Online Brief Report: Self-reported fatigue in children following intensive care treatment

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The study took place at Great Ormond Street Hospital for Children, London UK

Reprints are not required

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Abstract

Objectives: Adults report high levels of fatigue after intensive care, but little is known about pediatric survivors. This study aimed to explore rates of self-reported fatigue in children after critical illness.

Design and Setting: Prospective cohort study carried out at a tertiary hospital.

Patients: Ninety-seven children aged 7y to 17y.

Measurements and Main Results: Children completed the PedsQL Multidimensional Fatigue Scale three months after discharge from PICU. Comparisons with normative data (n=209) showed that PICU survivors reported similar mean (SD) total fatigue scores to their healthy peers (79.6 (16.3) v 81.8 (12.5), p=0.239), but greater cognitive fatigue (77.4 (21.9) v 82.4 (16.4), p=0.048). Also children who had sustained a traumatic brain injury reported *less* sleep/rest fatigue (84.6 (15.0) v 76.8 (16.3), p=0.006) Baseline indices of severity of illness were not associated with fatigue.

Conclusions: The PedsQL Multidimensional Fatigue Scale appears to be a promising tool for use in outcomes research with PICU survivors. These results highlight the need to bear in mind the heterogeneity of PICU patients and the multidimensional nature of fatigue symptoms.

Fatigue is often reported by adult ICU survivors. Griffiths and Jones (2007) report that muscle wasting and fatigue are major issues in their adult ICU follow up clinics (1) and others describe reduced exercise tolerance and chronic fatigue in this population, for many months after discharge (2-4). Less is known about fatigue in children after intensive care treatment, although significant sleep problems have been observed (5) and fatigue has been identified as an area on which more data are required (6).

This study aimed to examine the extent of fatigue in PICU survivors, using a promising self-report measure, the PedsQL Multidimensional Fatigue Scale (7). It was hypothesised that Pediatric Intensive Care Unit (PICU) survivors would report higher levels of fatigue than healthy controls and that children who had been admitted for traumatic brain injury (TBI) would report higher cognitive fatigue (8).

METHOD

Design: This was a prospective cohort study, nested within another study which examined children's self-reported quality of life following critical illness (9). Ethical permission was granted by the hospital Ethics Committee (Ref: 03AR12). Parents and children were provided with age-appropriate research information sheets, and written informed consent was obtained.

Sample/Procedure: Families of surviving children aged over 7 years, admitted consecutively for >= 24 hours to a 21-bed ICU in a tertiary Children's Hospital over an 18-month period, were approached about the study by letter, 6 weeks after discharge from PICU. (Exclusion criteria were non-accidental injury; significant learning difficulties; readmission; palliative care; no registered General Practitioner.)

Demographic and medical data were obtained from the child's medical record. Illness severity was determined using the Paediatric Index of Mortality (PIM) score (10) and, for the TBI group, the Glasgow Coma Scale (GCS) (11).

Measures: The 18-item PedsQL Multidimensional Fatigue Scale (7) is made up of three separate 6-item subscales which measure 'general fatigue', 'sleep/rest fatigue' and 'cognitive fatigue'. Total and subscale Scores range from 0-100, with higher scores indicating better functioning, ie *lower* fatigue.

The scale was originally first described in 2002, has good reliability and validity and a factor structure demonstrated to be independent of gender or age (12). Until relatively recently data on healthy controls was limited, but norms for 209 healthy controls are now available as are comparative scores for children with a number of common conditions (13-17). There are versions for different age groups and for parents to complete if the child is not able. Participants also completed the generic PedsQL Quality of Life Inventory (18) for the main longitudinal study (9).

Statistical Analysis: Children's scores on the PedsQL Multidimensional Fatigue Scale were compared with norms using Student's t tests (19). Associations with baseline measures were examined using non-parametric Spearman correlations. Analyses were performed using the IBM Statistical Package for the Social Sciences (SPSS) version 25, using $p<0.05$ for statistical significance.

RESULTS

Median age of the sample was 11y (range 7-17y) and median length of stay was 2d (range 1-38d). The majority (n=90 (93%)) were ventilated. In relation to the TBI group (n=36), n=19 (53%) had sustained severe injury (GCS<=8); n=10 (28%) moderate injury (GCS 9-12) and n=7 (19%) mild injury (GCS >=13) (20). Fifteen children were admitted electively, mainly for spinal or transplant surgery, with the remainder (n=46) admitted for other emergency conditions. Further sample information is available elsewhere (9).

