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ORIGINAL CONTRIBUTION

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Abstract The objective of this study was to investigate, under circumstances of routine care, the impact of paediatric delirium (PD) on length of stay in the paediatric intensive care unit (PICU) as well as on direct financial costs. A five-year prospective observational study (2002–2007) was carried out in a tertiary eight-bed PICU in the Netherlands. Critically ill children aged 1 to 18 years who were acutely, non-electively and consecutively admitted to the PICU and detected as having PD in routine care were compared to critically ill children aged 1 to 18 years without signs of PD. PD, population characteristics and severity of illness at admission were used as predictors for length of PICU stay. Differences in length of stay yielded short-term, direct medical costs associated with PD. Forty-nine children with and 98 children without PD were included. PD prolonged length of PICU stay with 2.39 days, independent of severity of illness, age, gender, mechanical ventilation and medical indication for admission ($B = 0.38$, $P < 0.001$). PD increased direct medical costs with 1.5%. The results suggest a negative prognostic influence of PD on duration of PICU stay in routine care, resulting in an increase of direct medical costs.

Keywords Delirium · Children · Paediatric intensive care unit · Length of stay · Costs

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Introduction

Delirium in adults, a frequently observed complication among intensive care patients, predicts prolonged hospital stay and is associated with a higher risk of morbidity and mortality during, as well as after hospital admission [1–3, 11]. Comparatively, little work has been carried out in the area of paediatric delirium (PD). Two studies reported incidences of 4 and 5% of PD in critically ill children in a paediatric intensive care unit (PICU) [6, 9]. It is likely that these represent an underestimate, as case finding depended on referral for emotional and behavioural disturbances, as noticed during daily routine care. The true rate of PD is probably higher, given the fact that (i) the prevalence of delirium in adult intensive care units is much higher (up to 42% of the non-ventilated [11] and 82% of the ventilated patients [2]) and (ii) children are considered to be more susceptible to delirium [1]. Turkel and Tavaré suggested that delirium in children may prolong hospital stay and increase mortality [12]. However, their study was uncontrolled, making it difficult to interpret the findings. The aim of this study was to investigate, in critical illness and under

circumstances of routine care with regard to diagnosis and treatment, the impact of PD on length of stay in the PICU while correcting for other prognostic factors including severity of illness (scored according to the Paediatric Risk of Mortality II (PRISM II) [4]), age, gender, mechanical ventilation and medical indication for admission.

Materials and methods

Design, setting and patients

From January 2002 to February 2007, a prospective, descriptive study was carried out in critically ill children aged 1 to 18 years in a tertiary eight-bed PICU in the Netherlands. In case of (a) agitation, confusion, anxiety, discomfort or behavioural disturbance without acceptable medical explanation or (b) failure of standard analgosedative treatment, children were routinely referred by the attending paediatric intensivist for assessment for the presence of PD by the child neuropsychiatrist. Assessment consisted of (a) evaluation using DSM-IV criteria for delirium, applied by anamnestic information of the parents, nurses and medical team about the child's behaviour(al changes) and (b) by child psychiatric examination. This way the child was categorized as having (probable) PD or not. The final diagnosis was made in a consensus meeting between child psychiatrist and paediatric intensivist, in order to rule out alternative diagnoses [9]. Diagnostic instruments for delirium, developed for the adult population (e.g. DRS-R-98, CAM-ICU), are not used in routine care at our PICU because of the absence of validation in critically ill children. Children younger than the age of one were excluded in order to reduce misclassification: cognitive functions and social interaction skills which are necessary for psychiatric examination are insufficiently developed below that age [5]. Elective admissions of non-critically ill children (e.g. elective post-operative observation, elective IC-procedures and diagnostic monitoring) were also excluded. Both mechanically ventilated and non-ventilated patients were included. This selection procedure yielded a sample of 49 critically ill children with PD. In addition to these delirious children, 98 critically ill children were randomly selected as control group out of the total group of acute PICU admissions due to critical illness in the period January 2002 to February 2007 ($n = 743$). These children also met the inclusion criteria and had not been psychiatrically examined because of the absence of psychiatric symptoms, behavioural disturbance and/or complicated analgosedation; for these reasons, they were considered as being non-delirious. Results were obtained during a quality of care improvement program regarding the assessment, diagnosis and treatment of emotional behavioural disturbances in critically ill children at the PICU, and all parents assented to clinical procedures as required under Dutch law, which stipulates that under these circumstances no institutional review board approval is required.

