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RESEARCH

Induction behaviour and race and its association with postoperative agitation in paediatric elective surgery

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Background: It has been suggested that preoperative agitation in children may be a risk factor for postoperative delirium and postoperative vomiting. Previous studies have suggested that adult African patients have a lower incidence of postoperative nausea and vomiting, but no such association has been shown in children.
Aim: To determine the incidence of both postoperative delirium and postoperative vomiting in elective paediatric surgical patients in a South African hospital and their association with preoperative agitation and patient race.
Methods: A retrospective database analysis was undertaken of patients 1–12 years of age undergoing elective surgery. The Watcha behavioural scale was used to assess pre- and postoperative agitation. A Watcha score > 2 defined significant preoperative agitation or postoperative delirium. Multivariable logistic regression evaluated ENT surgery, sex, age, volatile type, significant preoperative agitation and race as predictors of postoperative delirium. Sex, race, significant preoperative agitation, ENT surgery and vomiting prophylaxis were evaluated as predictors of postoperative vomiting.
Results: Significant preoperative agitation occurred in 13.5% (125/928); postoperative delirium in 3.4% (32/928) and postoperative vomiting in 1.4% (12/856) of patients. Postoperative delirium occurred in 3.1% of African patients as compared with 10.4% of non-African patients ($p = 0.007$); and postoperative vomiting in 1.2% of African patients as compared with 4.4% of non-African patients ($p = 0.074$). The predictors of postoperative delirium were non-African race (odds ratio [OR] 3.67; 95% confidence interval [CI] 1.22–11.07; $p = 0.021$), significant preoperative agitation (OR 3.54; 95% CI 1.55–8.09; $p = 0.003$), and ENT surgery (OR 2.5; 95% CI 1.0–6.0; $p = 0.040$). Only non-African race predicted postoperative vomiting (OR 3.73; 95% CI 1.01–13.79; $p = 0.049$), which included other variables like ENT surgery, significant preoperative anxiety, PONV prophylaxis.
Conclusion: Preoperative agitation, non-African race and ENT surgery were predictors of postoperative agitation. Postoperative vomiting was predicted only by non-African race, which correlates with the trend seen in adults, even though incidence difference between African and non-African patients was not statistically significant.

Keywords: emergence agitation, emergence deliriuminduction behaviour, preoperative agitation, preoperative anxiety

Introduction

It has been suggested that significant preoperative agitation in children may be a risk factor for postoperative delirium and postoperative vomiting (POV). The incidence of emergence delirium in children occurs in the order of 15% of patients, but incidences as high as 50% have been reported.[1–4] It is important to identify risk factors for emergence delirium, so that clinicians may prophylactically treat high-risk patients. The association between agitation at induction and emergence delirium has not been clearly delineated with contradictory results being reported.[5–9] The incidence of POV in children has been reported as 34%.[10] While preoperative anxiety and agitation have been implicated as possible risk factors for postoperative nausea and vomiting (PONV) in adults,[11–15] its role as a risk factor in children remains unclear.[16,17] Further, local South African data have suggested that adult African patients have a lower incidence of PONV than non-African patients[18] but no such association has yet been shown in children.

We undertook a retrospective database analysis to: (1) determine the incidence of both postoperative delirium and postoperative vomiting in children in a South African hospital; and (2) determine their association with significant preoperative agitation and patient race.

Methods

We undertook a retrospective analysis of the Grey's Hospital (Pietermaritzburg, KwaZulu-Natal, South Africa) anaesthesia paediatric database (University of KwaZulu-Natal Bio-medical Ethics Committee REF: BE452/14). This database consists of quality improvement data routinely completed by anaesthetists and recovery nursing staff. Patients were considered eligible if they were aged 1–12 years and underwent elective surgery at Grey's Hospital from March 21, 2014 to November 9, 2015. This included paediatric, orthopaedic, maxillofacial, ophthalmology, plastic, and ear, nose and throat (ENT) surgery cases.

Preoperative and postoperative agitation was measured using the Watcha behavioural scale. This was assessed during the induction period in theatre and in the recovery room with the presence of a Zulu-speaking nurse. The four points of the scale are as follows: 1 = asleep or calm; 2 = crying—can be consoled; 3 = crying—cannot be consoled; 4 = agitated—thrashing around. For the purposes of this analysis a Watcha score > 2 defined significant preoperative agitation or postoperative delirium. Any episodes of vomiting before discharge from the recovery room were also extracted.

The baseline characteristics of the included patients were reported as mean (standard deviation [SD]) for continuous variables and count (per cent) for categorical variables. Comparisons between normally distributed data were done using Student's t-test. Where three or more groups were analysed, analysis of variance was used. Categorical data were analysed using a chi-squared test. A p-value of < 0.05 was used for defining statistical significance.

