation of the metabolic and hormonal response to surgery

There are thought to be two main initiators of the stress response to surgery, namely afferent neuronal input from the operative site, both somatic and autonomic, and the release of cytokines from damaged tissue resulting from surgical trauma.

Afferent neuronal input from the surgical site activates hypothalamo–pituitary hormone secretion and the sympathetic nervous system. As early as 1959, Hume and Egdahl were able to demonstrate the important role of somatic afferent fibre activity in initiating the hormonal changes, by showing that section of peripheral nerve, spinal cord or medulla oblongata could prevent the adrenocortical response to limb injury in animals. More recently, the use of extradural anaesthesia has demonstrated how autonomic afferent activity is also important in the initiation of the response. (See Chapter Three).

Damaged tissues, resulting from either surgery or accidental injury, release cytokines. The cytokines are a group of low–molecular–weight glycoproteins that include the interleukins (IL 1–15 so far), the interferons and tumour necrosis factor (TNF–α and –β) (Hall and Desborough 1992). They are synthesised mainly by cells of the macrophage and monocyte series, but are also produced by many other cell types, such as fibroblasts, glial cells and endothelial cells. TNF–α and IL–1β are thought to be mediators of the sepsis syndrome (Bone 1991).

Interleukin–6 is the main cytokine released after routine surgery, becoming detectable 2–4 h after the onset of surgery. Circulating IL–1β and TNF–α values do not change. Cruickshank and colleagues (1990) have shown that the IL–6 response is proportional to the severity of the surgery. Surface surgery was associated with only a transient increase in IL–6 whereas major vascular surgery and hip arthroplasty were associated with large and sustained rises in circulating values.

The biochemical and immunological aspects of IL–6 have been reviewed by Heinrich and colleagues (1990) and Van Snick (1990). Interleukin–6 stimulates acute phase protein synthesis in the liver; a good correlation was observed between the increase in circulating IL–6 values during surgery and the increase in serum

C–reactive protein (CRP) (Cruickshank et al, 1990). It also has effects on the immune system and haematopoiesis, which include B cell proliferation and T differentiation, T cell costimulation and plasmacyte proliferation (Hall and Desborough, 1992). Spangelo and colleagues (1989) and Imura, Fukata and Mori (1991) have shown a possible role of IL–6 in the control of anterior pituitary hormone secretion, suggesting a link between the endocrine and immune systems.

Other factors can also alter the stress response to surgery. These include anxiety, fear, dehydration and starvation preoperatively, and fluid or blood loss and hypothermia intraoperatively. Postoperatively, infection, hypoxia, immobilisation and alteration of diurnal rhythms may also affect the response (Desborough and Hall, 1990). Salmon (1992) has shown that patients' personality and preoperative mental state influence not only surgical recovery, but also alter catabolic hormone secretion after surgery. However, none of these factors, except severe haemorrhage, is able to initiate the hormonal and metabolic changes.

Modification of the metabolic and endocrine response to surgery

There are two main methods available for modifying the metabolic and endocrine response to surgery. First, the use of afferent neuronal blockade to inhibit both somatic and autonomic impulses from the site of trauma; secondly, large doses of opiate analgesics can be given intravenously to block hypothalamic–pituitary function. Neither of these two techniques are completely effective in all situations. Autonomic afferent fibre activity is difficult to abolish in many surgical sites, and high–dose opiate anaesthesia is inappropriate for many surgical operations, because of the respiratory depression that follows.

Hormonal manipulations have also been tried, either using agents to inhibit the secretion or action of the catabolic hormones, or infusing anabolic hormones, such as insulin. Alpha– and β–adrenoceptor blocking drugs have been given but the results are conflicting. Beta–adrenoceptor blockade with propanolol 0.15mg/kg had little effect on circulating metabolites during pelvic surgery, but caused an even greater insulin suppression than that observed in a control group (Cooper et al, 1980). However, propanolol 0.3mg/kg was found to inhibit the surgically induced increase in plasma glucose, lactate and free fatty acids values (Tsuji et al, 1980). Alpha–adrenoceptor blockade with phentolamine, infused at 0.5mg/min to patients undergoing pelvic surgery, resulted in an increase in insulin secretion and a decrease in the glucose response (Walsh et al, 1982).

Growth hormone administration improved nitrogen balance in burn patients (Wilmore et al, 1974), probably as a result of the increase in insulin secretion, while the administration of somatostatin, which inhibits the secretion of insulin, glucagon and growth hormone, caused a small decrease in the hyperglycaemic response to major abdominal surgery, together with a reduction in glucagon secretion (Hall, 1985). This effect on blood glucose occurred even though plasma insulin concentration was further decreased by the somatostatin, showing that glucagon contributes to the rise in hepatic glucose output during major abdominal surgery.

Hall and colleagues (1983) investigated the effects of a low–dose insulin infusion on circulating metabolites during pelvic surgery. Blood glucose was found to decline progressively, together with a reduction in plasma NEFA values, showing an inhibition of lipolysis. Cortisol secretion was unaffected, and sympathetic activity may have even been enhanced as shown by an augmented lactate response.

Nursing patients in a thermoneutral environment may help to mitigate the response to surgery. Cuthbertson and colleagues (1972) reported a decrease in protein catabolism in patients with major fractures of the lower limb maintained at an environmental temperature of 28–30°C, while Carli, Clark and Woollen (1982) found a reduction in postoperative nitrogen loss when they prevented heat loss with space blankets, warmed intravenous fluids and a hot-water mattress. However, Spivey and Johnston (1969) were unable to show any improvement in nitrogen balance by raising the environmental temperature from 24°C to 29°C after surgery.

Cytokine secretion occurs in response to tissue damage and therefore cannot be modified by the use of neuronal blockade. Moore and colleagues (1994) found that epidural analgesia had no effect on the IL–6 changes after pelvic surgery. Large doses of alfentanil, however, may decrease IL–6 secretion (Crozier et al, 1994). Schulze and colleagues (1992) investigated the use of high–dose steroids, such as prednisolone 30mg/kg intravenously. They found that IL–6 production was attenuated, but there were associated problems with wound healing and dehiscences of intestinal anastomoses.

The following chapter will review the effect that anaesthesia has on the endocrine and metabolic changes which occur with surgery.

Chapter Three

Literature Review

This literature review will be presented in two parts. Firstly, studies will be reviewed that compare the way general and local anaesthesia affect the metabolic and hormonal response to surgery. Secondly, there will be a review of the studies performed to compare the effects of local and general anaesthesia on cataract surgery.

Effect of anaesthesia on the metabolic and hormonal responses to surgery

Much work has been done to study the effect that anaesthesia has on the stress response to surgery. The subject has been reviewed by Kehlet (1984) and Hall (1985) and more recently by Hall and Desborough (1996).

Regional Anaesthesia

The effect of epidural anaesthesia with local analgesics on the metabolic and hormonal response to pelvic surgery has been investigated extensively by Kehlet and colleagues (Kehlet, 1982; Kehlet, Brandt and Rem, 1980). Neither spinal nor epidural anaesthesia alone affected plasma cortisol, growth hormone, lactate, free fatty acids or ketone concentrations (Kehlet, 1982). However, plasma adrenaline and noradrenaline concentrations decreased progressively as the sensory level extended to T_9–T_{10} and higher (Pflug and Halter, 1981). High thoracic blocks (to T_2–T_6) also inhibited the insulin response to glucose, while low dermatome blockade (T_9–T_{10}) had no effect on pancreatic islet function (Halter and Pflug, 1980). This suggests that resting adrenergic tone is important for normal pancreatic islet cell function.

Epidural blockade extending from T_4–S_5 has been shown to inhibit completely the glucose and cortisol response to pelvic surgery (Enquist et al, 1977). However, a less extensive block, from T_6–S_5, while providing excellent analgesia and abolishing the hyperglycaemic response, failed to prevent the increase in cortisol concentration. These findings showed that not only somatic afferent, but also sympathetic afferent blockade was necessary to prevent activation of pituitary secretion and thus cortisol production. The less extensive blockade was able to abolish the glucose response because of efferent blockade of the adrenal medulla preventing catecholamine secretion.

Although an epidural blockade from T_4–S_5 established before the onset of surgery is able to abolish the changes in circulating hormones and metabolites, Moller and colleagues (1982) showed that such a block, established after surgery had started, caused a decrease in blood glucose, but did not affect the plasma cortisol. Once the hypothalamic–pituitary–adrenal axis has been activated, afferent neuronal blockade is ineffective. Moore and colleagues (1994) have shown that the cytokine–mediated responses to pelvic surgery, such as acute phase protein synthesis and a decrease in the divalent cations (Fe^{2+} and Zn^{2+}), are not altered by epidural anaesthesia.

Spinal anaesthesia has been shown to have similar effects to epidural anaesthesia on the metabolic and hormonal changes (Moller et al, 1982). The dermatomal level of the block was again demonstrated to be important.

The effects of epidural anaesthesia on upper abdominal surgery were investigated initially by Bromage, Shibata and Willoughby (1971). They found that, even with an epidural blockade extending as high as C_6, the cortisol response to upper abdominal and thoracic surgery was unaltered. Hyperglycaemic changes were prevented by the efferent sympathetic blockade, but unblocked vagal afferent activity was thought to have caused the ACTH secretion.

Subsequent attempts to block vagal afferent fibres in addition to thoracic epidural blockade failed to decrease the cortisol response to upper abdominal surgery (Traynor et al, 1982). It is possible that epidural blockade does not completely block sympathetic afferent fibres, as the addition of a coeliac plexus block to epidural blockade decreased plasma cortisol in major abdominal surgery (Tsuji et al, 1983). It is also possible that stimulation of the diaphragm (C_3–C_5) and free nerve endings in the peritoneum may contribute to the hormonal response to upper abdominal surgery.

It is difficult to assess accurately the level of blockade. Bengtsson and colleagues (1983, 1985) have shown that the level of sympathetic blockade may be unexpectedly lower than the level of somatic blockade. Somatosensory evoked potentials have been used to try to assess the adequacy of somatic afferent blockade during epidural analgesia. Using either dermatomal stimulation with scalp recording of the evoked potential (Lund et al, 1987) or stimulation of a mixed peripheral nerve with measurement of the potential in the cervical epidural space (Loughnan et al, 1990), it has been shown that neither bupivacaine 0.75% or lignocaine 2% is capable of completely inhibiting afferent transmission in the cord (Loughnan et al, 1990; Dahl et al, 1990). Etidocaine was the most effective local anaesthetic agent in abolishing the somatosensory evoked potential (Dahl, Rosenberg and Kehlet, 1992; Lund et al, 1991). It may be that the inability of epidural blockade with bupivacaine to prevent the cortisol response to upper abdominal surgery was due partly to inadequate afferent somatic neuronal blockade.

Other local anaesthetic blocks have been used to try to obtund the metabolic and hormonal responses to upper abdominal surgery. The sympathetic chain lies in the paravertebral space, and blocks of the interpleural, intercostal and paravertebral spaces may act like a thoracic epidural blockade (Hall and Lacoumenta, 1988). Again, the glucose response to surgery is prevented, but the cortisol response is not affected (Giesecke et al, 1988; Pither, Bridenbaugh and Reynolds, 1988).

Epidural and intrathecal opioids provide good analgesia, but do not prevent the metabolic and hormonal changes associated with surgery because of the lack of sympathetic blockade. Neither epidural morphine nor diamorphine have been shown to have any effect on the metabolic response to surgery, although some decrease in plasma cortisol concentration was found postoperatively, possibly reflecting the excellent analgesia (Christensen et al, 1982; Normandale et al, 1985).

High–dose opioid anaesthesia

With the discovery of opiate receptors in the central nervous system and especially in the hypothalamus, many studies have examined the effect of "high–dose" opioid anaesthesia on the stress response to surgery. In 1959, McDonald and colleagues were able to show that morphine could inhibit the hypothalamic–pituitary–adrenal axis in man, and in 1974, George and colleagues demonstrated a decrease in endocrine changes occurring with major surgery using large doses of intravenous (IV) morphine (1–4mg/kg). Fifty μg/kg fentanyl IV has been shown to prevent changes in glucose, lactate, cortisol and growth hormone concentrations during pelvic surgery (Hall et al, 1978), while 15 μg/kg IV was sufficient only to modify these hormones and metabolites, and also secretion of ACTH and β endorphin (Lacoumenta et al, 1987). However, use of opioids in this way is impractical for most types of surgery because of postoperative respiratory depression.

Most studies investigating the effects of high–dose opiates on the stress response to surgery have used open heart surgery as their model, as postoperatively, ventilation is usually controlled artificially in these patients. The effects of high–dose morphine and fentanyl have been investigated (Brandt et al, 1978; Walsh et al, 1981) and more recently sufentanil and alfentanil (de Lange et al, 1982; deLange et al, 1983; Sebel, Bovill, van der Haven, 1982; Bovill et al, 1983). All these studies have shown that the catecholamine, ACTH, cortisol, GH, vasopressin and glucose changes are abolished by the opioids, but only until the start of cardiopulmonary bypass. The physiological changes associated with cardiopulmonary bypass, including hypothermia, haemodilution and non–pulsatile flow, evoke endocrine responses that cannot be inhibited by opiates. Studies of high–dose fentanyl or alfentanil anaesthesia during abdominal surgery also showed that, although there was a reduction in the stress response intraoperatively, this did not last postoperatively (Moller et al, 1984).

In all these studies, the opioid was given before the start of surgery. Bent and colleagues (1984) investigated the effect of giving fentanyl 50 μg/kg after pelvic surgery was established, and found that there was no change in circulating glucose, NEFA or cortisol values. The same dose, given before surgery, prevented these changes (Hall et al, 1978). Thus, as was found for epidural anaesthesia, the metabolic and hormonal changes are easily prevented, but cannot be reversed once they are established.

General anaesthesia

General anaesthesia, *per se*, appears to have little effect on the metabolic and hormonal response to surgery. Laryngoscopy and intubation might be expected to induce a response, as cardiovascular variables are often affected at this time. However, Carli and Elia (1991) studied 2h of anaesthesia alone, including laryngoscopy and intubation, before the start of surgery and found no changes in circulating concentrations of various metabolites, including glucose and lactate. Klingstedt and colleagues (1987) studied patients before cholecystectomy and found no change in adrenaline concentrations during intubation. Halter, Pflug and Porte (1977) found no increase in adrenaline or noradrenaline following intubation. An increase in both these variables occurred during surgery, with further increases seen after extubation. It is not clear whether there was a gradual increase in catecholamine concentrations due to surgical trauma, or this was because of the extra stimulus of extubation. However, results obtained may depend on how the samples are collected. Derbyshire and Smith (1984) found, with the use of rapid blood sampling, that increased concentrations of adrenaline and noradrenaline may occur for 5–10 min after intubation.

Intravenous induction agents

Etomidate, an imidazole derivative, has been shown to inhibit adrenal steroidogenesis both *in vitro* and *in vivo* (Kenyon et al, 1984; Wagner et al, 1984; Moore et al, 1985). It inhibits the mitochondrial, cytochrome P–450–dependent, 11β–hydroxylase step of the biosynthetic pathway, resulting in suppression of cortisol and aldosterone secretion. Moore and colleagues (1985) showed that cortisol production may be inhibited for up to 24h after an etomidate infusion of 1–2h duration. Lacoumenta and colleagues (1986a) showed that prolonged inhibition of cortisol secretion by etomidate did not alter cardiovascular stability during pelvic surgery, and that the only metabolic effect was a reduction in the hyperglycaemic response to surgery. However, long–term sedation with etomidate has been shown to be associated with increased mortality in critically ill patients, presumably because of cortisol suppression (Ledingham and Watt, 1983) and the drug is no longer licensed for this use. Udelsman and colleagues (1986) have produced evidence in chronically adrenalectomized primates to support the clinical observations that cortisol suppression during and after routine surgery has few deleterious effects. They found that, when these animals underwent a standardised upper abdominal procedure, only 10% of the usual daily steroid requirements was necessary for survival, and normal daily replacement therapy of steroid ensured a smooth operative course. There is little risk, therefore, in maintaining circulating cortisol concentrations within the normal range throughout routine surgery.

Both diazepam and midazolam have also been shown to inhibit cortisol production from isolated bovine adrenocortical cells *in vitro* (Holloway et al, 1989). Midazolam, which has an imidazole ring in addition to its basic benzodiazepine structure, was found to decrease the cortisol response to peripheral surgery (Crozier *et al,* 1987) and major upper abdominal surgery (Desborough *et al,* 1991). Desborough and colleagues (1991) also found that the production of growth hormone was augmented, showing that midazolam had a mixed inhibitory and stimulatory effect on pituitary hormone secretion.

Ketamine activates the sympathetic nervous system (White, Way and Trevor, 1982) and has been shown to be associated with significant increases in blood glucose and plasma cortisol concentrations and heart rate. (Lacoumenta *et al,* 1984). However, these authors showed that once surgery was established, there was no difference in the metabolic response between ketamine and halothane anaesthesia, and they concluded that ketamine produces only transient hormonal and metabolic changes which are minor in comparison with the superimposed surgical stimulation.

Volatile anaesthetic agents

Volatile anaesthetic agents appear to have little effect on endocrine and metabolic function. Von Werder and colleagues (1970) found no change in plasma cortisol with 7h of halothane anaesthesia without surgery, whereas Halter, Pflug and Porter (1977) found a slight decrease in plasma adrenaline concentration after 30min of halothane anaesthesia. Likewise, enflurane anaesthesia alone produced no changes in plasma glucose or cortisol (Oyama et al, 1979; Carli and Elia, 1991). However, Oyama, Latto and Holaday (1975) showed an insignificant increase in plasma glucose and cortisol concentrations with 30min of isoflurane anaesthesia.

Volatile anaesthetic agents also have little effect on the endocrine and metabolic response to a surgical stimulus. In all the above studies, once surgery was superimposed, there was the expected increase in circulating metabolites and hormones. There may be some effect on the sympathetic response to surgical stress as shown by catecholamine concentrations. Brown and colleagues (1982) showed that plasma noradrenaline values were significantly lower in patients receiving enflurane compared with low–dose fentanyl anaesthesia, although adrenaline concentrations were similar. Roizen, Horrigan and Frazer (1981) found that high concentrations of halothane and enflurane (minimum alveolar concentration (MAC) of 1.5) suppressed the surgically–induced increase in plasma noradrenaline to surface surgery, but Lacoumenta and colleagues (1986b) found that a MAC dose of 2.1 halothane was ineffective in preventing the sympathoadrenal and pituitary hormone responses to pelvic surgery.