Statistical analysis

Data concerning population characteristics (e.g. age and sex, given the fact that younger children and males are more susceptible to delirium [1]), severity of illness at admission (measured by PRISM II) and length of PICU stay of delirious and non-delirious children were compared. Independent sample t tests and χ^2 tests were carried out to investigate differences in population characteristics between the PD group and the controls. A linear regression model, yielding unstandardised coefficients, was used to test whether PD prolonged PICU stay after adjustment for possible confounders. Since PICU stay was not normally distributed, the variable was log-transformed. The log-transformed variable was the dependent variable and PD, age, gender, PRISM II, mechanical ventilation and medical indication for admission were the independent variables. Although five medical indications for admission were classified (respiratory, neurological, circulatory, surgical and 'other'), only three of these groups were used for inferential statistics, as the numbers for the surgical and 'other' indication for admission were too small. Analyses were carried out using SPSS 15.0 software.

Results

Descriptive statistics

PICU stay varied from 1 to 62 days, with a median stay of 4 days and an interquartile range of 2 to 9 days (Fig. 1 for uncorrected graphical group comparison).

Children with PD were older than children without PD ($P = 0.001$), received more mechanical ventilation ($P < 0.001$) and had a trend towards higher PRISM II scores ($P = 0.073$). There were no other differences between the delirious and non-delirious group. One out of 49 children with PD died (2.0%), versus 6 out of 98 controls (6.1%). Overall mortality in critically ill children aged 1 to 18 years was 27 out of 743 (3.6%, period January 2002 to February 2007) (Table 1).

Inferential statistics

PD significantly increased the duration of PICU stay ($B = 0.38$, SE $= 0.062$, $P < 0.001$). The log-transformed effect size represents a difference in PICU stay of 2.39 days,

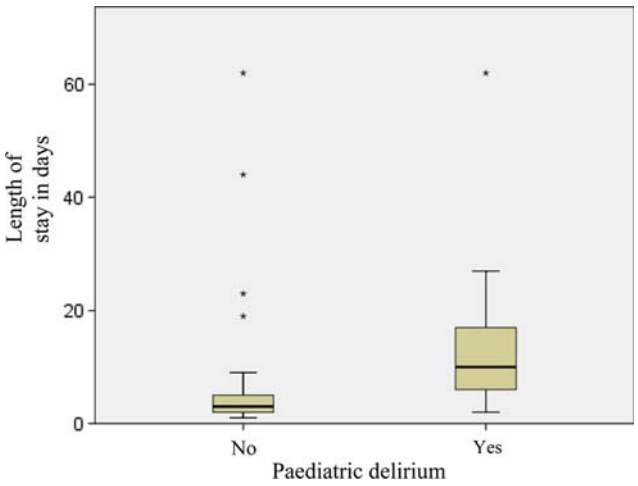

Fig. 1 Length of stay in non-delirious and delirious children. Distribution of length of PICU stay (days) for children with and without PD. Length of PICU stay is graphically displayed in *boxplots*. Presented are sample minimum, lower quartile (Q1), median (Q2), upper quartile (Q3) and maximum. *Asteriks* represents outlier observations. For non-delirious children the PICU stay varied from 1–62 days, with a Q1 of 2 days, Q3 of 3 days and Q3 of 5 days, respectively. For children with PD the PICU stay varied from 2–62 days, with a Q1 of 6 days, Q2 of 10 days and Q3 of 18 days

Table 1 Population characteristics

	Children with delirium $n = 49$	Children without delirium $n = 98$
Age in years[a]	8.8 ± 5.4	5.9 ± 4.7
PRISM II score[b]	18.3 ± 23.4	11.2 ± 22.0
Male sex	63%	61%
Mechanical ventilation[a]	84%	42%
Mortality[d]	2.04%	6.12%
Reason for admission[c]		
Respiratory	$n = 19$ (39%)	$n = 34$ (35%)
Neurological	$n = 15$ (31%)	$n = 25$ (26%)
Circulatory	$n = 11$ (22%)	$n = 29$ (30%)
Surgical[e]	$n = 4$ (8%)	$n = 8$ (8%)
Others[e]	$n = 2$ (4%)	$n = 7$ (7%)

[a] Significant at level $\alpha < 0.005$

[b] Trend towards significance, $P = 0.073$

[c] Admission may be associated with multiple medical indications

[d] 50% of the cells have an expected count less than 5

[e] 25% of the cells have an expected count less than 5. Bivariate frequencies of these indications for admission groups were too skewed for inferential statistics and are therefore excluded from the analysis

independent of severity of illness (measured by PRISM II), age, gender, mechanical ventilation and medical indication for admission. Apart from the hypothesized association between length of PICU stay and PD, post-hoc associations with the following variables were observed: mechanical ventilation ($B = 0.143$, SE $= 0.063$, $P = 0.024$), respiratory indication for admission ($B = 0.352$, SE $= 0.069$, $P < 0.001$) and circulatory indication for admission ($B = 0.177$, SE $= 0.073$, $P = 0.017$). In contrast, severity of illness (measured by PRISM II score) was not associated with length of PICU stay ($B = 0.002$, SE $= 0.001$, $P = 0.205$).