Psychometrics: In this sample, the PedsQL Multidimensional Fatigue Scale demonstrated acceptable reliability (Cronbach's $\alpha = 0.88$ for whole scale; 0.82 for general fatigue; 0.65 for sleep/rest fatigue and 0.87 for cognitive fatigue). The proportion of children scoring at the extremes of the scale of the scale (ceiling 6%; floor 0%) was also acceptable at <15%. Evidence of construct validity was provided by the positive correlation between total fatigue score and concurrent generic quality of life score ($r=0.48$, $p<0.001$). In terms of general feasibility the scale was straightforward to administer, taking under 5 minutes to complete with each child and the proportion of missing items was low (0.4%).

Comparisons with healthy controls (see Table 1): PICU survivors' total fatigue scores were similar to those of healthy children (n=209), but the proportion of the sample scoring >2SD below norms (indicative of severe fatigue (8)) was higher than would be expected at 9/97 (9%). Also although scores on the 'general fatigue' and 'sleep/rest fatigue' subscales were not significantly different to the norms, scores on the 'cognitive fatigue' subscale were significantly worse, both for the sample as a whole and for the 'other emergency group' in particular

The only other finding of note, related to the TBI group, was that they reported that they had less sleep/rest fatigue, ie they slept *better* than their healthy peers.

Associations with illness severity (see Table 2): None of the four baseline variables examined (PIM score; length of stay; days on opiates/benzodiazepines; GCS) were significantly associated with total fatigue score for the whole sample, but there was an association between higher PIM score and *lower* fatigue in the elective sub-group, suggesting greater improvements in functioning after intensive care treatment for the sicker children in this group.

DISCUSSION

The hypothesis that PICU survivors would report higher total fatigue than healthy children was not upheld. This is interesting given that their self-report ratings of general quality of life were significantly lower at three months than those of controls (9). It also contrasts with the adult ICU literature, and may indicate that, in general, children regain energy at a faster rate than adults after critical illness.

However the fact that nearly one in ten reported severe fatigue shows that this was not the case for all, and increased 'cognitive fatigue' was found in the sample, indicating that some PICU survivors may benefit from further assessment consistent with recent recommendations relating to pediatric Post Intensive Care Syndrome (PICS-p) (21)and the reports of neuropsychological deficits in particular groups of PICU survivors, such as those who have had sepsis (22) and those who have required extra corporeal membrane oxygenation therapy (23), who may benefit from additional support on return to school.

Cognitive fatigue was not however found to be a specific problem for the TBI group in this sample, as had been originally hypothesised. A recent study of 32 children who had sustained

mainly mild to moderate TBI (8), which used the same fatigue scale, reported above average fatigue, but these data were collected earlier, at six weeks post-injury. Further research could establish whether significant improvements in fatigue occur between six weeks and three months post-injury in this subset of patients.

The lack of association between objective indices of severity of illness and fatigue is consistent with the literature (8) and highlights the need for more information on the trajectories of recovery of children after critical illness. Finally, the finding that the sickest children who were admitted electively reported the lowest fatigue at follow up is a reminder that, although PICU treatment can be associated with poor long term outcomes for some, it is also be associated with significant improvements in health status and quality of life in others.

Limitations of the study include the fact that children were excluded if they had significant learning difficulties, whether these pre-dated admission or resulted from injury. This, together with the number of short stay patients who were admitted electively, may mean that this sample is not representative of the PICU population as a whole.

Nevertheless, in conclusion, these findings support the potential value of the PedsQL Multidimensional Fatigue Scale for use with children after critical care. It was straightforward to administer, demonstrated acceptable psychometric properties and discriminated between PICU survivors and healthy children. Furthermore, the results relating to cognitive fatigue in the 'other emergency' subgroup and sleep/rest fatigue in the TBI subgroup (which may reflect their need for extra sleep during recovery) illustrate the value of a *multidimensional* measure of fatigue.

In the context of the growing appreciation of the heterogeneity of long-term outcomes in this group (6, 24), this scale could prove useful in the characterization and monitoring of children's recovery after PICU.

REFERENCES

1. Griffiths RD, Jones C. Seven lessons from 20 years of follow-up of intensive care unit survivors. Curr Opin Crit Care 2007; 13:508–513

2. Steenbergen S, Rijkenberg S, Adonis T et al. Long-term treated intensive care patients outcomes: the one-year mortality rate, quality of life, health care use and long-term complications as reported by general practitioners. BMC Anesthesiol. 2015;15:142.