In conclusion, there is general agreement from all the studies comparing the effects of general and regional anaesthesia on the metabolic and endocrine responses to surgery that these responses are little altered by general anaesthesia unless high–dose opioids are used. This effect lasts only as long as a high concentration of opioid can be maintained in the blood and tissues. However, regional anaesthesia prevents the stress response, provided that a complete neuronal blockade, both somatic and autonomic, can be achieved.

Comparison of general and local anaesthesia for cataract surgery

Although there has been much discussion of the relative merits of either general (GA) or local (LA) anaesthesia for cataract surgery (Rubin, 1990), there have been few studies attempting a prospective, controlled evaluation of the two techniques. Much of the work has been directed at comparing different general anaesthetic techniques for such surgery, or at comparing and contrasting different local anaesthetic techniques, as described in Chapter One.

Some studies have looked at the effects of combining general and local anaesthesia. Lytle and Thomas (1992) added topical oxybuprocaine to the eyes of patients under general anaesthesia and prevented the pressor response to surgical stimulation, decreasing the concentration of enflurane required compared with those patients receiving general anaesthesia alone.

A few studies have compared surgical complications following either general or local anaesthesia. Scott and Clearkin (1994) looked at surgically–induced diffuse scleritis (SIDS) following cataract surgery, and found that there was a higher incidence of this problem in the younger patients and in those having a general anaesthetic. Ropo, Ruusuvaara and Nikki (1992) compared the incidence and duration of postoperative ptosis following cataract surgery and concluded that ptosis is common after both local and general anaesthesia, but in most cases is shortlasting. It may be related to the volume or myotoxicity of the local anaesthetic drug, as their four-point technique, using twice as much LA as their two-point technique, caused a greater incidence of ptosis both immediately and after one week. The use of a lid speculum and/or the superior rectus muscle bridle suture may be important in provoking ptosis of a longer duration.

Nagle and Cooper (1993) investigated the aetiology of nasopharyngeal secretion reflux under anaesthesia and found that nasal secretions could drain into the conjunctival sac and contaminate the surgical field. These were more commonly seen on the face at the end of surgery in patients under general anaesthesia.

Wolf, Lynch and Berlin (1975) found no difference in surgical outcome after cataract surgery in patients under either LA or GA, whereas Vernon and Cheng (1985) found more patients (5 out of 97) required additional surgery after LA cataract extraction, than after GA (0 out of 97). The reasons for this observation were not apparent in this retrospective study.

Robinson and Nylander (1989) looked at the effects of continuing warfarin treatment throughout cataract surgery on 10 occasions and observed that, although three cases of hyphaema occurred, none of the four patients receiving LA had a retrobulbar haemorrhage. They suggested that warfarin can be continued throughout cataract surgery providing the international normalised ratio (INR) is within the recommended therapeutic range and is closely monitored, especially if additional drugs are given. Topical indomethacin was shown to reduce the miosis which occurs during cataract surgery, whether performed under LA or GA (Searle, Pearce and Shaw, 1990).

Campbell and colleagues (1993) noted that 19% of patients under GA experienced at least one episode of oxygen desaturation during the procedure, compared with none in the LA group. Heart rate and arterial pressure were stable in the LA group compared with the GA group, where marked fluctuations were noted. 61% of patients under GA experienced falls in systolic arterial pressure greater than 30% of the preinduction value.

There have been some studies to investigate the difference in postoperative morbidity after cataract surgery. No difference in oxygen saturation was demonstrated between those patients receiving GA or LA the night before surgery, immediately postoperatively, or during their first postoperative night (McCarthy, Mirakhur and Elliott, 1992). The overall incidence of significant desaturation was low.

Postoperative pain was shown to be minimal in one study (Koay et al, 1992); 55% of patients having no pain, and 32% reporting slight discomfort. 8% reported mild pain and only 5% had moderate to severe pain. Patients receiving LA were found to be more comfortable postoperatively on the day of operation in this study, but 84% of these patients had received papaveretum 10mg and promethazine 50mg preoperatively. None of the GA patients had received any analgesic.

Cognitive function was tested 24h, two weeks and three months after cataract surgery under GA or LA in 169 patients (Campbell et al, 1993). The GA patients performed marginally less well than the LA group at 24h, but recovery to preoperative values had occurred in all patients by two weeks. There was no evidence of long term dysfunction detected in either group, with no significant differences between the performances of the two groups at any time.

Karhunen and Jonn (1982) examined memory function following LA or GA for cataract surgery using the Wechsler Memory Scale and Luria tests. They found there was a diminution in performance one week postoperatively, but there was no difference between GA and LA, although all the LA patients in this study had received fentanyl and diazepam sedation.

Backer and colleagues (1980) looked at the myocardial reinfarction rate following ophthalmic surgery and found a zero reinfarction rate after 288 operations under LA. Nine of these operations were performed within three months, and nine between three to six months, of the myocardial infarction. There was also a zero reinfarction rate after 26 operations under GA. The small number in the GA group made it difficult to undertake comparisons, but the authors concluded that LA does not pose special risks for myocardial reinfarction.

Three studies have looked at mortality in association with ophthalmic surgery (Duncalf, Gartner and Carol, 1970; Petruscak, Smith and Breslin, 1973; and Quigley, 1974). Death was shown to be much less common after ophthalmic surgery than after general surgery, with no difference between LA and GA. However, this was thought to be heavily dependent on patient selection; death was rare after GA in young, healthy patients, and LA was used more frequently in the elderly. Patients with retinal detachment were at greater risk, and prolonged bed rest contributed to a higher mortality (Quigley, 1974). Mortality in the younger patients seemed to be the result of poor anaesthetic technique, for example, hypoxia from inadequate airway control, whereas in the older patients, with both LA and GA, cardiovascular status played an important role (Duncalf, Gartner and Carol, 1970).

General and local anaesthesia for cataract surgery has also been compared looking at costs, throughput and staffing levels needed. Percival and Setty (1992) found that LA was 15 times less expensive in material, led to a faster throughput of patients in the operating theatre and halved the expenditure on staff (ophthalmologists gave the local anaesthetic). The place of day surgery for cataract treatment has been considered, and general anaesthesia has been shown to be just as applicable in this setting as local anaesthesia, provided strict admission criteria are met (Strong et al, 1992; Moffat and Cullen, 1995).

Lastly, few studies have looked at patients' opinions on the different forms of anaesthesia for cataract surgery, but a small study of 24 patients suggested a preference for local anaesthesia (Rassam and Thomas, 1989).

Thesis Plan

The choice of LA or GA for cataract surgery is currently the subject of much discussion in this country. While in some countries, LA is the technique of choice with very few general anaesthetics being given, there remains a significant number of patients and surgeons who prefer GA to LA in the United Kingdom. It is important to know if there is any increased risk to providing a GA for this group of patients. One aspect which has not so far been considered, is the metabolic and hormonal alterations which may occur during cataract surgery. This is the subject of this thesis. I have set out to discover whether there are any metabolic or hormonal changes during cataract surgery in the elderly patient, and if so, are these changes affected by the choice of general or local anaesthesia.

Chapter Four

Methods

This thesis comprises five separate studies involving 138 patients, all of whom had their cataract surgery undertaken at Edgware General Hospital by Miss G. Vafidis. The concluding study is a questionnaire on 231 patients who were asked about morbidity following their cataract surgery. The studies are summarised in Table 4.1, which also shows the Chapters in which each one is reported. The studies were approved by the local Ethical Committee and informed consent was obtained from each patient.

Patients studied

All patients studied were scheduled for extracapsular cataract extraction of one eye with intraocular lens implantation. They were otherwise healthy and were not receiving any therapy known to interfere with the hormonal and metabolic response to surgery, apart from oral hypoglycaemic agents in Study 5. All patients were suitable for either general anaesthesia (GA) or local anaesthesia (LA) and were allocated randomly to receive either GA or LA.

General Anaesthesia

No premedication was given. Anaesthesia was induced with thiopentone, the trachea intubated after administration of vecuronium, and the lungs were ventilated with 66% nitrous oxide in oxygen supplemented with 0.6–1.0% enflurane. On completion of surgery, residual neuromuscular block was antagonised with neostigmine and glycopyrronium.

Retrobulbar Anaesthesia

The local anaesthetic used was a mixture of equal volumes of 2% lignocaine and 0.75% bupivacaine without adrenaline. 3ml was injected as a retrobulbar block using a transcutaneous inferotemporal approach with the eye in the primary gaze position. 2ml was placed at the side of the eye to block the facial innervation of the orbicularis muscle and produce akinesia. Oxygen, at 4l/min, was piped beneath the sterile drapes during the operation. No premedication or sedation was used in any of the patients receiving local anaesthesia.

Peribulbar Anaesthesia

Peribulbar blockade was undertaken with the same mixture of local anaesthetic used for retrobulbar block. A transcutaneous approach was utilised with 3ml inferotemporal to the globe and 3ml superomedially. Pressure of 60mmHg was maintained on the orbit with a Honan balloon for at least 5min after the block. These patients also received oxygen, piped at 4l/min, beneath the sterile drapes during the operation, and did not receive any premedication or sedation.

Monitoring

All patients had their arterial pressure measured non–invasively, and their electrocardiogram and pulse oximetry monitored continuously throughout the induction, surgery and recovery periods. The patients in the GA groups had their ventilation adjusted to maintain an end–tidal CO_2 tension above 4.0kPa.

Blood Samples

On arrival in the anaesthetic room, all patients had a central venous catheter introduced percutaneously through an antecubital fossa vein under local anaesthetic for collection of blood samples. After a ten minute rest period, a control blood sample was collected. Further venous blood was collected after induction of either general or local anaesthesia, at the time of nuclear extraction, on completion of surgery, and at 30 and 60min after completion of surgery in Studies 1 and 2. Studies 3 and 4 had a further sample collected at 120min after surgery was complete, and Study 5 collected an eighth sample at 240min post–surgery. The samples were centrifuged immediately and the supernatant stored at –20°C before analysis.

Glucose

Plasma glucose concentration was measured in Studies 1 and 2, whereas blood glucose concentration was estimated in Studies 3, 4 and 5. For the determination of plasma glucose values, the thawed supernatant was deproteinised with uranyl acetate before assay, but for whole blood determination, the sample was deproteinised immediately in uranyl acetate and the supernatant stored at –20°C. The glucose concentration was determined enzymatically using a glucose oxidase / peroxidase method (Werner, Rey and Wielinger, 1970).

Plasma glucose values are 10–15% greater than whole blood glucose values, as intracellular concentrations are kept low by metabolism, and therefore inclusion of erythrocytes in the sample "dilutes" the plasma. The difference between blood and plasma values depends on the haematocrit (Zilva, Pannall and Mayne, 1988a). However, plasma must be removed promptly from blood, or collected in the presence of an inhibitor of glycolysis, such as fluoride, or the formed elements will utilise glucose to produce lactate, and the plasma glucose value will be lowered. The concentration can drop from 4.8 mmol/litre at time zero, to 3.9 mmol/litre at 4 hours and 1.9 mmol/litre by 24 hours (Zilva, Pannall and Mayne, 1988b). This

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problem is avoided by the use of blood glucose, and was the reason for changing to blood glucose estimations in the later studies.

Lactate

Plasma lactate was measured in Study 1, and blood lactate in Studies 3, 4 and 5 for the reasons given above. Lactate concentrations were also measured enzymatically using lactate dehydrogenase (Hohorst, 1965). Either thawed plasma or whole blood was deproteinised with 0.6M perchloric acid before measurement in a similar method to that described above.

Non-Esterified Fatty Acids (NEFA)

Plasma NEFA concentrations in Studies 1 and 5 were measured enzymatically using acyl-CoA synthetase linked to chromogen production. This is specific for fatty acids with carbon chain lengths from 6 to 18 (Shimizu et al, 1979).

Beta-Hydroxybutyrate (βOH)

Blood βOH concentrations in Study 5 were measured enzymatically using β hydroxybutyrate dehydrogenase (Williamson and Mellanby, 1974).

Cortisol

Plasma cortisol concentrations were measured in Study 1, and serum cortisol concentrations were measured in Studies 3, 4 and 5. Serum was chosen for the later studies because the fibrin strands in the plasma interfered with the automatic pipettes. Cortisol concentrations were measured with a sensitive and specific radioimmunoassay (Seth and Brown, 1978).

Catecholamines

Plasma for catecholamine determination was stored after the addition of 200 μlitre of an antioxidant solution. This consisted of 100 mmol/litre of reduced glutathione and 100 mmol/litre of EGTA. Plasma noradrenaline and adrenaline concentrations were later measured by HPLC with electrochemical detection (Davis, Kissinger and Shoup, 1981). The limits of detection of the assay were 0.1 nmol/litre for noradrenaline and 0.05 nmol/litre for adrenaline. The coefficients of variation for a pooled plasma sample (about 1.5 nmol/litre noradrenaline and 0.3 nmol/litre adrenaline) were 4.5% for noradrenaline and 8.2% for adrenaline.

Insulin

Serum insulin was measured by a sensitive and specific radioimmunoassay (Soeldner and Slone, 1965).

Growth Hormone

Serum growth hormone was measured by a sensitive and specific radioimmunoassay (Boden and Soeldner, 1967).

Variability of Assays

The coefficients of variation for the metabolite assays are shown in Table 4.2, and for the hormone assays in Table 4.3.

Statistical analysis

The data are presented as mean values (SEM). Statistical analysis was undertaken using Fisher's exact test for the patients' demographic details. Two–way analysis of variance (ANOVA) with Dunnett's test (Dunnett, 1964) was used to show differences within each group compared with the control value, and one–way ANOVA to examine differences between groups at the same time point (Armitage and Berry, 1994). A p value of <0.05 was considered statistically significant.

	Number of Patients	*Anaesthetic technique*	*Measurements*	*Duration of study*	*Chapter*
Study 1	18	9 GA 9 Retrobulbar	Circulating Glucose, Lactate, NEFA and Cortisol values	up to 60 min postoperatively	5
Study 2	20	10 GA 10 Retrobulbar	Circulating Glucose, Noradrenaline and Adrenaline values Heart Rate and Mean arterial pressure	up to 60 min postoperatively	5
Study 3	30	10 GA 10 Retrobulbar 10 GA + Retrobulbar	Circulating Glucose, Lactate and Cortisol values	up to 120 min postoperatively	6
Study 4	30	10 GA 10 Retrobulbar 10 Peribulbar	Circulating Glucose, Lactate and Cortisol values	up to 120 min postoperatively	7
Study 5	40	10 GA 10 Retrobulbar 10 NIDDM GA 10 NIDDM Retrobulbar	Circulating Glucose, Lactate, βOH, NEFA, Cortisol, Insulin and Growth hormone values	up to 240 min postoperatively	8
Study 6	231	119 GA 112 LA - Retrobulbar and Peribulbar	Questionnaire		9

Table 4.1. *Summary of Studies in this Thesis. (GA =general anaesthesia, LA = local anaesthesia, NEFA = non-esterified fatty acids, βOH = β-hydroxybutyrate, NIDDM = non-insulin-dependent diabetes mellitus)*

Metabolite	Coefficient of variation
Glucose	1.2%
Lactate	3.2%
Non-esterified fatty acids	1.8%
β-hydroxybutyrate	4.2%

Table 4.2 *Coefficients of variation for metabolite assays.*

Hormones	Within assay c.v.	Between assay c.v.
Cortisol	6.0%	10.3%
Growth Hormone	7.1%	6.3%
Insulin	8.2%	11.4%

Table 4.3 *Coefficients of variation (c.v.) for hormone assays.*

Chapter Five

The investigation of the effects of general and local anaesthesia on the metabolic and hormonal changes during cataract surgery.

Introduction

Ophthalmic surgery offers a useful model for investigating the effects of local anaesthesia (LA) on the endocrine and metabolic changes associated with surgery. Local anaesthetic applied to the ciliary ganglion by means of a retrobulbar block is able to completely denervate the eye, providing not only somatic afferent, but also autonomic, blockade of the eyeball. Under general anaesthesia (GA), innervation of the eye remains intact. Thus, comparing the metabolic and hormonal responses under LA with those under GA, gives an indication of the role of afferent neuronal stimulation in surgical stress.

This chapter describes two studies to explore the stress response to cataract surgery in elderly patients, comparing the metabolic and hormonal responses when the surgery is undertaken with either GA or LA. The first study was a pilot study looking at changes in three metabolic and one hormonal variable in 18 patients. The second study looked at a further 20 patients, and compared catecholamine concentrations as well as cardiovascular variables.

Study 1

Cortisol and glycaemic responses to cataract surgery.

Methods

18 elderly patients admitted for cataract surgery were studied. They were

otherwise healthy and not receiving any therapy known to interfere with the hormonal or metabolic responses to surgery. They were allocated randomly to receive either GA or LA. The method of LA used was retrobulbar blockade.

Central venous access via an antecubital fossa vein was obtained before the administration of general anaesthesia or retrobulbar blockade as described in Chapter Four. Blood samples were taken for plasma glucose, lactate, NEFA and cortisol concentrations before induction, (the control sample), after induction, at lens extraction, at the end of surgery, and at 30 and 60 min after the end of surgery. The samples were centrifuged, stored and assayed as described in Chapter Four.

Results

There was no significant difference between the groups except for the duration of surgery, which was longer in the LA group (30 min compared with 25 min; $p<0.05$) (Table 5.1). The overall theatre time, however, was similar in both groups (49 min LA group; 47 min GA group).

Plasma cortisol (Figure 5.1)

In the GA group, cortisol concentrations increased progressively throughout the study from a control value of 348 nmol/litre to 747 nmol/litre 60 min after completion of surgery. In contrast, in the LA group plasma cortisol concentration did not change during surgery from the control value of 320 nmol/litre, and then decreased slowly to 223 nmol/litre 60 min after surgery ($p<0.05$). There was a significant difference between the groups during surgery ($p<0.01$) and after surgery ($p<0.001$).

Circulating metabolites

Plasma concentration of glucose increased in the GA group from 4.7 to 5.2 mmol/litre on completion of surgery, but this change was not significant (Figure 5.2). In the LA group, plasma concentration of glucose did not alter more than 0.2 mmol/litre from the control value of 4.4 mmol/litre throughout the study. There was a significant difference in plasma concentration of glucose between the groups at nuclear extraction, at the end of surgery and 30 min after completion of surgery ($p<0.05$).

In the GA group, plasma concentration of lactate did not alter significantly during surgery from the control value of 1.22 mmol/litre, but declined significantly to 0.99 mmol/litre 60 min after completion of surgery ($p<0.05$) (Figure 5.3). In contrast, in the LA group plasma concentration of lactate decreased slowly during the study and this resulted in a significant difference between the groups at the end of surgery and 60 min after completion of surgery ($p<0.05$).