Direct costs analysis

In the current sample, PD increased the duration of PICU stay with 2.39 days. Given the fact that the direct costs associated with a single day at the PICU are close to € 2.000 (source: financial control, Maastricht University Medical Center+, The Netherlands), these extra 2.39 days of intensive care would result in € 4.780 of extra costs. With a very conservatively estimated prevalence of PD of 5% [6, 9] and 300 acute, non-elective admissions per year, 15 children with delirium would generate an extra cost of € 71.700 per year, corresponding to an increase of 1.5% in direct medical costs due to PD.

Discussion

To our knowledge, this is the first study which demonstrates the negative prognostic influence of PD on PICU stay in routine care. This association was previously described in adult and geriatric intensive care patients with delirium [1–3, 11]. Turkel and Tavaré retrospectively investigated the outcome of PD in terms of length of stay and mortality rate, identifying 84 delirious children out of 1,027 consecutive psychiatric consultations in a paediatric hospital [12]. The length of stay of these delirious children was long (mean 41 days, range 1–255 days) and the mortality was high (20%). However, since only length of stay and mortality of delirious children were reported and data pertaining to a non-delirious control group were absent, it is not possible to make a comparative interpretation of the findings. It is probable that the extended length of stay, reported by Turkel and Tavaré, is the consequence of the very high level of severity of illness, as inferred from the high mortality rate. In addition, the prognostic impact of PD was, in contrast to our prospective study, investigated retrospectively.

In contrast to the generally accepted positive association between PRISM II score and length of stay in children admitted to a PICU, there was no evidence for an association in the current study. A likely reason is the effect of sample selection on PRISM II score; the PRISM II score is calculated from six cardio-respiratory, six biochemical, but only two neurological parameters and tends to underestimate severity of illness in patients with an (isolated)

encephalopathy. In this study, 31% percent of the delirious children and 26% of the non-delirious children had an underlying neurological illness. Therefore, it is recommended to incorporate delirium parameters into the severity of illness assessment of critically ill children (i.e. PRISM II), representing the sixth vital sign: mental status [10].

In contrast to our expectations—given the known vulnerability of young children for delirium [1]—delirious children were older than non-delirious children. It is likely that this is related to the lower sensitivity of psychiatric examination, as an instrument to detect PD, in younger children; since cognitive abilities and social interactions are developed to a lower degree in the youngest. In these cases, PD may have been misdiagnosed, resulting in more false negatives among young children. The direction of this misclassification would have been conservative rather than anti-conservative with regards to the reported results.

Limitations

First, although we attempted to control for confounders, some residual confounding cannot be excluded, due to the complicated multifactorial causation of PD. Therefore, effect sizes may also be smaller than reported. For example, the use of psychotropic medications, such as benzodiazepines and opioids, notorious for their increased risk of ICU delirium [7, 8] was not examined directly. However, effects of benzodiazepines and opioids arguably were controlled for indirectly, given the fact that their use is predominantly associated with mechanical ventilation—in our PICU, this would typically be the case—and this was included in the analyses. Second, PD was diagnosed on the basis of referral procedures in routine care. The control group consisted of children without evident symptoms who were not referred for psychiatric examination. In the control group, we may thus have missed children who were suffering from (a hypoactive or subclinical) PD, leading to the inclusion of false-negatives in the control group. This may have biased our results conservatively to the null, i.e. the real effect of PD on length of PICU stay may be larger than reported. Third, although the study demonstrated an association between PD and PICU stay, inferences on direction of causality can not be made with confidence. It is theoretically possible that a prolonged PICU stay increases the risk to develop PD, rather than delirium prolonging the duration of PICU stay. However, this may be unlikely given the direction of causality in adult and geriatric patients. Fourth, this study was conducted in a tertiary facility in a university hospital; therefore, results cannot be generalized automatically to other settings.

Finally, costs associated with further hospital, post-PICU stay were not examined and indirect costs similarly could not be calculated.

Conclusion

This study suggests a negative prognostic influence of PD on duration of PICU stay resulting in an increase of direct medical costs. This extra expense, together with the burden of PD for the child, parents, family and staff, makes it all the more important to increase awareness regarding this neglected clinical entity. Further research is needed to investigate whether PD can be prevented or diagnosed earlier and whether earlier treatment may yield health as well as costs benefits.

Conflict of interest statement Jim van Os is an independent speaker with or unrestricted grant receiver from Eli Lilly, Lundbeck, Organon, BMS, GSK, Janssen-Cilag and Astra Zeneca. The other authors have no financial relationships to disclose.

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