2. Chaboyer W, Grace J. Following the path of ICU survivors: a quality-improvement activity. Nurs Crit Care. 2003;8(4):149–155

3. Herridge MS, Cheung AM, Tansey CM et al. One-year outcomes in survivors of the acute respiratory distress syndrome. N Engl J Med. 2003 Feb 20;348(8):683-693

5. Als LC, Picouto MD, Hau SM et al:.Mental and physical well-being following admission to pediatric intensive care. Pediatr Crit Care Med 2015;16:e141-149

6. Watson RS, Choong K, Colville G et al: Life after Critical Illness in Children-Toward an Understanding of Pediatric Post-intensive Care Syndrome. J Pediatr. 2018; 198:16-24 doi: 10.1016/j.jpeds.2017.12.084

7. Varni JW, Burwinkle TM, Katz ER et al. The PedsQLin pediatric cancer: reliability and validity of the Pediatric Quality of Life Inventory Generic Core Scales, Multidimensional Fatigue Scale, and Cancer Module. Cancer. 2002;94:2090–2106

8. Crichton AJ, Babl F, Oakley E et al:.Prediction of multidimensional fatigue after childhood brain injury. J Head Trauma Rehabil 2017;32:107-16

9. Colville GA, Pierce CM. Children's self-reported quality of life after intensivel care treatment. Pediatr Crit Care Med 2013;14:e85-92

10. Pearson G, Stickley J, Shann F: Calibration of the paediatric index of mortality in UK paediatric intensive care units. Arch Dis Child2001; 84:125–128

11. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A Practical scale. Lancet 1974;2:81-84

12. Varni JW, Beaujean AA, Limbers CA. Factorial invariance of pediatric patient self-reported fatigue across age and gender: a multigroup confirmatory factor analysis approach utilizing the Peds QL Multidimensional Fatigue Scale Qual Life Res 2013; 22:2581-2594

13. Panepinto JA, Torres S, Bendo CB, et al. PedsQ multidimensional fatigue scale in sickle cell disease: feasibility, reliability, and valid-ity. Pediatr Blood Cancer. 2014;61(1):171–177

14. Varni JW, Burwinkle TM, Szer IS. The PedsQLMultidimensional Fatigue Scale in pediatric rheumatology: Reliability and validity.Journal of Rheumatology. 2004;31:2494–2500

15. Marcus SB, Strople JA, Neighbors K, et al. Fatigue and health-related quality of life in pediatric inflammatory bowel disease. Clinical Gastroenterology and Hepatology. 2009;7:554–561

16. Varni JW, Limbers CA, Bryant WP, et al. The PedsQLMultidimensional Fatigue Scale in Type 1 diabetes: Feasibility, reliability, and validity. Pediatric Diabetes. 2009;10:321–328

17. Varni JW, Limbers CA, Bryant WP, et al. The PedsQLMultidimensional Fatigue Scale in pediatric obesity: Feasibility, reliability, andvalidity. International Journal of Pediatric Obesity. 2010;5:34–42

18. Varni JW, Seid M, Kurtin PS. PedsQL 4.0: Reliability and validity of the Pediatric Quality of Life Inventory Version 4.0 Generic Core Scales in healthy and patient populations. Medical Care. 2001;39:800–812

19. Upton P, Eiser C, Cheung I, et al: Measurement properties of the UK-English version of the Pediatric Quality of Life Inventory 4.0 (PedsQL) generic core scales. Health Qual Life Outcomes 2005; 3:22

20. Anderson V, Catroppa C, Morse SA et al: Functional plasticity or vulnerablility after early brain injury? Pediatrics 2005;116:1374-1382

21. Manning JC, Pinto NP, Rennick JE et al. Conceptualizing Post Intensive Care Syndrome in Children-The PICS-p Framework. Pediatr Crit Care Med. 2018 Apr;19(4):298-300 doi: 10.1097/PCC.0000000000001476.

22. Als LC, Nadel S, Cooper M et al..Neuropsychologic function three to six months following admission to the PICU with meningoencephalitis, sepsis, and other disorders: a prospective study of school-aged children. Crit Care Med 2013;41:1094-
103.

23. Boyle K, Felling R, Yiu A et al. Neurologic Outcomes After Extracorporeal Membrane Oxygenation: A Systematic Review. Pediatr Crit Care Med. 2018;19:760-766. doi: 10.1097/PCC.0000000000001612.

24. Typpo K, Mendelson J. After the fairytale ending: functional impairment after pediatric critical illness. Pediatr Crit Care Med. 2016 May;17(5):473-474 doi:10.1097/PCC.0000000000000712.