Plasma NEFA concentrations did not change significantly in either group during the study (Figure 5.4).

Discussion

The results show clearly that cataract surgery under general anaesthesia evokes an endocrine and metabolic response, and that this response can be prevented completely by local analgesia. In the GA group, the plasma cortisol values increased more than two–fold, but the changes in circulating metabolites were relatively small.

The retrobulbar block used to provide LA necessitates the injection of a local analgesic solution around the ciliary ganglion in the apex of the orbit. The ciliary ganglion is a peripheral parasympathetic ganglion of the oculomotor nerve and also contains sympathetic and somatic afferent fibres (Williams et al, 1989). The parasympathetic root contains both sensory and motor fibres, the latter supplying the ciliary muscle and sphincter pupillae. The sympathetic fibres arise from the superior cervical ganglion, traverse the ciliary ganglion without synapsing, and supply the dilator pupillae and blood vessels of the eyeball. The somatic afferent component of the ganglion consists of sensory fibres from the eyeball in the short ciliary nerves (ophthalmic branch of the trigeminal nerve). These fibres also traverse the ganglion without synapsing and continue in the nasociliary nerve. Thus a correctly placed retrobulbar block provides not only somatic afferent, but also autonomic, block of the eyeball. The results of this study are important confirmatory evidence of the effectiveness of complete deafferentation of the operative site in preventing catabolic hormone secretion during surgery.

The main cause for the glycaemic response to surgery is activation of the sympathoadrenal system (Hall, 1985). It can be inferred from this initial study, therefore, that the comparatively small glycaemic response to surgery of 0.5 mmol/litre in the GA group reflected only a modest increase in circulating plasma concentrations of catecholamine. This contention is supported by the lack of a significant increase in plasma concentration of lactate in the GA group, as it has been postulated that the lactic acidaemia of surgery is an indirect indicator of increased sympathetic activity (Lacoumenta et al, 1987). Both plasma glucose and lactate concentrations decreased significantly in the LA group, suggesting reduced catecholamine secretion.

The effects of age on the metabolic and endocrine response to surgery have received little attention. Blichert-Toft and colleagues (1979) compared the response to inguinal herniorrhaphy in men aged 20–30 yr and 70–75 yr and observed only small differences. Similarly, age was found not to be a significant variable in determining the hormonal and metabolic changes associated with cholecystectomy (Hakanson et al, 1984). It would seem likely, therefore, that the metabolic response to cataract surgery under GA was minor because of the nature of the surgery rather than the age of the patients.

There was no difference between the groups in the total time spent in the operating theatre, although the duration of surgery was longer in the LA group (Table 5.1). Thus, perhaps surprisingly, LA offered no advantage over GA in theatre utilization. It was my impression, however, that patients who received LA felt symptomatically better in the immediate postoperative period. This opinion is similar to the observations of Rassan and Thomas (1989), who noted the excellent recovery of patients undergoing cataract surgery with LA and patients' preference for this form of anaesthesia. Chapter Nine of this thesis details the results of my study to investigate this aspect.

In conclusion, this pilot study showed that the hormonal and metabolic response to cataract surgery was abolished by LA. It clearly demonstrated the metabolic stability offered by LA in a group of patients who often have severe endocrine and metabolic disorders.

Table 5.1 *Details of patients studied in Study 1 (mean values (SEM)).*

** Significant difference between mean values (p<0.05)*

	LA group (n=9)	GA group (n=9)
Age; years	74 (2.8)	68 (5.2)
Weight; kg	76 (2.9)	70 (5.4)
Sex	6M : 3F	2M : 7F
Induction time; min	13 (2.7)	12 (1.9)
Duration of surgery; min	30 (2.5) *	25 (1.4) *
Start of induction to leaving theatre; min	49 (2.9)	47 (2.1)

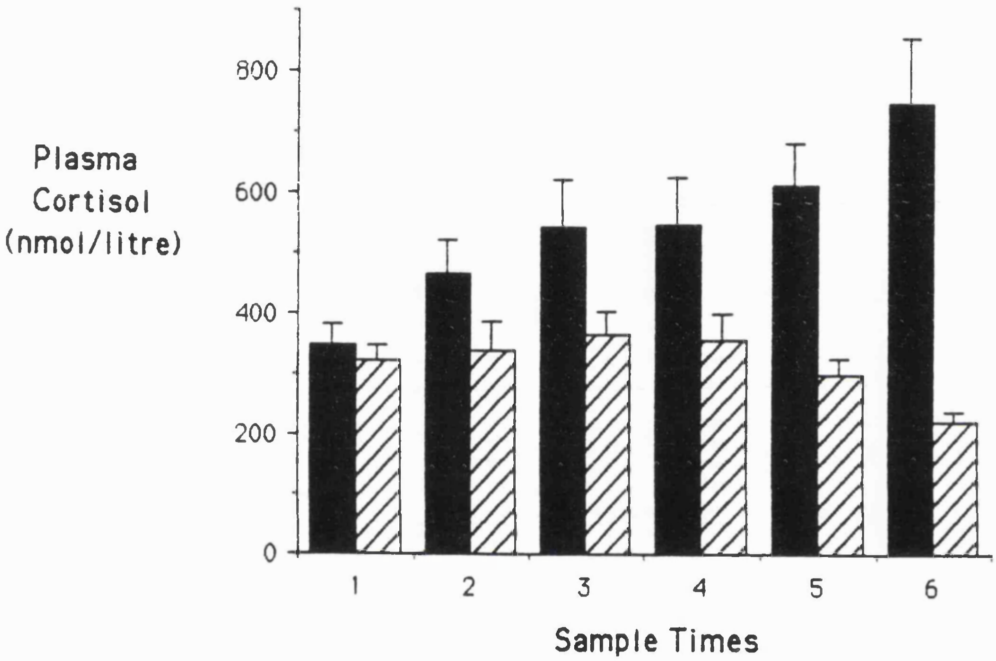


Fig 5.1 *Mean (SEM) plasma concentration of cortisol in the GA group (solid bars) and LA group (hatched bars).*

Sample 1 = before induction of anaesthesia; 2 = after induction of anaesthesia; 3 = nuclear extraction; 4 = end of surgery; 5 = 30 min after completion of surgery; 6 = 60 min after completion of surgery.

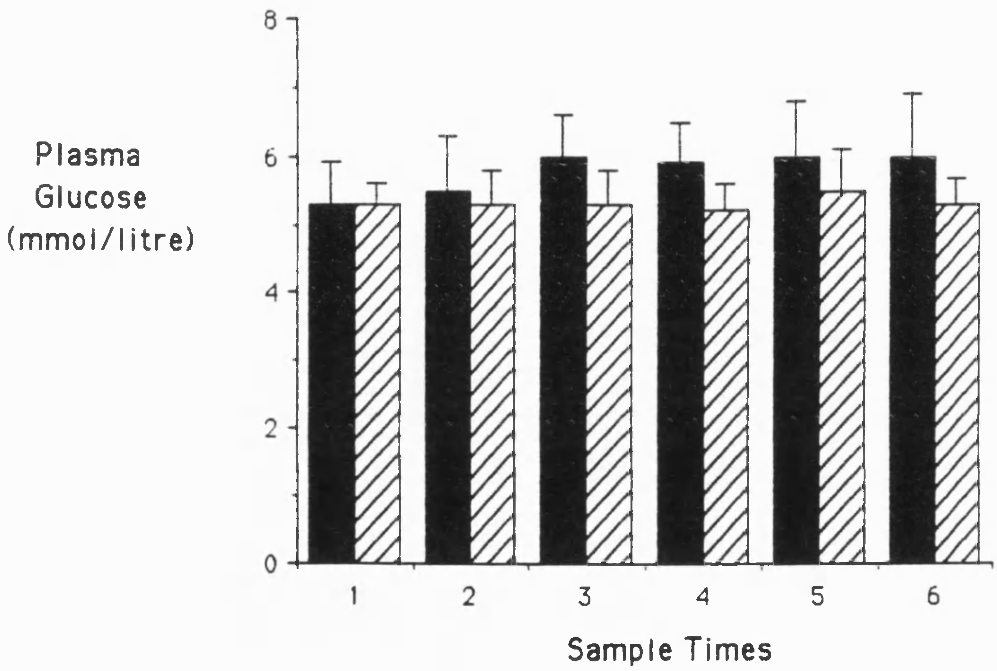


Fig 5.2 *Mean (SEM) plasma concentration of glucose in the GA group (solid bars) and LA group (hatched bars).*

Sample 1 = before induction of anaesthesia; 2 = after induction of anaesthesia; 3 = nuclear extraction; 4 = end of surgery; 5 = 30 min after completion of surgery; 6 = 60 min after completion of surgery.

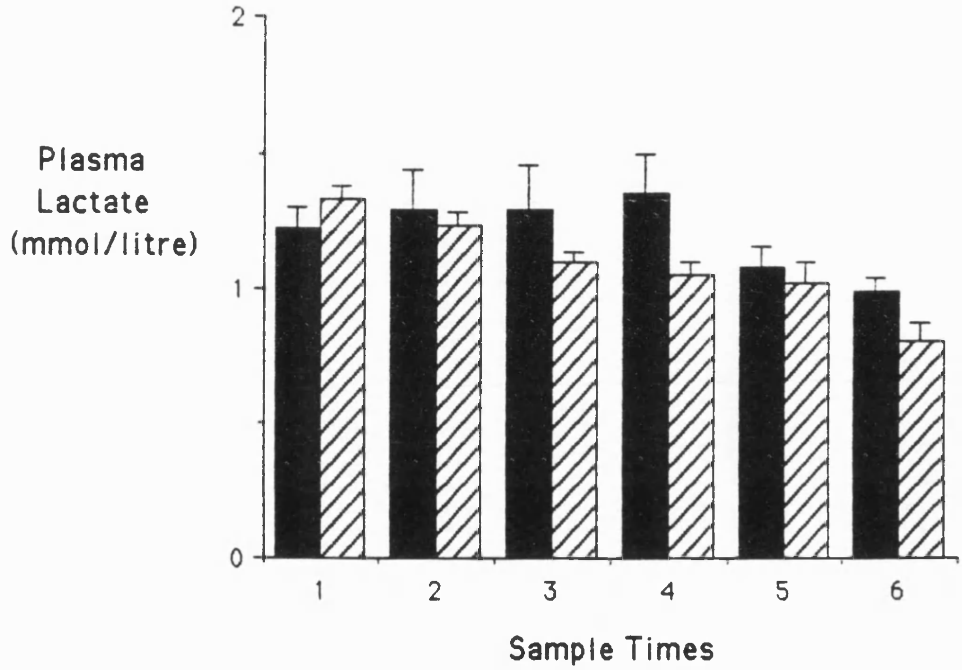


Fig 5.3 *Mean (SEM) plasma concentration of lactate in the GA group (solid bars) and LA group (hatched bars).*

Sample 1 = before induction of anaesthesia; 2 = after induction of anaesthesia; 3 = nuclear extraction; 4 = end of surgery; 5 = 30 min after completion of surgery; 6 = 60 min after completion of surgery.

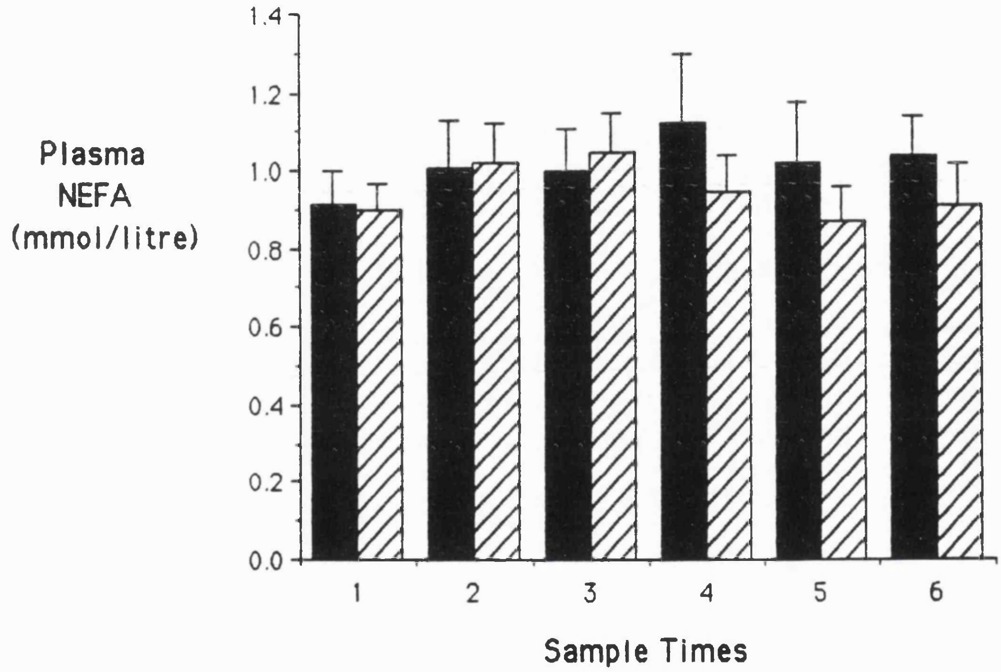


Fig 5.4 *Mean (SEM) plasma concentration of non-esterified fatty acids (NEFA) in the GA group (solid bars) and LA group (hatched bars). Sample 1 = before induction of anaesthesia; 2 = after induction of anaesthesia; 3 = nuclear extraction; 4 = end of surgery; 5 = 30 min after completion of surgery; 6 = 60 min after completion of surgery.*

Study 2

Plasma catecholamine response to cataract surgery

Encouraged by the results of the pilot study, I was keen to quantify the catecholamine response to cataract surgery under GA. Study 1 indicated a relatively small metabolic response, as shown by changes in circulating glucose and lactate values, and suggested only a limited increase in catecholamine secretion. The object of Study 2 was to compare the plasma catecholamine response associated with cataract surgery in patients receiving either GA or LA. Concurrent changes in plasma glucose, arterial pressure and heart rate were also measured.

Methods

20 elderly patients admitted for cataract surgery were investigated in this study. The selection of patients and their randomisation for either GA or LA, again using retrobulbar blockade, was as described previously. The method of collection of blood samples, the techniques of GA and LA used, and the timing of the sampling was described in Chapter Four.

In this study, blood was collected from the patients and assayed for plasma glucose, noradrenaline and adrenaline concentrations up to 60 min after the end of surgery. Arterial pressure was measured noninvasively in both LA and GA groups, and the ECG and pulse oximetry were monitored continuously throughout the study.

Results

There was no significant difference between the groups with respect to age, body weight, sex distribution, time for induction of anaesthesia and duration of surgery (Table 5.2). The overall operating theatre time was significantly longer in the GA group (48 min GA group, 40 min LA group, $p<0.05$).

Plasma catecholamines (Figures 5.5 and 5.6)

Plasma noradrenaline concentrations in the GA group increased from a control value of 1.25 nmol/litre to a peak value of 1.74 nmol/litre on completion of surgery. In the LA group, however, plasma noradrenaline varied little from the control value of 1.18 nmol/litre. Plasma noradrenaline values were significantly decreased in the LA group compared with the GA group at the end of surgery ($p<0.01$), and at 30 and 60 min after completion of surgery ($p<0.05$).

Plasma adrenaline values in the GA group increased from 0.52 nmol/litre in the control period to only 0.63 nmol/litre 30 min after completion of surgery. In the LA group plasma adrenaline concentrations were stable intraoperatively and then declined from a control value of 0.44 nmol/litre to 0.34 nmol/litre 60 min after completion of surgery. Plasma adrenaline values were significantly decreased in the LA group compared with the GA group at both 30 and 60 min after completion of surgery ($p<0.05$).

Plasma glucose (Figure 5.7)

Plasma glucose increased intraoperatively and postoperatively in the GA group from 5.3 to 6.0 mmol/litre. There was little change in glucose values in the LA group with the result that there was a significant difference between the groups both during and after surgery ($p<0.05$).

Mean arterial pressure and heart rate (Figures 5.8 and 5.9)

Heart rate and mean arterial pressure were similar in both groups in the control period. Mean arterial pressure increased significantly in both groups after induction of anaesthesia, by 20 mmHg in the GA group ($p<0.01$) and by 10 mmHg in the LA group ($p<0.05$). In the GA group arterial pressure decreased below control values during the rest of the study, whereas arterial pressure remained significantly higher in the LA group before declining to control values postoperatively. Arterial pressure was significantly higher in the LA group at nuclear extraction, on completion of surgery and 30 min after completion of surgery ($p<0.05$).

In contrast, heart rate varied little in the LA group throughout the study. In the GA group, however, there was a marked increase in heart rate after induction of anaesthesia from 76 to 96 beats/min ($p<0.01$), but this was not sustained during and after surgery. Heart rate was significantly higher in the GA group compared with the LA group only after induction of anaesthesia ($p<0.01$).

Discussion

The results of Study 2 show clearly that LA prevented the increase in catecholamine secretion associated with cataract surgery under GA. The plasma noradrenaline and adrenaline values found in the control period were similar to those reported in unstressed, healthy individuals (Buhler et al, 1978), showing that the patients were comparatively stress–free in spite of the lack of premedication. Although increased sympathoadrenal activity during surgery mainly results from afferent stimuli from the operative site, it is also augmented by hypoxaemia, hypercarbia and blood loss. Although in this study, these physiological variables were not specifically examined, there is no reason to suggest that they were not comparable in the two groups, so that the abolition of sensory neuronal input from the eye in the LA group is likely to have been the cause of the difference in circulating catecholamines. The increases in plasma catecholamines in the GA group were only small (noradrenaline 0.49 nmol/litre, adrenaline 0.11 nmol/litre) and much less than those found in upper abdominal and pelvic surgery in which increases of up to 1.0 nmol/litre adrenaline have been observed (Lacoumenta et al, 1986; Klingstedt et al, 1987). This modest rise in sympathoadrenal activity is reflected in the small size of the glycaemic response, only 0.7 mmol/litre.

Local anaesthesia was associated with improved stability of arterial pressure and heart rate. The significant increase in mean arterial pressure found after neural blockade, which persisted for the intraoperative period, was only 10 mmHg and may have been caused by apprehension and fear. Induction of GA resulted in the expected tachycardia and hypertension, since no attempt was made to obtund the response to laryngoscopy and intubation, but subsequently the arterial pressure was well controlled in the GA group. It is possible that in hypertensive patients, the increase in arterial pressure seen during LA and persisting throughout the operation, may reach unacceptable levels. GA may be the preferred option, providing the pressor response at induction can be obtunded, either by avoiding intubation and using a laryngeal mask, or by the use of agents such as lignocaine, as discussed in Chapter One. The changes in cardiovascular variables found at induction of anaesthesia in the GA group were not associated with a marked increase in circulating noradrenaline values. This discrepancy may be accounted for by the observation that circulating noradrenaline values probably only represent about 20% of the noradrenaline activity at the synapse and so grossly underestimate sympathetic nervous activity (Silverberg et al, 1978). A possible effect of thiopentone on decreasing tonic sympathetic activity may also have obtunded the noradrenaline response (Joyce, Roizen and Eger, 1983). Previous studies have shown that general anaesthesia, *per se*, has little effect on the classical endocrine and metabolic response to surgery which results from surgical stimulation (Kehlet, 1984; Carli and Elia, 1991).

The overall operating theatre time was significantly decreased in the LA group. This finding was in contrast to Study 1, in which I failed to find any benefit in theatre utilisation. It is notable that in this study, the duration of surgery was similar in the two groups, whereas previously it was significantly longer in the LA group. The results from both studies emphasise that the saving in overall time in the LA group occurs on completion of surgery and not on induction of anaesthesia.

In conclusion, Study 1 showed that the hormonal and metabolic response to cataract surgery was abolished by LA. Study 2 reinforced these results and showed that not only the plasma glucose, but also plasma catecholamine responses are abolished by LA, and that this technique improves cardiovascular stability.

Table 5.2 *Details of patients in Study 2. Mean values (SEM).*

** Significant difference between mean values (p<0.05)*

	LA group (n=10)	GA group (n=10)
Age; years	80 (1.5)	76 (4.5)
Weight; kg	58 (4.0)	63 (4.7)
Sex	2M : 8F	1M : 9F
Induction time; min	13 (0.9)	13 (1.2)
Duration of surgery; min	22 (1.3)	25 (1.9)
Start of induction to leaving theatre; min	40 (2.1) *	48 (1.8) *

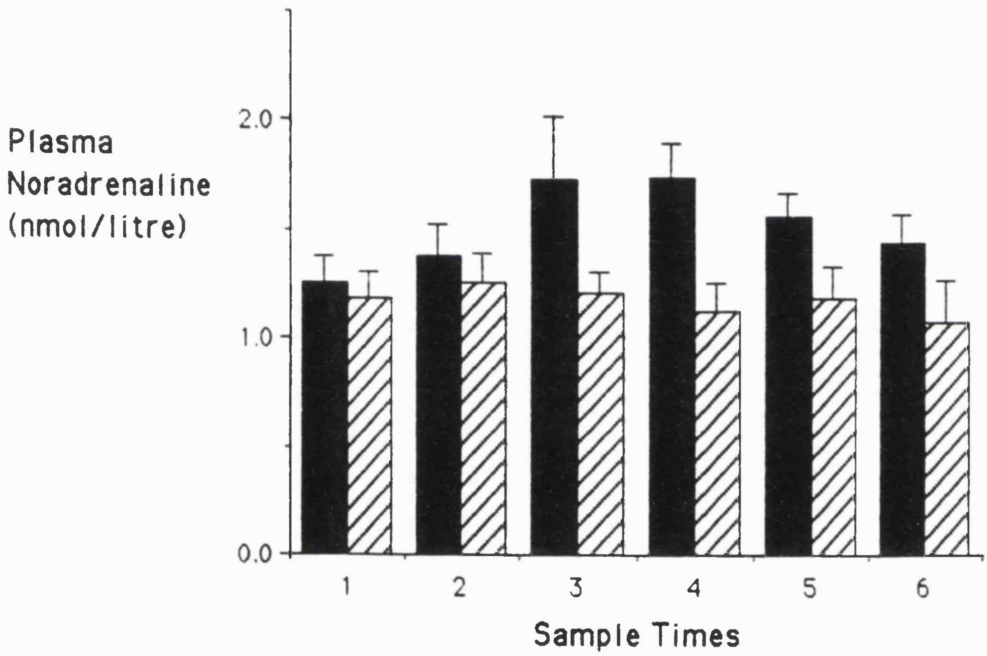


Fig 5.5 *Mean (SEM) plasma noradrenaline concentration (nmol/litre) in the GA group (solid bars) and LA group (hatched bars).*

Sample 1 = before induction of anaesthesia; 2 = after induction of anaesthesia; 3 = nuclear extraction; 4 = end of surgery; 5 = 30 min after completion of surgery; 6 = 60 min after completion of surgery.

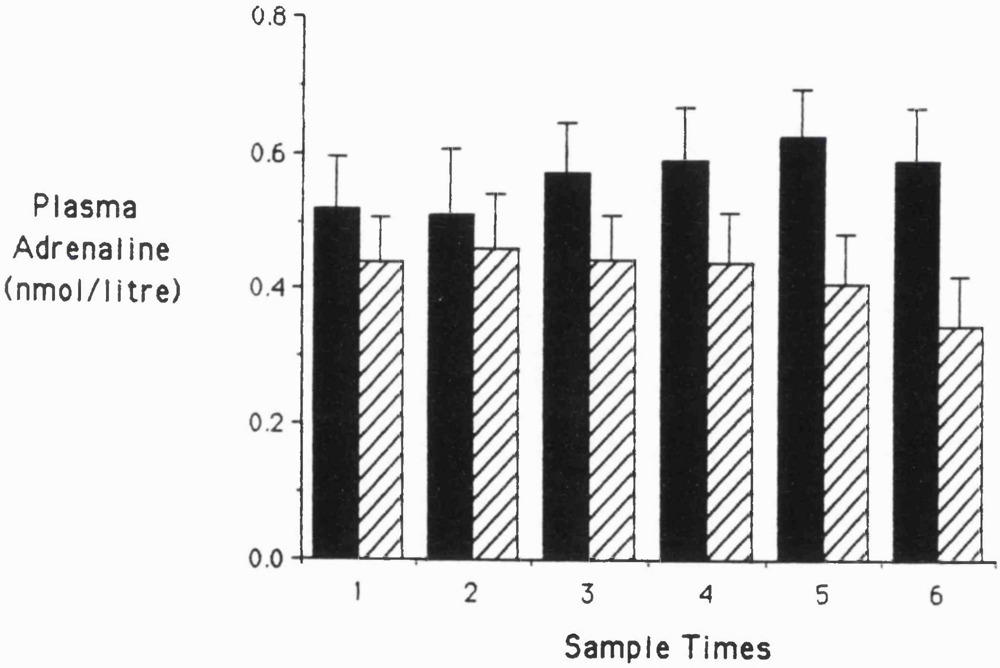


Fig 5.6 *Mean (SEM) plasma adrenaline concentration (nmol/litre) in the GA group (solid bars) and LA group (hatched bars).*

Sample 1 = before induction of anaesthesia; 2 = after induction of anaesthesia; 3 = nuclear extraction; 4 = end of surgery; 5 = 30 min after completion of surgery; 6 = 60 min after completion of surgery.

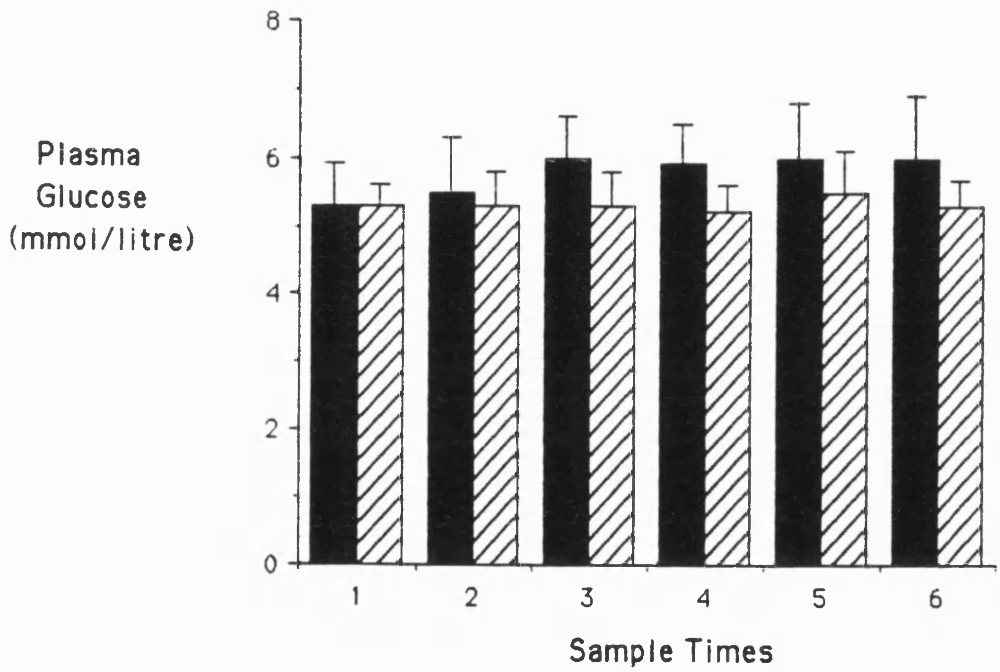


Fig 5.7 *Mean (SEM) plasma glucose concentration (mmol/litre) in the GA group (solid bars) and LA group (hatched bars).*

Sample 1 = before induction of anaesthesia; 2 = after induction of anaesthesia; 3 = nuclear extraction; 4 = end of surgery; 5 = 30 min after completion of surgery; 6 = 60 min after completion of surgery.

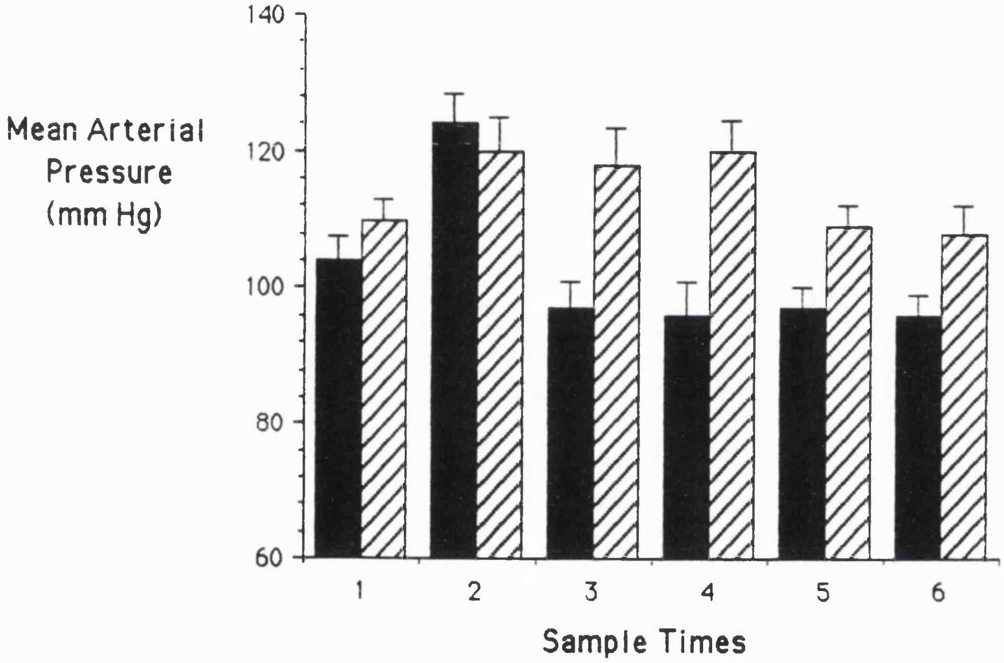


Fig 5.8 *Mean (SEM) arterial pressure (mmHg) in the GA group (solid bars) and LA group (hatched bars).*

Sample 1 = before induction of anaesthesia; 2 = after induction of anaesthesia; 3 = nuclear extraction; 4 = end of surgery; 5 = 30 min after completion of surgery; 6 = 60 min after completion of surgery.

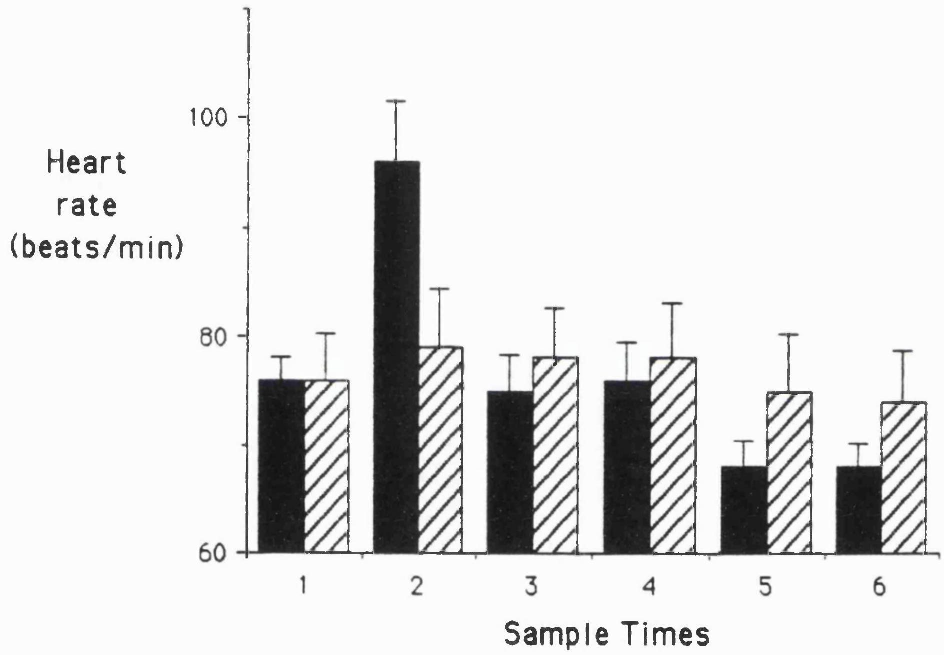


Fig 5.9 *Mean (SEM) heart rate (beats/min) in the GA group (solid bars) and LA group (hatched bars).*

Sample 1 = before induction of anaesthesia; 2 = after induction of anaesthesia; 3 = nuclear extraction; 4 = end of surgery; 5 = 30 min after completion of surgery; 6 = 60 min after completion of surgery.

Chapter Six

The investigation of the effects of combining general and local anaesthesia on the metabolic and hormonal changes during cataract surgery.

Introduction

It was shown in the last chapter that, although induction of general anaesthesia and intubation was associated with a rise in arterial pressure and heart rate, this was not associated with a significant increase in circulating catecholamine concentrations. The increase in metabolite and hormone values, in particular cortisol, during cataract surgery in the previous two studies was seen after surgery had started and is considered to be caused by the surgical stimulus itself. Studies of the effect of general anaesthesia on its own suggest little, if any, increase in circulating metabolites and hormones (Kehlet, 1984; Carli and Elia, 1991). However, in all studies, surgery is superimposed on general anaesthesia thus masking any further effects from the anaesthetic itself. The object of Study 3 was to determine the part played by the general anaesthetic on the hormonal and metabolic response during and after cataract surgery.

Study 3

Methods

Thirty elderly patients admitted for cataract surgery were studied after informed consent had been obtained. They were randomised into one of three groups, to receive either general anaesthesia (GA), local anaesthesia by retrobulbar blockade (RB), or general anaesthesia followed by retrobulbar blockade (GA+RB). The techniques of GA and LA were as described in Chapter Four. In the GA+RB group, general anaesthesia was induced as in the GA group, and the retrobulbar block administered after the trachea was intubated.

Venous blood samples were collected as in Chapter Four, and assayed for blood glucose and serum cortisol concentrations up to 120 min after completion of surgery.

Results

There was no significant difference between the groups with respect to age, weight or sex, although there was a preponderance of females in all groups (Table 6.1). There was also no significant difference in the times for induction of anaesthesia, duration of surgery or overall time in theatre between the three groups. Once in the recovery room, no patient in the RB or GA+RB groups complained of pain or discomfort in the operated eye.

Serum Cortisol (Figure 6.1)

Serum cortisol concentrations in the GA group increased from a baseline of 407 nmol/litre to a peak of 801 nmol/litre 30 min post-operatively ($p<0.01$), while in the RB group cortisol concentrations did not change significantly from a baseline of 360 nmol/litre throughout the study period. In contrast, in the GA+RB group, cortisol concentrations changed little during surgery from the baseline of 381 nmol/litre but increased to 660 nmol/litre 30 min post-operatively ($p<0.05$)

before declining over the next two hours. There was a significant difference between the GA group and both the RB and GA+RB groups at the end of surgery ($p<0.01$). However, postoperatively there was a significant difference between the RB group and the GA+RB group ($p<0.05$) as well as the GA group ($p<0.01$), with no significant difference between the GA and GA+RB groups.

Blood Glucose (Figure 6.2)

Blood glucose concentrations in the GA group increased from 4.8 mmol/litre pre–operatively to a peak of 6.0 mmol/litre 60 min post–operatively, although this change was not statistically significant. However, in both the RB and GA+RB groups, blood glucose changed little from the baseline values of 4.5 mmol/litre in the RB group and 4.2 mmol/litre in the GA+RB group until 2h after surgery. At this time, blood glucose concentration in the RB group increased to 7.1 mmol/litre ($p<0.01$), because the patients who had had local anaesthesia only, had eaten by this time. There was a significant difference between the GA group and the RB and GA+RB groups 30 min postoperatively ($p<0.05$), and between the GA group and the GA+RB group 60 min postoperatively ($p<0.05$). At 120 min post surgery, there was a significant difference between the RB group and the GA+RB group ($p<0.01$).

Discussion

The results of this study confirm the findings in Chapter Five that local anaesthesia given as a retrobulbar block is able to prevent the metabolic and hormonal response to cataract surgery which is observed under general anaesthesia alone. The combination of general anaesthesia with retrobulbar blockade also provides stable cortisol and glucose concentrations during surgery, suggesting that the increases seen under general anaesthesia alone are due to surgical stimulation. However, an unexpected finding was a significant increase in cortisol concentration 30 min post–operatively in patients with the combined technique at a time when, with retrobulbar block alone, there was still no change from baseline values. This increase in cortisol concentration could result from a variety of causes, namely the use of neostigmine and glycopyrronium, extubation of the trachea, emergence from anaesthesia, and/or events in the recovery period such as nausea or coughing.

Extubation of the trachea is unlikely to be the cause of the increase in cortisol concentration. The results showed no increase in glucose concentrations post–operatively, which indicates that a marked increase in sympathetic activity could not have occurred. It has been shown that extubation is no more stimulating than intubation (Holden et al, 1991; Lowrie et al, 1992), and I found no metabolic or hormonal response to intubation in this study. Neostigmine, by producing an increase in acetylcholine (ACh) concentration, could have been the cause of the elevated cortisol concentration. ACh has been found to stimulate release of hypothalamic corticotrophin releasing factor (CRF) (Hillhouse, Burden and Jones, 1975), but neostigmine, a quaternary compound, cannot pass the blood–brain barrier. There is little evidence that ACh is able to act directly on the pituitary to cause release of ACTH, although acetylcholine has been shown recently to be synthesised and released by rat corticotrophs (Carmeliet and Denef, 1989).

The immediate recovery period for the patients in this study showed no major complications. Three of the ten patients in the GA+RB group suffered from minor complaints: nausea in two and coughing in one. These were brief episodes and required no treatment. It may be that emergence from anaesthesia itself was the cause of the increase in cortisol concentration, and that, just as with the diurnal rhythm in which cortisol concentrations are elevated on waking in the morning, it is also increased on awakening from anaesthesia. This increase in cortisol concentration on emergence from anaesthesia has not been described previously. All the studies that have examined the metabolic and hormonal effects of anaesthesia have surgery superimposed before the patient is woken.

In conclusion, cataract surgery performed under general anaesthesia results in a marked hormonal and metabolic response which can be prevented by local anaesthesia alone. However, the combination of both general and local anaesthesia only provided stable conditions intra-operatively. Plasma cortisol concentration increased in the postoperative period. I suggest that antagonism of neuromuscular blockade or emergence from anaesthesia, or both, evokes an adrenocortical response which may obtund the beneficial effects of local anaesthesia.

Table 6.1 *Details of patients studied in Study 3 (mean values (SEM)).*

	RB group (n=10)	GA group (n=10)	GA+RB group (n=10)
Age; years	82 (2.2)	77 (1.9)	75 (2.3)
Weight; kg	64 (5.9)	67 (3.8)	72 (3.9)
Sex	4M : 6F	1M :9F	4M :6F
Induction time; min GA→start of surgery	–	18 (1.6)	18 (1.4)
Induction time; min LA→start of surgery	16 (1.9)	–	13 (1.3)
Duration of surgery; min	30 (2.9)	24 (1.7)	25 (1.5)
Start of induction to leaving theatre; min	49 (4.2)	53 (2.5)	51 (1.6)

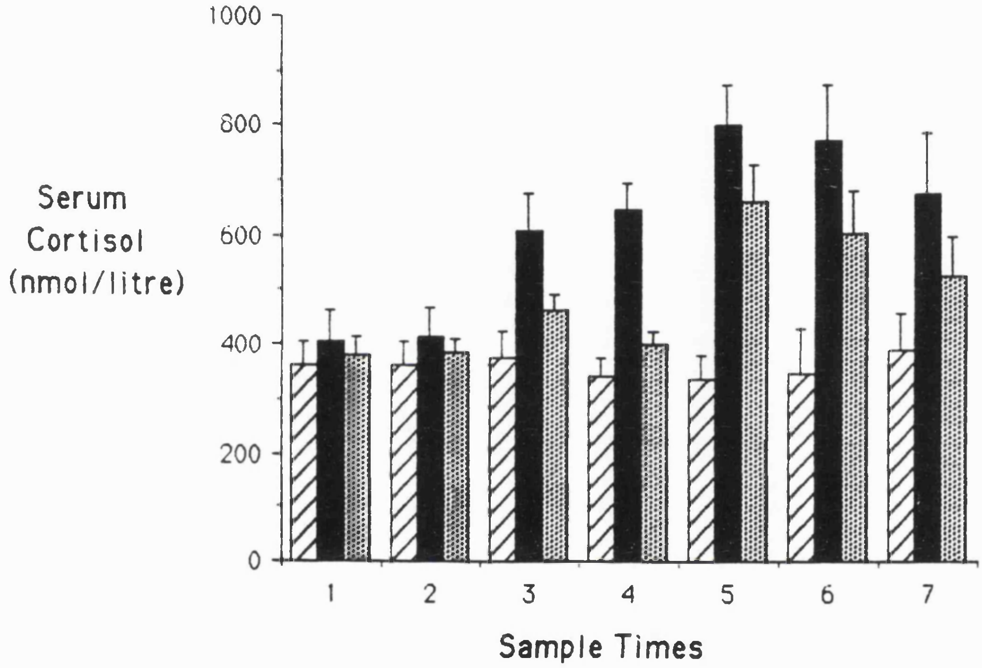


Fig 6.1 *Mean (SEM) serum cortisol concentration in the RB group (hatched bars), GA group (solid bars) and GA+RB group (stippled bars). Sample 1 = before induction of anaesthesia; 2 = after induction of anaesthesia; 3 = nuclear extraction; 4 = end of surgery; 5 = 30min after completion of surgery; 6 = 60min after completion of surgery; 7 = 120min after completion of surgery.*

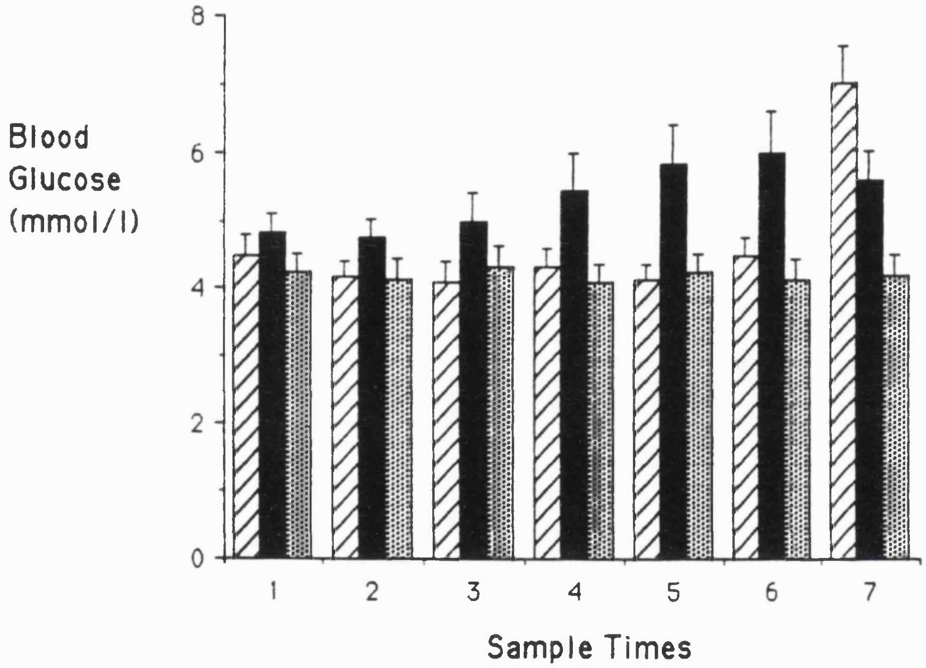


Fig 6.2 *Mean (SEM) blood glucose concentration in the RB group (hatched bars), GA group (solid bars) and GA+RB group (stippled bars). Sample 1 = before induction of anaesthesia; 2 = after induction of anaesthesia; 3 = nuclear extraction; 4 = end of surgery; 5 = 30min after completion of surgery; 6 = 60min after completion of surgery; 7 = 120min after completion of surgery.*

Chapter Seven

The investigation of the effect of peribulbar blockade on the metabolic and hormonal response to cataract surgery.

Introduction

The previous two chapters have shown that local anaesthesia given by retrobulbar blockade inhibited the endocrine, and markedly decreased the metabolic, changes occurring in patients undergoing cataract surgery with general anaesthesia. Today retrobulbar block is performed less commonly, as peribulbar blockade is becoming the technique of choice. In peribulbar blockade a larger volume of local anaesthetic is injected around the orbit of the eye at one or two injection sites, whereas in retrobulbar block a smaller volume is injected intraconally towards the ciliary ganglion (Hamilton, 1990). Although the time to onset of analgesia may be longer, peribulbar block has been shown to be as effective as retrobulbar block in providing sensory blockade and akinesia (Weiss and Deichman, 1989). Furthermore, serious side effects are decreased as the needle is further from the dura and major blood vessels. The object of Study 4 was to determine whether peribulbar block, with its anaesthetic solution placed more peripherally, is as effective as retrobulbar block in decreasing the metabolic and hormonal changes associated with cataract surgery performed under general anaesthesia.

Study 4

Methods

30 elderly patients admitted for cataract surgery were investigated in this

study. They were allocated randomly to receive either general anaesthesia (GA), local anaesthesia by retrobulbar blockade (RB), or local anaesthesia by peribulbar blockade (PB). Venous blood samples were collected up to 120 minutes after completion of surgery and assayed for blood glucose and lactate and serum cortisol concentrations. The techniques used for anaesthesia and the methods of analysis of the blood samples are described in Chapter Four.

Results

There was no significant difference between the groups with respect to age, weight, sex distribution, time for induction of anaesthesia or duration of surgery. (Table 7.1) One patient in the RB group was excluded as he was found to be diabetic on the basis of his baseline blood glucose concentration.

Serum Cortisol (Figure 7.1).

In the GA group, serum cortisol concentration increased from a baseline of 407 nmol/litre to a peak of 801 nmol/litre ($p<0.01$) 30 min postoperatively. In both local anaesthetic (LA) groups, serum cortisol values varied little from the baseline values of 441 nmol/litre in the PB group and 360 nmol/litre in the RB group. The peribulbar data were consistently, but insignificantly, higher than the retrobulbar values. Serum cortisol results in the PB and RB groups were significantly decreased compared with those in the GA group during, and at the end of surgery ($p<0.05$) and 30 and 60 min postoperatively ($p<0.01$).

Blood Glucose (Figure 7.2).

Blood glucose concentration in the GA group increased from a baseline of 4.8 mmol/litre to a peak of 6.0 mmol/litre 60 min postoperatively, although this increase was not statistically significant. In contrast, both LA groups showed a slight decrease in blood glucose concentrations from a baseline of 4.1 mmol/litre in the PB group to 3.6 mmol/litre 30 min postoperatively, and from 4.5 mmol/litre to 4.1 mmol/litre in the RB group. However, two hours post–surgery there was a significant increase in blood glucose ($p<0.01$) in both PB and RB patients because both groups of patients had eaten. Blood glucose values were significantly increased in the GA group compared with both RB and PB groups, at the end of surgery and at 30 and 60 min post surgery ($p<0.01$).

Blood Lactate (Figure 7.3).

Blood lactate concentrations in the PB and RB groups decreased steadily during surgery from their control values of 0.86 mmol/litre in the PB group and 0.70 mmol/litre in the RB group. This was more pronounced with PB, which fell to a nadir of 0.53 mmol/litre at the end of surgery ($p<0.01$ during, and at the end of surgery, and 60 min postoperatively), than with RB which fell to 0.51 mmol/litre at the end of surgery ($p<0.05$). Lactate values increased 120 min post–surgery in the PB and RB groups, coincident with the increase in blood glucose (Figure 7.2). In the GA group, the blood lactate concentration showed a more gradual decline during surgery, from 0.87 mmol/litre at the start to 0.57 mmol/litre 60 min postoperatively ($p<0.05$). There were no significant differences between the three groups.

Discussion

The results show clearly that peribulbar blockade is as successful as retrobulbar blockade in preventing the metabolic and hormonal response associated with cataract surgery under general anaesthesia.

Retrobulbar anaesthesia was first described by Knapp in 1884, and has for many years been an effective means of providing local anaesthesia for eye surgery.

Rare, but nevertheless sight and life–threatening, complications have been reported, the incidences varying in different studies from 1:375 (Ahn and Stanley, 1987) to 1:750 (Nicoll et al, 1987) (0.26 – 0.13%). Complications have included retrobulbar haemorrhage (Davis and Mandel, 1986), optic nerve damage (Pautler et al, 1986), bulbar perforation (Grizzard et al, 1991; Ramsay and Knobloch, 1978), central retinal artery occlusion (Goldsmith, 1967), brain stem anaesthesia (Hamilton, 1985; Javitt et al, 1987), respiratory arrest (Wittpenn et al, 1986; Rigg and James, 1989), grandmal seizure (Meyers, Ramirez and Boniuk, 1978) and cardiopulmonary arrest (Rosenblatt, May and Barsoumian, 1980). Local anaesthetic solution is deposited within the muscle cone at the back of the orbit for a retrobulbar block (Fig 7.4). In this anatomical space lie the ciliary ganglion, the optic nerve and the central retinal artery. Thus, there is the danger of arterial injection leading to retrobulbar haemorrhage or cardiorespiratory arrest, and of optic nerve damage leading to visual loss. The optic nerve is covered by extensions of the meninges and it has been shown that when solutions are injected beneath this meningeal sheath they can pass posteriorly along the subdural space of the optic nerve to the subdural space surrounding the pons and midbrain (Drysdale, 1984). This explains the occurrence of central nervous symptoms, such as apnoea, reported after retrobulbar block.

Peribulbar block was first described by Davis and Mandel in 1986, the same paper being reprinted in a different journal in 1988. It utilises an extramuscular injection, depositing local anaesthetic outside the muscle cone so that the needle is kept well away from the site of the optic nerve and major vessels (Fig 7.5). Spread of the injectate then occurs through the intermuscular septum into the intramuscular compartment within the cone by simple diffusion aided by pressure applied to the orbit (Hamilton, 1990). This accounts for the slightly longer onset of action with peribulbar block which, however, these results show is insignificant in practice (Table 7.1). This orbital diffusion carries local anaesthetic to the third, fourth, fifth, sixth and seventh cranial nerves and also to the ciliary ganglion (Davis and Mandel, 1986), to provide good analgesia and also akinesia, without the need for a separate seventh nerve block. Scleral perforation is less of a danger with this technique but is still a possibility and has been reported (Kimble et al, 1987; Grizzard et al, 1991).

Davis and Mandel (1994) have conducted a large prospective multicentre study of 16,224 peribulbar blocks and have shown that peribulbar is as effective as retrobulbar anaesthesia in providing analgesia and akinesia, while leading to fewer sight- and life-threatening complications. The incidence of orbital haemorrhage was 0.074%, globe perforation 0.006%, expulsive haemorrhage 0.013% and grandmal seizure 0.006%. There were no cases of cardiac or respiratory depression, or deaths.

In conclusion, Study 4 shows that peribulbar is as effective as retrobulbar block in preventing the metabolic and hormonal response to cataract surgery, and that diffusion of the local anaesthetic into the muscular cone is sufficient to provide neural blockade of the ciliary ganglion.

Table 7.1. *Details of patients studied in Study 4. Mean values (SEM).*

	GA group (n=10)	RB group (n=9)	PB group (n=10)
Age; years	77 (1.9)	82 (2.2)	80 (1.9)
Weight; kg	67 (3.8)	64 (5.9)	61 (3.6)
Sex	1M:9F	4M:5F	4M:6F
Induction time; min	18 (1.6)	16 (1.9)	19 (1.7)
Duration of surgery; min	24 (1.7)	30 (2.9)	28 (2.7)
Start of induction to leaving theatre; min	53 (2.5)	49 (4.2)	51 (3.7)

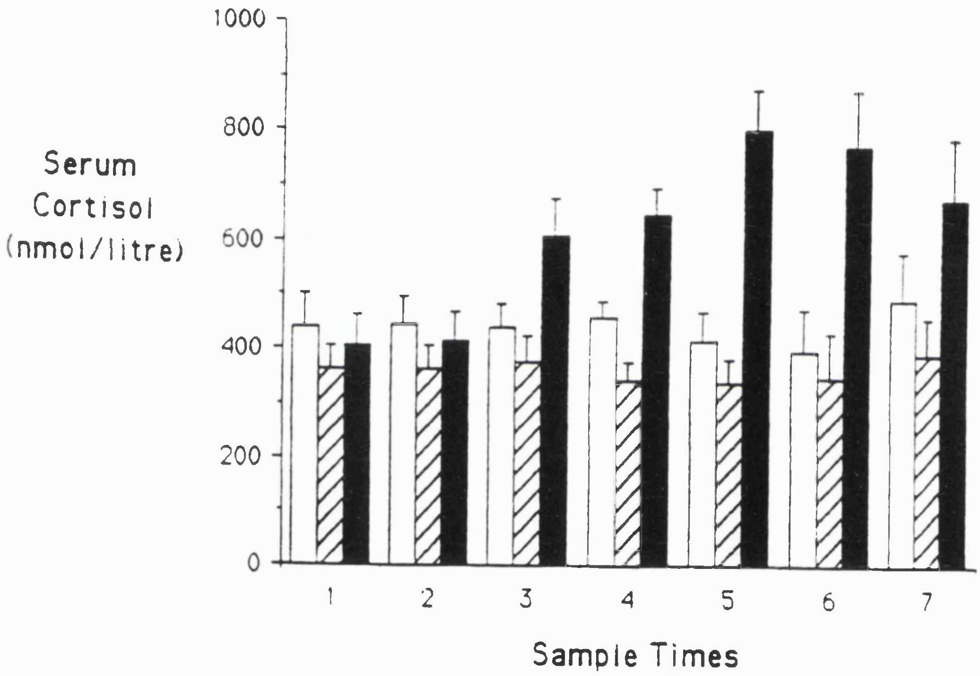


Fig 7.1. *Mean (SEM) serum cortisol concentration in the PB group (open bars), RB group (hatched bars), and GA group (solid bars). Sample 1 = before induction of anaesthesia; 2 = after induction of anaesthesia; 3 = nuclear extraction; 4 = end of surgery; 5 = 30min after completion of surgery; 6 = 60min after completion of surgery; 7 = 120min after completion of surgery.*

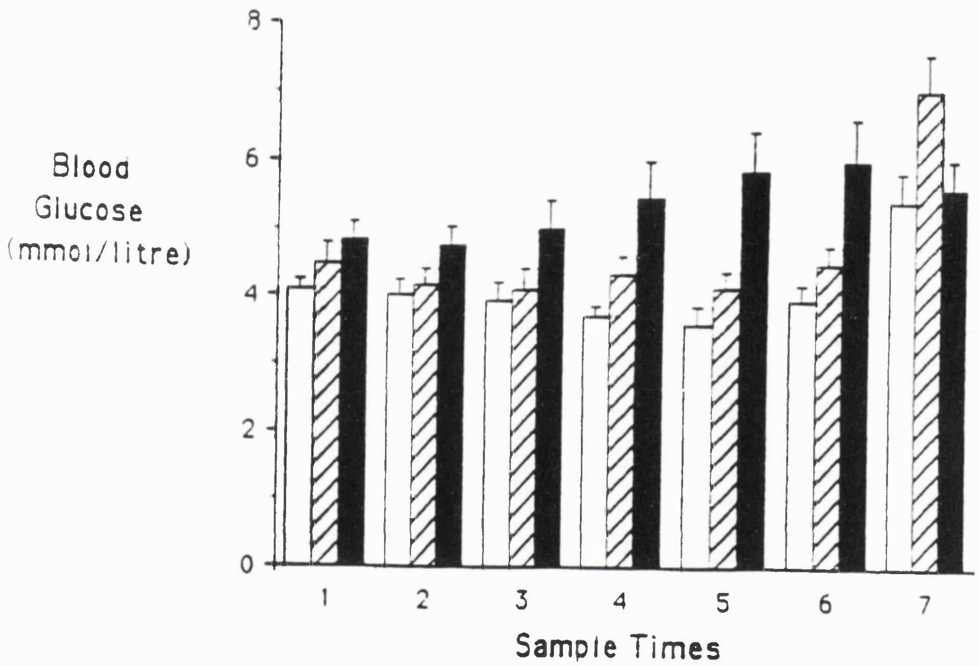


Fig 7.2. *Mean (SEM) blood glucose concentration in the PB group (open bars), RB group (hatched bars), and GA group (solid bars). Sample 1 = before induction of anaesthesia; 2 = after induction of anaesthesia; 3 = nuclear extraction; 4 = end of surgery; 5 = 30min after completion of surgery; 6 = 60min after completion of surgery; 7 = 120min after completion of surgery.*

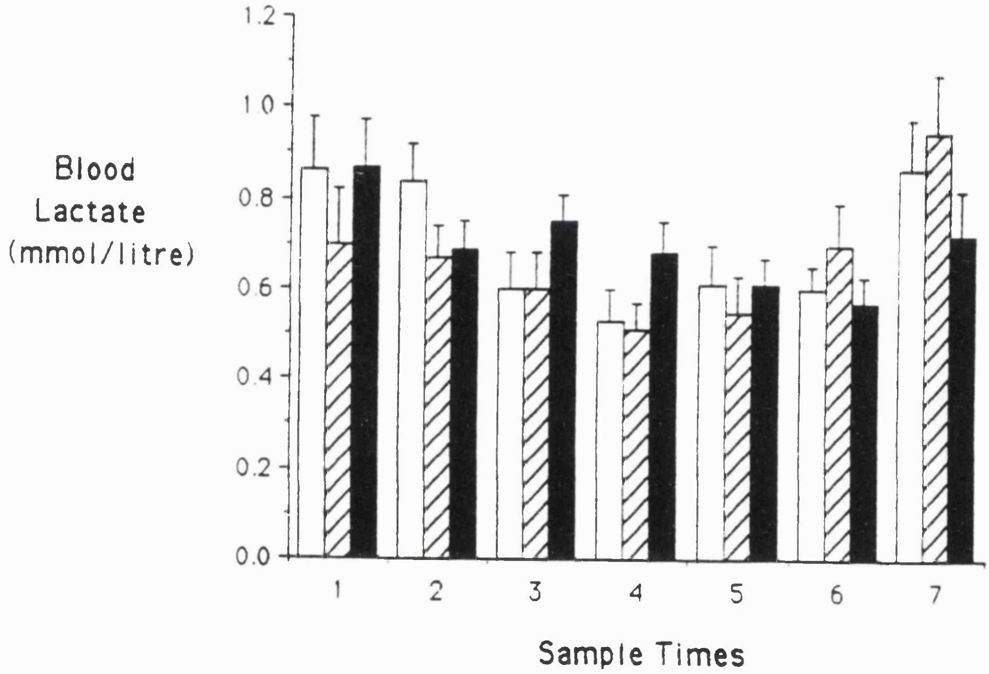


Fig 7.3. *Mean (SEM) blood lactate concentration in the PB group (open bars), RB group (hatched bars), and GA group (solid bars). Sample 1 = before induction of anaesthesia; 2 = after induction of anaesthesia; 3 = nuclear extraction; 4 = end of surgery; 5 = 30min after completion of surgery; 6 = 60min after completion of surgery; 7 = 120min after completion of surgery.*

Fig 7.4 *Lateral view of injection site for retrobulbar blockade.*

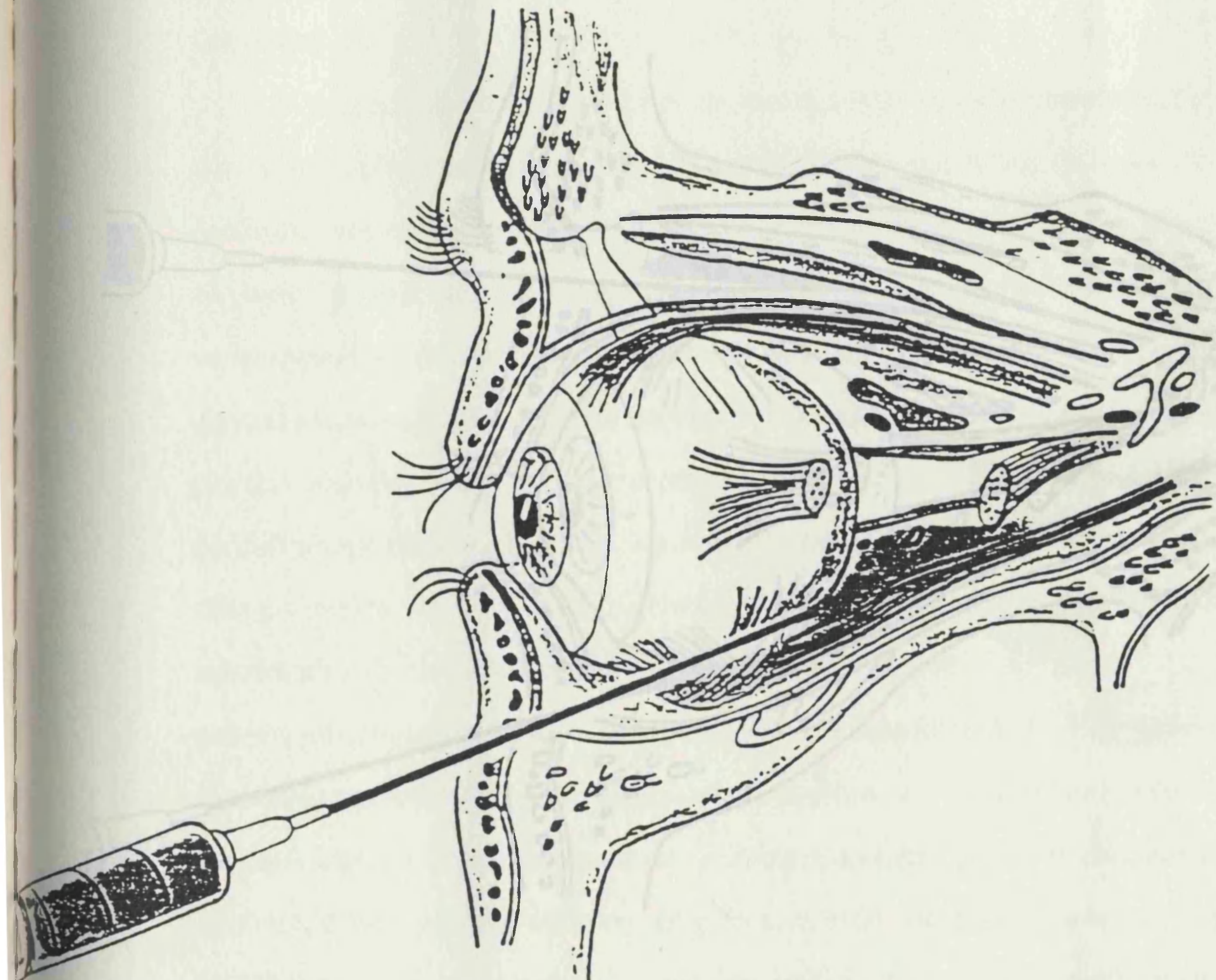
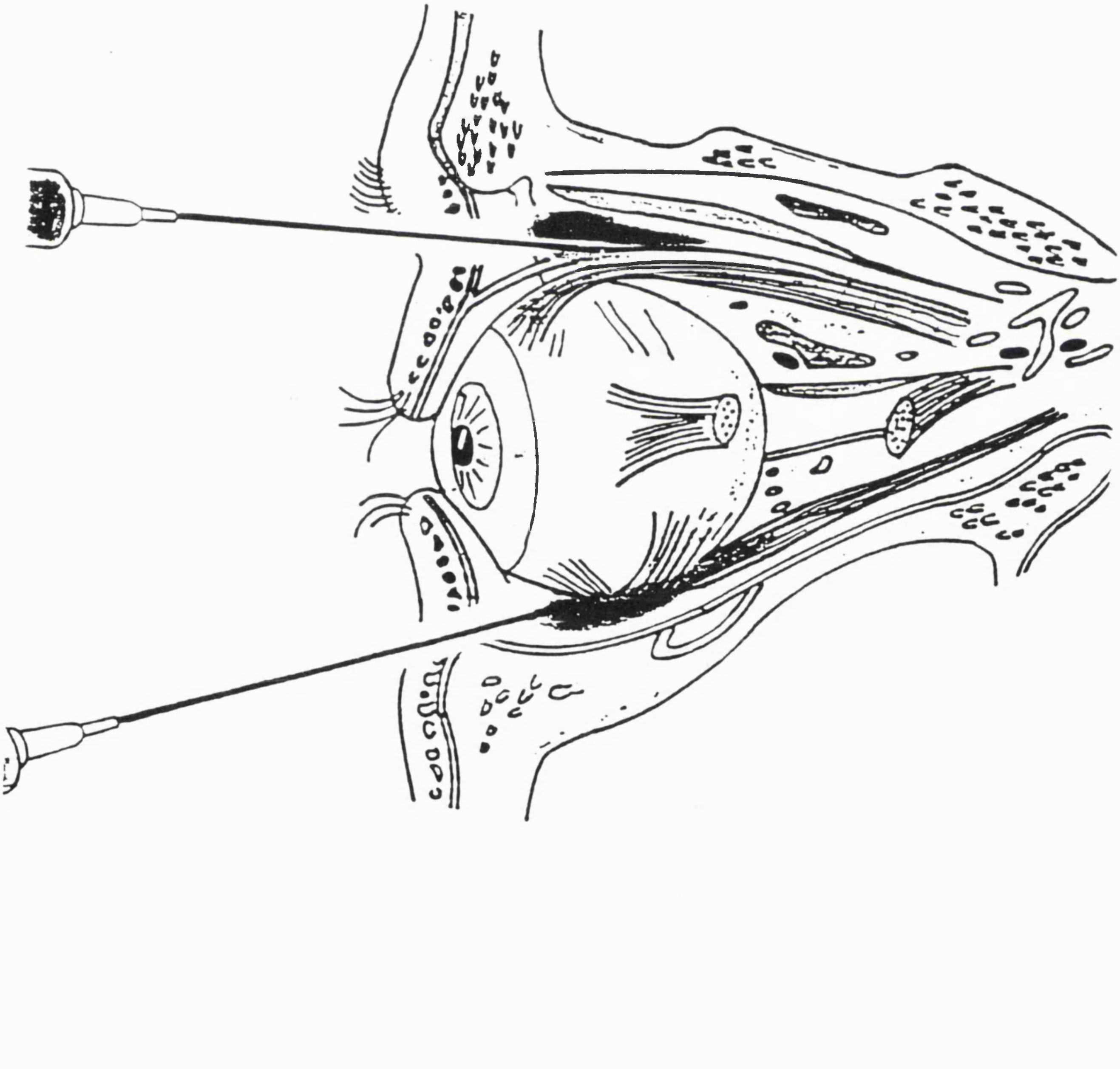


Fig 7.5 *Lateral view of injection sites for peribulbar blockade.*



Chapter Eight

The investigation of the effects of general and local anaesthesia on the metabolic and hormonal changes during cataract surgery in non–insulin–dependent diabetic patients.

Introduction

The management of diabetic patients undergoing surgery is complicated by the preoperative starvation necessary when general anaesthesia is used, the postoperative starvation that is inevitable and the endocrine and metabolic responses to that surgery. Using local anaesthesia, postoperative starvation is unneccessary, as is starvation preoperatively, providing there is no conversion to general anaesthesia. The previous chapters have described studies of non–diabetic patients showing that cataract surgery under local anaesthesia, using either peribulbar or retrobulbar blockade, markedly decreases the hormonal and metabolic changes which occur in these patients undergoing their surgery with general anaesthesia. The response of non–insulin dependent diabetes mellitus (NIDDM) patients to surgical stress has not been fully elucidated, but there is general agreement that control of blood glucose concentration, avoiding either hyper– or hypoglycaemia, is of prime importance in the perioperative period (Milaskiewicz and Hall, 1992). Study 5 compares the effects of local and general anaesthesia in NIDDM patients undergoing cataract surgery on metabolic control in the immediate perioperative period to determine whether there is an improvement when the surgery is performed under local anaesthesia.

Study 5

Methods

Forty elderly patients admitted for cataract surgery were studied after informed consent had been obtained. They were otherwise healthy and, apart from oral hypoglycaemic agents, were not receiving any medication known to interfere with the hormonal and metabolic responses to surgery. Twenty NIDDM patients were allocated randomly to receive either general anaesthesia (GA) or local anaesthesia (LA) by retrobulbar blockade, and twenty non–diabetic controls were also studied after randomisation to general or retrobulbar anaesthesia.

General anaesthesia and retrobulbar blockade were administered as described in Chapter Four. No intravenous fluids were given to any group throughout the study. Postoperatively, LA patients were allowed to eat within 2h of their operations, whereas the GA patients did not eat until after 4h had passed. This is accordance with usual clinical practice in our unit.

Venous blood was collected from an antecubital fossa vein, as described in Chapter Four. In this study, two control blood samples were collected ten minutes apart, with further samples after induction of GA or LA, at the time of nuclear extraction, on completion of surgery, and 30, 60, 120 and 240 min after completion of surgery. Samples were assayed for blood glucose and lactate, plasma non–esterified fatty acid and beta–hydroxybutyrate, and serum cortisol, insulin and growth hormone concentrations.

A baseline value was obtained for each hormone and metabolite by calculating the mean from the two control samples obtained before induction of anaesthesia. The results are presented as mean (SEM) difference from baseline as there were significant differences between baseline glucose and hormone values in diabetic and control patients.

Results

There was no significant difference between the groups with respect to age, weight, sex distribution, time for induction of anaesthesia or duration of surgery. (Table 8.1) One patient in the LA control group was excluded from the results as insufficient data were collected. In the GA NIDDM group, six patients were taking long–acting oral hypoglycaemic agents (glibenclamide or chlorpropamide), one was taking short–acting tolbutamide, and three were treated by diet alone. In the LA NIDDM group, four were taking long–acting agents (glibenclamide), one was taking short–acting metformin and five were treated by diet alone.

Serum Cortisol (Figure 8.1).

Baseline values for serum cortisol were greater in the diabetic patients (GA and LA NIDDM - 498 nmol/litre, GA and LA control - 401 nmol/litre ($p<0.05$)). In both LA groups, serum cortisol concentrations changed little during and after surgery, with a decrease in the diabetic patients postoperatively of 122 nmol/litre ($p<0.05$) at 2h. In contrast, both GA groups had serum cortisol concentrations which were unchanged after induction of anaesthesia, but increased during surgery to reach a peak 30 min postoperatively. The GA NIDDM group increased by 399 nmol/litre ($p<0.01$) and the GA control group by 376 nmol/litre ($p<0.01$). By 4 hours postoperatively the concentrations in both GA groups had returned to baseline. There was no statistically significant difference between the two LA groups or the two GA groups, but the difference between the GA groups and the LA groups was significant ($p<0.05$ at lens extraction, end of surgery and 1 hour postoperatively, and $p<0.01$ 30 min postoperatively).

Blood Glucose (Figure 8.2).

Baseline glucose values were also significantly greater in the diabetic patients than the controls (GA and LA NIDDM - 6.6 mmol/litre, GA and LA controls - 4.6 mmol/litre ($p<0.01$)). In both LA groups, the blood glucose concentrations varied little from their respective baselines until 2h postoperatively when the LA patients ate. In contrast, blood glucose concentrations in the GA NIDDM patients increased by 2.0 mmol/litre ($p<0.05$) by 2h postoperatively, while the GA control group increased by only 1.2 mmol/litre ($p<0.05$) by 1h postoperatively. The increase in glucose concentrations in the GA patients was significantly greater than that in both the LA groups at the end of surgery and at 30 and 60 min postoperatively ($p<0.05$).

Serum Insulin (Figure 8.3).

Baseline insulin concentrations were greater in the diabetic patients compared with the controls, but this was not significant. (GA and LA NIDDM - 17.7 mU/litre, GA and LA control - 11.9 mU/litre). All four groups followed a similar pattern during surgery, with serum insulin concentrations falling by 5.7 mU/litre ($p<0.01$) in the GA NIDDM group, 3.9 mU/litre ($p<0.01$) in the LA NIDDM group, 3.2 mU/litre ($p<0.05$) in the GA controls, and 2.3 mU/litre ($p<0.01$) in the LA controls at the end of surgery. Postoperatively, serum insulin concentration increased by 7.4 mU/litre ($p<0.01$) in the GA control group at 1h to coincide with the peak in blood glucose concentrations, but in the GA NIDDM group, there was no rise in serum insulin despite the greater blood glucose concentrations seen in that group. There was no significant difference in insulin concentrations between the two GA groups. In both LA groups, insulin concentrations increased markedly postoperatively when the patients ate, by 16.8 mU/litre ($p<0.01$) at 4h in the LA NIDDM group, and by 30.2 mU/litre ($p<0.01$) at 2h in the LA control group. Thus, there was a significant difference in the response between the GA and LA groups at 2 and 4h postoperatively ($p<0.05$).

Blood Lactate (Table 8.2).

There was no significant difference in baseline blood lactate concentrations between the groups (GA and LA NIDDM – 0.98 mmol/litre, GA and LA control – 0.76 mmol/litre). In the LA controls, concentrations decreased by 0.20 mmol/litre at the end of surgery ($p<0.01$), before rising 2h postoperatively by 0.23 mmol/litre ($p<0.05$) when the patients ate. The LA NIDDM patients followed a similar pattern, with concentrations decreasing by 0.23 mmol/litre 1h postoperatively ($p<0.05$), but with no subsequent rise at 2 and 4h as in the control group, even though these patients also ate at this time. In the GA control group, concentrations gradually declined throughout the study period, reaching statistical significance ($p<0.05$) at 30, 60, and 240 min postoperatively, whereas in the GA NIDDM group, concentrations increased by 0.09 mmol/litre at the end of surgery, then decreased by 0.24 mmol/litre ($p<0.01$) 2h postoperatively. There were no significant differences between the groups.

Plasma Non–Esterified Fatty Acids (Table 8.2).

There was no significant difference in baseline plasma non–esterified fatty acids (NEFA) concentrations between the groups (GA and LA NIDDM – 0.88 mmol/litre, GA and LA controls – 1.05 mmol/litre). In all groups, concentrations fell gradually throughout the study, with a sudden decrease in the LA control group of 0.8 mmol/litre ($p<0.01$) at 4h postoperatively when the patients ate. The other three groups also had concentrations which decreased, although less markedly, by 0.22 mmol/litre ($p<0.01$) in the GA NIDDM group, 0.41 mmol/litre ($p<0.05$) in the LA NIDDM group, and 0.30 mmol/litre ($p<0.05$) in the GA controls after 4h. There was a significant difference between the LA control group and the other three groups ($p<0.05$) at 2h, and between the LA control group and both GA groups ($p<0.05$) at 4h postoperatively.

Plasma Beta-Hydroxybutyrate (Table 8.2).

Baseline values for plasma beta-hydroxybutyrate (bOH) were GA and LA NIDDM - 43 μmol/litre, GA and LA controls - 54 μmol/litre. Concentrations varied little in all four groups during the study, until declining postoperatively in LA control patients when they ate, from 69 μmol/litre to 8 μmol/litre at 2h.

Serum Growth Hormone.

There was little change in growth hormone concentrations, with the majority of values falling below the concentration measurable with the assay technique. (<1.0 mU/litre)

Discussion

The results of Study 5 show that NIDDM patients undergoing cataract surgery under general anaesthesia have a marked cortisol and glucose response to surgery which is prevented by performing the surgery under local anaesthesia, in the same way as it is in non-diabetic patients. The previous chapters have demonstrated the extent of the metabolic and hormonal response to cataract surgery in non-diabetic subjects when this is performed under GA, and shown how this is completely abolished by performing the surgery under LA, whether by retrobulbar or peribulbar blockade. This is now shown to occur in NIDDM patients.

Non-insulin dependent diabetes mellitus affects 5-7% of the population (Yki-Jarvinen, 1994) and 10% of those over 70 years (Williams, 1994). It is a common problem in patients needing cataract surgery, 16% of whom, in one study, had diabetes (Fisher and Cunningham, 1985). It is characterised by impaired β cell function and is associated with insulin resistance (Yki–Jarvinen, 1994), but is not usually associated with ketoacidosis (Milaskiewicz and Hall, 1992), and normal circulating beta–hydroxybutyrate values were found in this study.

A diagnosis of diabetes is considered when the fasting blood glucose concentration is more than 7.0 mmol/l (WHO criteria). It can be seen that the fasting glucose values in our diabetic patients were relatively low, indicating adequate treatment. Many of them had only a mild form of NIDDM, since 8 out of 20 NIDDM patients were on diet alone. Ten out of 20 were taking the long–acting oral hypoglycaemic agents, chlorpropamide and glibenclamide. These agents are known to have a prolonged action; chlorpropamide because it is cleared slowly and excreted unchanged, and glibenclamide because it accumulates in the β cells and its metabolites retain hypoglycaemic activity (Williams, 1994). Although the patients had not taken their morning medication, the effects of agents taken the previous night might account for the relatively low glucose values. These low values are likely to be beneficial to patients. One study of diabetic patients having coronary artery bypass surgery, found the preoperative blood glucose concentration to be an important predictor of late mortality (Lawrie, Morris and Glaeser, 1986).

The acceptable upper limit of fasting blood glucose concentration recommended in NIDDM patients on treatment is 7.8 mmol/l (Williams, 1994). Wound healing is impaired and infection more likely with higher glucose concentrations. In experimental animals, concentrations above 13.7 mmol/l have been shown to impair granulocyte phagocytosis, granulocyte chemotaxis, granulocyte killing of bacteria, granulocyte adherence, synthesis of proto–collagen and collagen, capillary ingrowth and fibroblast proliferation (Milaskiewicz and Hall, 1992). Recent work in insulin dependent diabetic patients has shown the importance of maintaining normal glucose concentrations in preventing diabetic complications (Diabetes Control and Complications Trial Research Group, 1993). The importance of good glycaemic control in NIDDM patients is one of the issues currently being examined by the UK Prospective Diabetes Study Group (1991), which is looking at 5000 NIDDM patients and is due to report in 1996.

Serum cortisol concentrations in the diabetic patients in this study also showed a similar pattern of response to those in the non diabetic patients (Figure 8.1 and see previous chapters). Under GA, serum cortisol concentrations in the diabetic patients increased nearly twofold by 30 min postoperatively, before decreasing to baseline values by 4h. In both LA groups, whether diabetic or not, concentrations remained relatively constant. Blood samples were taken for 4h after operation as pilot studies had indicated that the hormonal response to cataract surgery was complete by this time. Baseline cortisol concentrations were higher in the diabetic patients than in the control patients, and although remaining relatively constant in the LA patients, were always greater in the diabetic than the non diabetic patients throughout the study. Some investigators have found hypercortisolism and elevated plasma ACTH levels in diabetic subjects (Cameron et al, 1987), whereas others have failed to demonstrate any alterations of the hypothalamic–pituitary–adrenal (HPA) axis in these patients (Asfeldt, 1972). It has been suggested that increased ACTH and cortisol values correlate positively with the duration of diabetes (Roy, Collier and Roy, 1990) and degree of retinopathy (Vermes et al, 1985; Roy, Collier and Roy, 1990), but not everyone has been able to show this association. However, it has been shown that there is a link between the activity of the HPA axis and diabetic polyneuropathy, which is almost invariably associated with autonomic nervous dysfunction (Tsigos, Young and White, 1993). It may be that central, as well as peripheral, catecholaminergic pathways are affected in long-term diabetes. Although this study demonstrates elevated baseline cortisol concentrations in the diabetic patients, they showed no signs of peripheral neuropathy nor obvious autonomic dysfunction, but these were not examined specifically.

Insulin concentrations remained fairly constant during surgery in all groups, even though blood glucose concentrations were elevated in the GA patients. One hour post surgery in the GA control patients, however, insulin concentrations increased in response to the hyperglycaemia. There was no insulin response to the raised glucose values in the GA diabetic patients, either intra– or post–operatively, even though their glucose concentrations were greater than the control patients and remained so for a longer time. In the LA control patients, insulin concentrations increased markedly when they ate; the response to eating in the diabetic LA patients was less marked but still present. The relative lack of insulin response to either hyperglycaemia during surgery or food intake in the diabetic patients can be explained by the β cell dysfunction characteristic of these patients (Hall, 1985).

There was little difference between the groups in lactate, non-esterified fatty acids and beta-hydroxybutyrate concentrations until the LA control patients ate, when their lactate concentrations increased, and their NEFA and beta-hydroxybutyrate concentrations fell. This occurred to a much lesser extent in the LA NIDDM patients. Glucose utilisation is associated with lactate production, while raised glucose values stimulate secretion of insulin, which inhibits lipolysis. Concentrations of beta-hydroxybutyrate decline when lipolysis is inhibited. These effects were all less pronounced in NIDDM patients due to the lack of insulin and resistance to its effects, thereby decreasing glucose utilisation and maintaining lipolysis.

In conclusion, the combination of preoperative and postoperative starvation, metabolic and endocrine responses to surgery under GA, and the aberrant metabolic responses of the diabetic patient leads to poor diabetic control. This study demonstrates that, by performing surgery under LA, the problem of the metabolic and endocrine response to surgery is prevented as is the necessity for postoperative starvation. These patients were starved preoperatively and did not receive their hypoglycaemic medication on the morning of surgery to standardise the LA and GA groups. It may be that there is no need to stop their normal medication or starve the patients for LA, as long as it is recognised there can be no conversion to GA or sedation used during the procedure, but this requires further investigation. However, even with preoperative starvation, early postoperative feeding means that the use of LA can provide minimal interruption of the normal daily routine of meals and treatment for the NIDDM patient, thus maintaining their metabolic stability.

Table 8.1. *Details of patients studied. Mean values (SEM), (ranges for age).*

	Group 1 GA – NIDDM (n=10)	Group 2 LA – NIDDM (n=10)	Group 3 GA – control (n=10)	Group 4 LA – control (n=9)
Age (years)	76 (47–87)	81 (72–87)	77 (69–88)	82 (71–91)
Weight (kg)	71 (5.3)	68 (2.4)	67 (3.8)	64 (5.9)
Sex	4M:6F	3M:7F	1M:9F	4M:5F
Induction time (min)	13 (0.9)	16 (1.5)	18 (1.6)	16 (1.9)
Duration of surgery (min)	31 (2.7)	26 (1.2)	24 (1.7)	30 (2.9)
Start of induction to arrival in recovery (min)	52 (2.5)	47 (1.7)	53 (2.5)	49 (4.2)
Oral hypoglycaemic drugs				
Glib	4	2		
Glib + Met	–	2		
Chlorpropamide	2	–		
Tolbutamide	1	–		
Metformin	–	1		
Diet alone	3	5		

	Baseline	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	Sample 7		
		After induction	Nuclear extraction	End of surgery	30 min	60 min	120 min	240 min	Differences between groups	
					post - operatively					
Lactate (mmol/l)										
GA control	0.81 (0.06)	−0.13 (0.06)	−0.07 (0.07)	−0.14 (0.08)	−0.21 (0.07)*	−0.24 (0.08)*	−0.10 (0.12)	−0.20 (0.06)*		
GA NIDDM	0.87 (0.13)	+0.03 (0.05)	+0.06 (0.07)	+0.09 (0.07)	−0.11 (0.08)	−0.22 (0.06)	−0.24 (0.08)**	−0.15 (0.11)	ns	
LA control	0.71 (0.09)	+0.01 (0.04)	−0.10 (0.07)	−0.20 (0.05)**	−0.16 (0.06)	−0.02 (0.09)	+0.23 (0.12)*	+0.08 (0.11)		
LA NIDDM	1.09 (0.16)	−0.01 (0.06)	−0.15 (0.07)	−0.05 (0.07)	−0.23 (0.07)	−0.23 (0.09)*	−0.22 (0.18)	−0.14 (0.11)		
NEFA (mmol/l)										
GA control	1.01 (0.10)	−0.13 (0.06)	−0.12 (0.10)	−0.07 (0.12)	−0.09 (0.15)	−0.04 (0.14)	−0.23 (0.11)	−0.30 (0.13)*	p<0.05	p<0.05
GA NIDDM	1.04 (0.07)	+0.01 (0.07)	−0.08 (0.09)	−0.12 (0.12)	−0.15 (0.09)	−0.15 (0.08)	−0.18 (0.11)	−0.22 (0.06)**	sample 6	sample 7
LA control	0.99 (0.17)	−0.10 (0.07)	−0.01 (0.09)	−0.08 (0.09)	−0.21 (0.13)	−0.14 (0.20)	−0.70 (0.17)	−0.80 (0.20)**	LAcontrol/	LAcontrol/
LA NIDDM	0.69 (0.17)	−0.12 (0.07)	−0.11 (0.07)	−0.08 (0.07)	−0.13 (0.11)	−0.04 (0.15)	−0.08 (0.20)	−0.41 (0.18)*	other groups	GA groups
bOH (umol/l)										
GA control	42 (11)	+24 (7)	+28 (10)	+40 (12)	+19 (12)	+38 (14)	+12 (10)			
GA NIDDM	45 (11)	+15 (6)	+14 (5)	+6 (8)	+15 (17)	+37 (25)	+36 (19)		ns	
LA control	69 (14)	+10 (9)	+23 (14)	+34 (15)	+28 (17)	−10 (14)	−61 (20)			
LA NIDDM	41 (11)	+1 (5)	+1 (5)	+3 (5)	+5 (13)	+22 (20)	+2 (18)			

Table 8.2 *Mean (SEM) difference from baseline of blood concentrations of lactate and beta hydroxybutyrate (bOH), and plasma concentrations of non−esterified fatty acid (NEFA). Significant difference from control: * = p<0.05, ** = p<0.01, ns = not significant. (Insufficient data obtained for analysis of bOH from sample 7).*

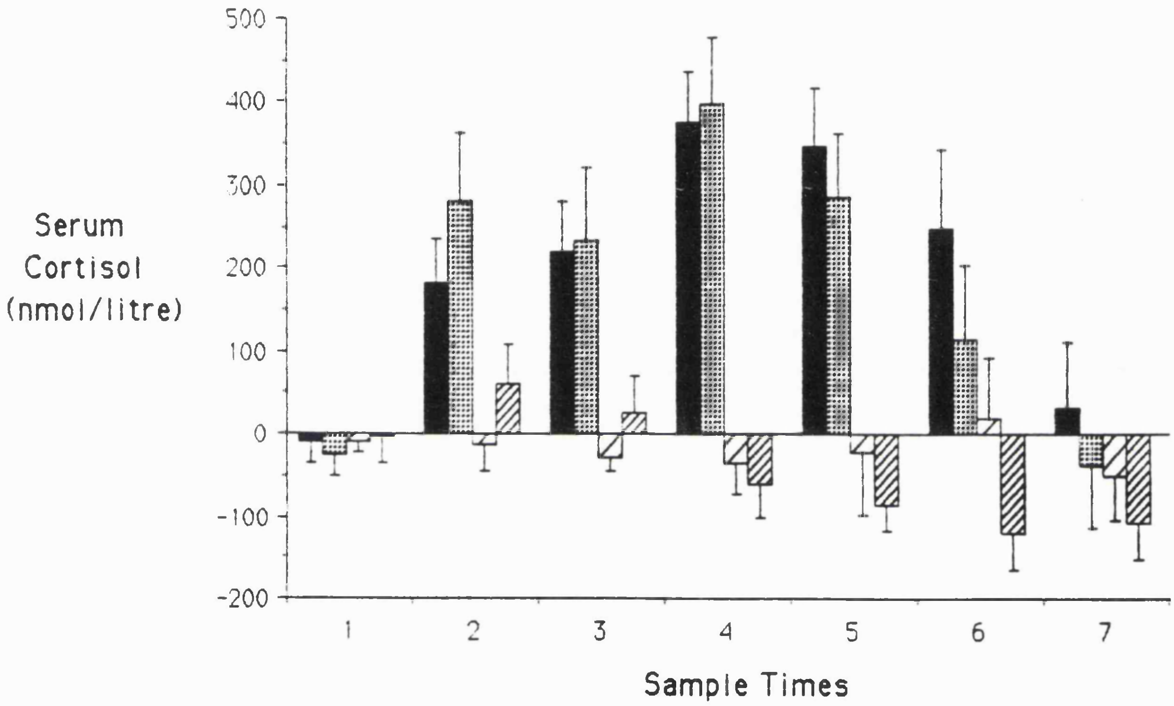


Fig 8.1. *Serum cortisol concentration (nmol/litre). Mean (SEM) difference from baseline in the GA control group (solid bars), GA NIDDM group (stippled bars), LA control group (broad hatched bars), and LA NIDDM group (narrow hatched bars).*

Sample 1 = after induction of anaesthesia; 2 = nuclear extraction; 3 = end of surgery; 4, 5, 6, 7 = 30, 60, 120 and 240 min after completion of surgery, respectively.

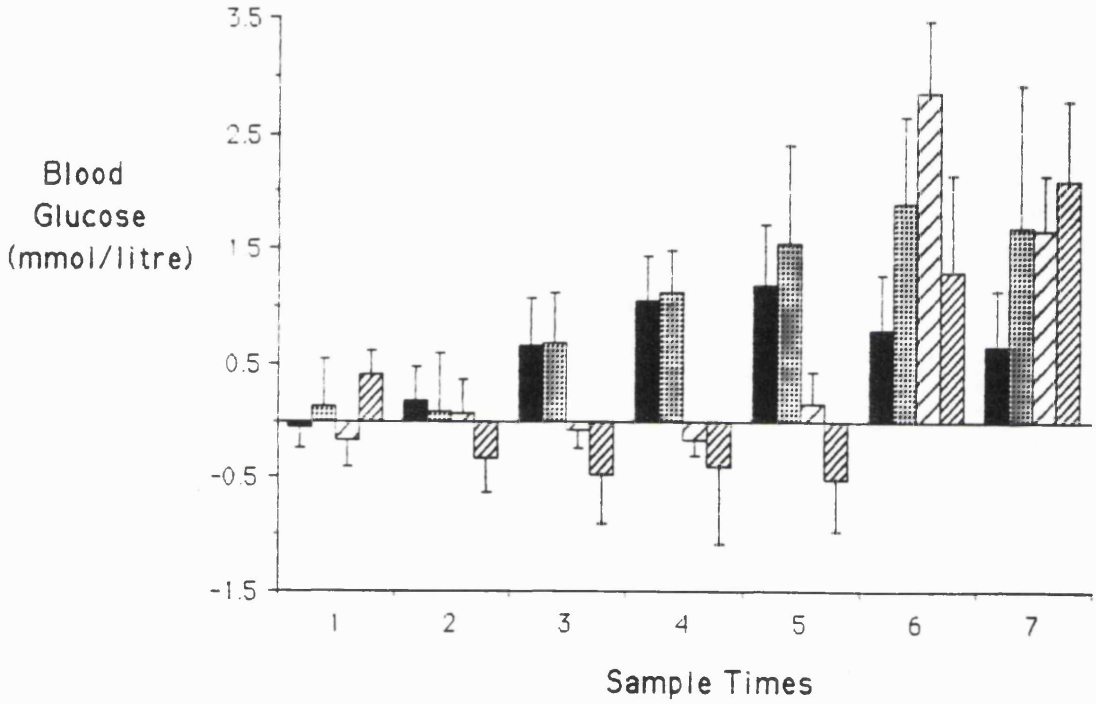


Fig 8.2. *Blood glucose concentration (mmol/litre). Mean (SEM) difference from baseline in the GA control group (solid bars), GA NIDDM group (stippled bars), LA control group (broad hatched bars), and LA NIDDM group (narrow hatched bars).*

Sample 1 = after induction of anaesthesia; 2 = nuclear extraction; 3 = end of surgery; 4, 5, 6, 7 = 30, 60, 120 and 240 min after completion of surgery, respectively.

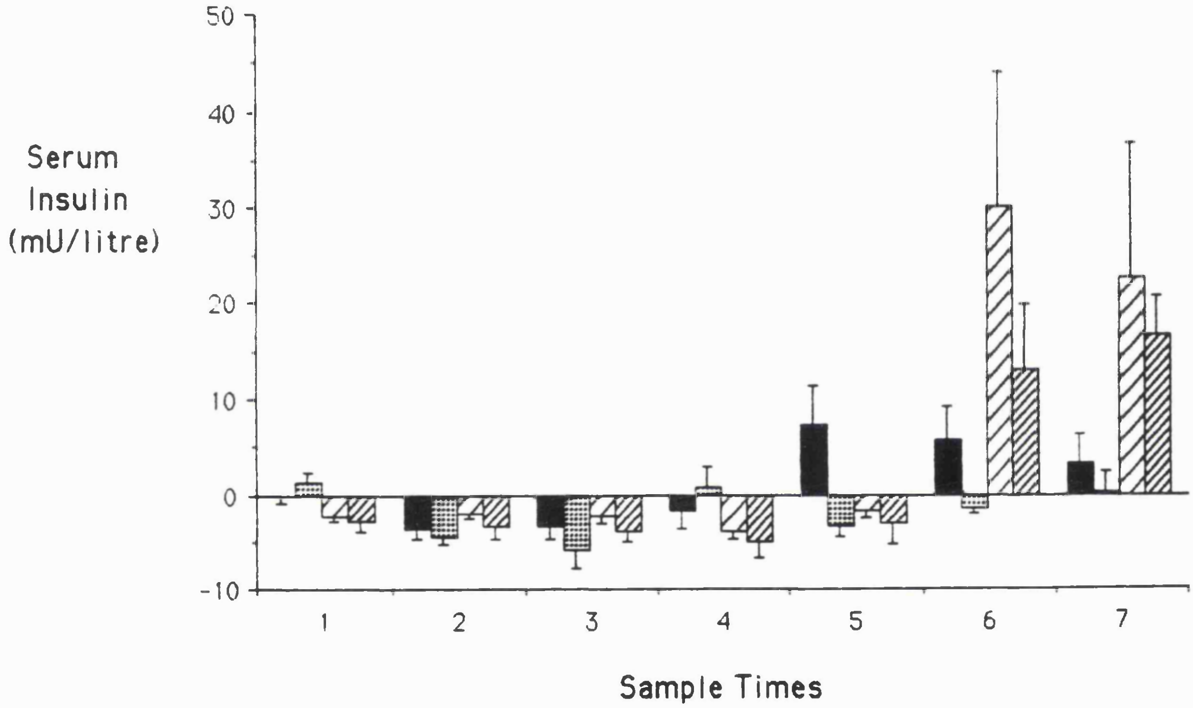


Fig 8.3. *Serum insulin concentration (mU/litre). Mean (SEM) difference from baseline in the GA control group (solid bars), GA NIDDM group (stippled bars), LA control group (broad hatched bars), and LA NIDDM group (narrow hatched bars).*

Sample 1 = after induction of anaesthesia; 2 = nuclear extraction; 3 = end of surgery; 4, 5, 6, 7 = 30, 60, 120 and 240 min after completion of surgery, respectively.

Chapter Nine

The investigation of postoperative morbidity following cataract surgery under either general or local anaesthesia.

Introduction

The previous chapters have shown that local anaesthesia (LA) for cataract surgery, using either retrobulbar or peribulbar blockade, prevents the metabolic and hormonal changes that occur when surgery is performed under general anaesthesia (GA), and provides better cardiovascular stability. The stability conferred may be beneficial in the elderly patients who frequently undergo this type of surgery. However, it is also important to the patient how they feel after their operation, and a questionnaire was devised to enquire about pain, nausea, vomiting and other common postoperative symptoms to see if either LA or GA conferred a benefit.

Study 6

Methods

Two hundred and thirty one patients undergoing cataract surgery were investigated. They were all operated on by one surgeon, and received either LA, using retrobulbar or peribulbar blockade, or GA. None of the patients were premedicated. The techniques used for retrobulbar and peribulbar blockade, and for general anaesthesia have been described in Chapter Four. No analgesics were given intraoperatively. Analgesics, either oral paracetamol or intramuscular pethidine, were available postoperatively if required. Next morning, before discharge, the patients were questioned by the nursing staff about postoperative sequelae, using the questionnaire shown on page 120.

The forms were collected and the difference between the groups analyzed using the chi-squared test.

Results

Of the 231 patients questioned, 119 received LA, and 112 received GA. There were no significant differences between the groups with respect to age and weight, although there were more females than males in both groups (Table 9.1). The results are shown in Table 9.2. There was no significant difference in the incidence of vomiting, headache or double vision between the two groups. 21% of the GA group had nausea as opposed to only 3% of the LA group ($p<0.01$), and 41% of the GA group complained of a sore throat compared with 3% in the LA group ($p<0.01$). Bruising of the eye occurred in 15% of the GA group, and 39% of the LA group ($p<0.01$).

The incidence of pain in the two groups was very similar, slightly more of the LA group experiencing severe pain in the eye postoperatively than the GA group (12% vs 8%, not significant (ns)). Similar proportions of patients in each group experienced mild pain (53% LA and 58% GA, ns) and no pain (35% LA, 34% GA, ns). All pain was controlled with oral analgesics.

The time from surgery to drinking and eating was markedly shorter in the LA group (1.3h and 1.8h respectively) than in the GA group (4.1h and 6.7h, $p<0.01$). While 45% of patients in the LA group considered they would have been able to go home on the day of surgery, 34% of the GA patients also felt this would have been possible (ns). The majority of patients in both groups would be prepared to repeat the same technique for a further eye operation (80% LA; 86% GA); however, 20% (24) would prefer not to have LA again, and 14% (16) would prefer not to have a GA. Thirteen LA patients and nine GA patients gave no reason for preferring to change their form of anaesthesia. Of those who did not want a GA again, four said it was because of the "after effects" of the anaesthetic; either it was non-specifically "unpleasant", or because of sickness. One patient thought that LA would have been "quicker", one patient said that they "did not like lying flat", and one patient said it was painful. Of those who did not want a repeat LA, four disliked the injection, one because it made her "tremble", the rest because it was painful; five found the operation painful. Two patients said they would just prefer to be asleep.

Discussion

Many patients currently undergo lens extraction under local anaesthesia, increasingly on a day stay basis. The previous studies have shown some advantages of LA, as regards metabolic, hormonal and cardiovascular stability, but it is important to find out if our practice is acceptable to the patients. Some patients express apprehension at the thought of being awake for their operation, but 80% of the LA group found this technique acceptable and would be prepared to have the same form of anaesthesia again. General anaesthesia tends to be given to those who specifically request this form of anaesthesia and this study found that 86% of the GA group would be happy to repeat this technique at a subsequent operation.

Retrobulbar injections, especially when combined with a facial block, can be painful; four patients in the LA group complained of this. Peribulbar injections are generally less so, and can be made almost painless by the use of a careful technique involving the use of local anaesthetic solutions at body temperature, diluted with balanced salt solution, and very fine 25 – 30 gauge needles (Bloom, Scheie and Yanoff, 1984; Korbon, Hurley and Williams, 1987). These techniques were not all in general use in the hospital at the time of this study. The use of such manoeuvres, combined with full explanations, can go a long way to reassure the patients and improve the acceptance of LA.

Some of the findings of the questionnaire were predictable. The incidence of nausea was greater in those receiving GA, and vomiting was also more common, although, fortunately, the incidence was low. This may have been because opioids were not used peroperatively. Sore throat occurred more frequently in the GA group as all these patients were intubated. The use of laryngeal masks, which is becoming increasingly popular, may help to reduce this problem. The incidence of headache was slightly increased in the GA group, which might be explained by the longer starvation time in these patients. Bruising of the eye was more common after the local anaesthetic injection.

Several interesting points arose from the questionnaire. The first is the incidence of postoperative pain. This was found to be similar in the two groups; an unexpected finding since one would expect the LA group to be fully pain-free on the completion of surgery, while the GA group had no intraoperative analgesics. Indeed a third of the patients had no pain at all. A little over half of all the patients suffered mild pain, although only a third took oral analgesics. A surprising finding was that there was slightly more pain rated as severe in the LA group. It could be that discomfort or pain occurred as the LA wore off, or that the bruising, which was more common after LA, was the cause of the increased pain. There was certainly no evidence from this study that the use of LA as a form of preemptive analgesia conferred any benefit over GA without analgesia.

Another question we asked concerned the acceptability of day surgery. At the time of this study most patients having cataract surgery were treated as inpatients. At present, a significant proportion have their surgery in the Day

Surgery Unit under LA. If patients are suitable medically and socially and agree to have LA and go home the same day, they are treated as day patients. Those that have inadequate social circumstances, such as a suitable escort, or prefer GA, are admitted for surgery. Our results show that 45% of the LA patients felt able to go home on the same day as their operation. No account was made of whether these patients met the Day Unit criteria for discharge; it was the patient's opinion, knowing what was entailed in their operation. A larger proportion may be encouraged to take up this option in the future, even though our data suggest that 55% of the patients were glad of the facility to stay in the hospital overnight. However, 34% of the GA patients also felt able to have gone home the same day. In most previous reports on day case cataract surgery, LA has been used exclusively (Lowe et al, 1992; Chell, Shah and Fielder, 1994). Nevertheless, modern general anaesthesia enables most patients, including the elderly, to be fully ambulant on the day of surgery, and recent papers describe the successful use of GA for cataract surgery in the Day Surgery Unit (Strong et al, 1992; Moffat and Cullen, 1995). Provided that the patient's medical condition is stable and they have suitable home circumstances, the results of this study suggest that cataract surgery under GA in the Day Unit is acceptable to some patients, even though this is an elderly population.

The patients in the LA group were drinking and eating within two hours of their operations; indeed some were eating their lunch within minutes of arriving back on the ward. It took several hours before the GA patients were able to do this. Thus LA proved less disruptive to patients' routine, which is especially beneficial in the case of the diabetic patient (see Chapter Eight).

In conclusion, the results of our questionnaire suggest that, although a patient having LA is more likely to get bruising around their eye, they are less likely to experience nausea and sore throat and will return to eating and drinking far sooner following their surgery, than if they were to receive a GA.

Table 9.1 *Details of patients studied in Study 6 (mean values (SEM)).*

	LA group n=119	GA group n=112
Age; years	80 (2.1)	75 (3.4)
Weight; kg	63 (1.6)	66 (2.0)
Sex	37M : 82F	31M : 81F

Table 9.2. *Incidence of postoperative complications. Significant difference between groups shown by ** p<0.01, otherwise differences were not significant.*

	LA n=119	GA n=112
Nausea	4 (3%) **	23 (21%)
Vomiting	2 (2%)	7 (6%)
Headache	35 (29%)	38 (34%)
Sore throat	3 (3%) **	46 (41%)
Double vision	8 (7%)	8 (7%)
Bruising of eye	46 (39%) **	17 (15%)
Pain – Severe	14 (12%)	9 (8%)
Mild	63 (53%)	65 (58%)
None	42 (35%)	38 (34%)
Required oral analgesics	33 (28%)	30 (27%)
Time to drink (h) mean(SD)	1.3 (1.3) **	4.1 (2.2)
Time to eat (h) mean(SD)	1.8 (1.8) **	6.7 (3.5)
Able to have gone home same day	54 (45%)	38 (34%)
Prepared to have same technique again	95 (80%)	96 (86%)

Name............................	Date..............................
LA/GA	Time of operation.................
Sex:	Recovery...........................

QUESTIONNAIRE

At any time after your operation yesterday –

Did you feel sick?	YES/NO
Did you vomit?	YES/NO
Did you have pain in your eye?	Severe/ Slight/ No pain
Did you have a headache?	YES/NO
Did you have a sore throat?	YES/NO
Did you have any double vision?	YES/NO
Did you need to take any pain killers	
yesterday?	YES/NO
today?	YES/NO
Do you now have bruising round your eye?	YES/NO
When did you first drink after your operation?	Time......................
When did you first eat after your operation?	Time......................
If it had been practical, would you have been happy to go home last night?	YES/NO
Would you have the same form of anaesthetic again?	YES/NO

If NO, why not?..

Would you rather try the other technique for a future operation?	YES/NO
Have you had the other eye operated on?	YES/NO GA or LA

COMMENTS:

Chapter Ten

Discussion

The studies that comprise this thesis have demonstrated the extent of the metabolic and hormonal responses to cataract surgery when this is performed under general anaesthesia (GA), and have shown how these responses are prevented when the surgery is performed under local anaesthesia (LA), whether by retrobulbar or peribulbar blockade. Study 2 demonstrated the cardiovascular stability associated with LA. Study 3 demonstrated that the changes occurred in response to the surgery, as opposed to general anaesthesia itself, although there were changes in plasma cortisol concentrations seen on waking from anaesthesia. Study 5 demonstrated that LA prevented the metabolic and hormonal alterations associated with cataract surgery in those patients with non–insulin dependent diabetes (NIDDM) in the same way as with the non diabetic patient. Finally, Study 6 showed the patients' acceptance of LA and the reduction in postoperative morbidity with this technique.

The changes associated with the stress response to surgery were detailed in Chapters Two and Three, and this thesis investigated these during cataract surgery. However, it is valid to ask whether these changes are a necessary phenomenon which are beneficial to the patient, or whether they are detrimental and better prevented.

It is thought that the hormonal response to trauma evolved to protect the injured animal in a primitive environment in which they may be unable to find adequate food and water. Thus sodium and water is conserved and substrate mobilisation is initiated in preparation for reparation of the tissues. However, during elective surgery, physiological homeostasis is maintained and it can be argued that there is no need for these changes. Kehlet (1982) has suggested that it may be beneficial to decrease the endocrine and metabolic response to surgery.

Studies of clinical outcome are needed to determine whether the stress response is beneficial or detrimental. Yeager and colleagues (1987) conducted a randomised trial of patients undergoing major surgery using either epidural anaesthesia with the neural blockade maintained for 8–79h (mean 31h) postoperatively, or fentanyl anaesthesia with parenteral narcotics postoperatively. Urinary cortisol secretion was significantly less in the epidural group in the first 24h postoperatively. These patients also had a significantly reduced overall complication rate, which included a decreased incidence of cardiovascular failure and major infections; hospital costs were significantly less in the epidural group. There were methodological problems with this study. The number of patients studied was small, and some aspects of the perioperative management of the patients were inadequately controlled. Firm conclusions cannot be made.

Scott and Kehlet (1988) also found beneficial effects of regional anaesthesia on postoperative morbidity, but only after conducting a meta–analysis of many studies. They looked at mortality after hip surgery; and at pulmonary and vascular complications, infections, blood loss, cerebral function and the incidence of deep venous thrombosis after various forms of major surgery. They concluded that morbidity decreased for operations below the umbilicus performed under regional anaesthesia, which could be associated with the reduced stress response with this technique. However, this improvement was not statistically significant. The only statistically significant findings were in the reduction of blood loss and the decreased incidence of deep venous thrombosis in hip and pelvic surgery. There was less evidence for a reduction in morbidity in upper abdominal and thoracic operations in which regional anaesthesia has little influence on the stress response.

Anand, Sipell and Aynsley-Green (1987) studied two different anaesthetic techniques in neonates undergoing surgery for patent ductus arteriosus repair. They found that fentanyl 15μg/kg prevented the increase in blood glucose and plasma adrenaline concentrations seen in neonates who were not given fentanyl, and clinical outcome was said to be improved.

An intact inflammatory response to injury is probably needed to aid healing as shown by attempts to suppress interleukin-6 production with high dose steroids (Schulze et al, 1992). This was associated with impaired wound healing. However, immunoendocrine reactions to stress may contribute to the development of postoperative immunosuppression. Rem, Brandt and Kehlet (1980) have shown that surgery is associated with lymphopenia and granulocytosis, which is prevented by epidural anaesthesia. They suggested that inhibiting the endocrine and metabolic response to surgery may prevent postoperative immunosuppression.

Thus, there are some studies which give limited support to the idea that the stress response is detrimental in the healthy patient undergoing routine surgery. This may not apply to the critically ill patient. When etomidate was used for sedation in critically ill patients, there was an increased mortality secondary to cortisol suppression (Ledingham and Watt, 1983). However, Lacoumenta and colleagues (1986) found no deleterious effects when etomidate infusions were used in healthy patients during routine surgery, despite the decrease in plasma cortisol which reached a nadir of 127 nmol/litre after two hours of surgery.

Further studies are needed to more fully elucidate the influence of the stress response on clinical outcome.

The general anaesthetic technique chosen for the patients in this thesis was in common use when the studies began. Premedication and opiate analgesics were avoided, as in pilot studies they were found to be unnecessary, and the technique needed to be standardised. General anaesthesia has progressed, such that laryngeal masks are now in common use. Future studies should look at the endocrine and metabolic changes associated with cataract surgery under GA with the patient breathing spontaneously on a laryngeal mask. The changes may be similar to those of the intubated and ventilated patient, but theatre times may be shortened, since there is no need to reverse neuromuscular blockade. It would be interesting to determine if the changes in plasma cortisol concentration immediately postoperatively in those patients receiving combined GA and LA were less with a GA involving a laryngeal mask and spontaneous respiration.

Future studies should also be directed at the effects of other anaesthetic agents during GA. Mivacurium, as an alternative to vecuronium, removes the need to use neostigmine at the end of surgery. Opiate analgesics could be given intraoperatively, although the available evidence suggests that doses compatible with cardiovascular stability and the ability to breathe postoperatively do not change the metabolic and hormonal response to surgery. Certainly the patients in these studies did not wake in pain, even though they had not received analgesics.

The effects of premedication should be examined, as might the effects of obtunding the pressor response to intubation. However, there was no indication from these studies of any change in the metabolic and hormonal response with intubation.

One important variable that was not measured during these studies was the interleukin–6 (IL–6) response to cataract surgery. Evidence from the studies in the thesis suggests that changes in IL–6 would be small, as the trauma to the tissues is slight. However, this supposition needs to be substantiated.

Other local anaesthetic techniques, as discussed in Chapter One, are also used for cataract surgery. It would be useful to determine how effective they are in obtunding the hormonal and metabolic changes caused by the surgery.

In conclusion, this thesis has demonstrated the benefits of local anaesthesia for cataract surgery in the elderly patient. Both retrobulbar and peribulbar blockade prevent the hormonal and metabolic changes associated with cataract surgery under general anaesthesia, and maintain cardiovascular stability. The importance of this in the non–insulin dependent diabetic patient is demonstrated and ideas for future research are discussed.

Chapter Eleven

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