To determine risk factors for postoperative delirium, we performed univariable logistic regression on the following candidate variables: significant preoperative anxiety, ENT surgery, sex, age, race, and type of volatile. Predictors associated with postoperative delirium (i.e. $p < 0.1$) were entered into a multivariable regression model. For all logistic regression analyses we used forced simultaneous entry (all candidate variables remained in the model) as opposed to automated stepwise selection, because simulation studies demonstrate a higher risk of overfitting with the latter approach. We assessed collinearity using the variance inflation factor (VIF), which measures the extent to which the variance of the model coefficients was inflated (because of the correlation of the variable with other predictor variables) if that variable was included in the model. We considered variables with VIF>10 co-linear, and we excluded the variable with the lowest OR on univariate analysis from the model; 95% confidence intervals (CI) were estimated by bootstrapping with 1000 repetitions.

We repeated this process to determine predictors for the outcome of postoperative vomiting using the following candidate variables: sex, race, significant preoperative anxiety, ENT surgery and vomiting prophylaxis. Because of the low number of candidate variables, no univariate analysis was conducted and all candidate variables were used in the multivariable regression model. All analyses were done using Stata/IC 13.1® (2015) for Windows (StataCorp LLC, College Station, TX, USA).

Results

From a total of 1001 patients we included 928 patients in the analysis of preoperative and postoperative agitation (880 African patients [95%] and 48 non-African patients [5%]) and 856 for analysis of the incidence of postoperative vomiting (811 African patients [95%] and 45 non-African patients [5%]). The analysis is outlined in Figure 1. Mean patient age was 5.2 (SD 3.21) years and 62% were male.

Significant preoperative agitation (Watcha score > 2) occurred in 13.5% (125/928); postoperative delirium (Watcha score > 2) in 3.4% (32/928); and postoperative vomiting in 1.4% (12/856) of patients. Postoperative delirium occurred in 3.1% (27/880) of African

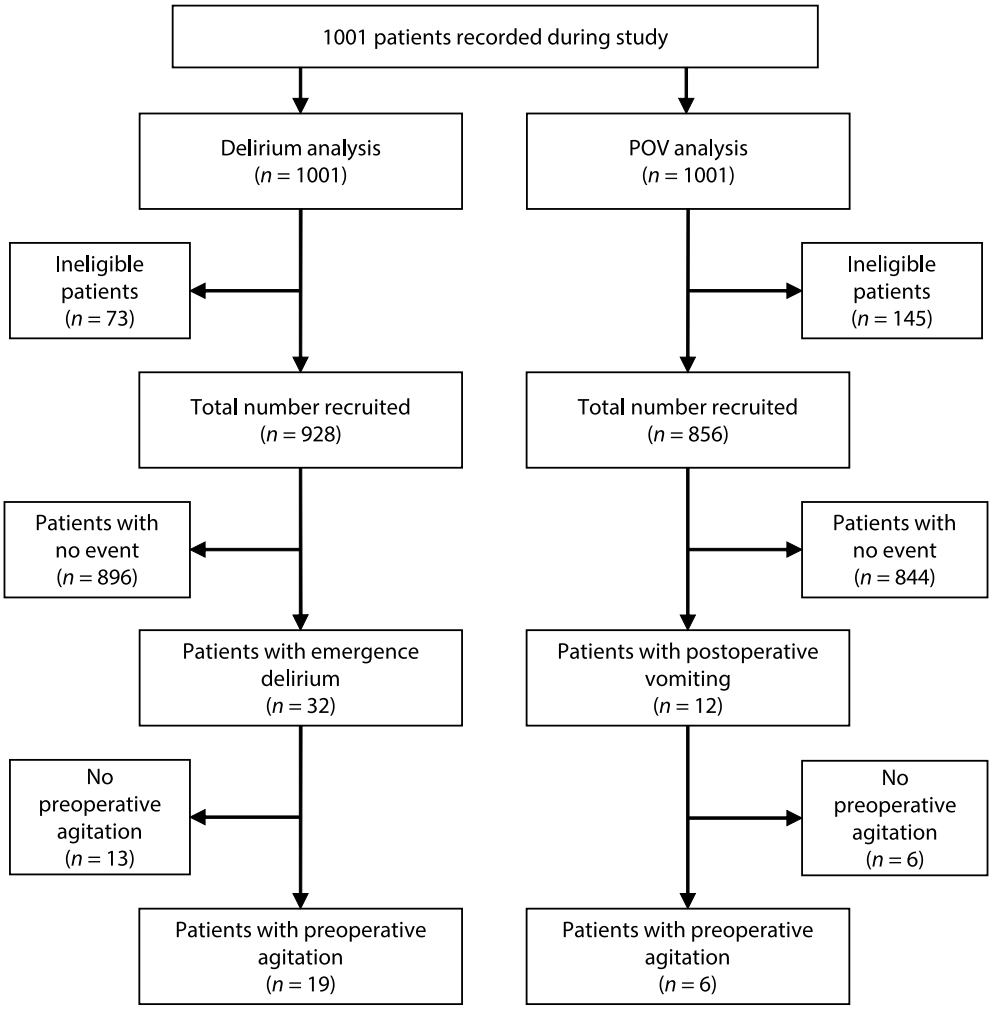

Figure 1: Study analysis

Table 1: Predictors for postoperative delirium

Predictors	Odds ratio	95% confidence interval	*p*-value
Non-African race	3.67	1.22-11.07	0.021
Significant perioperative agitation	3.54	1.55-8.06	0.003
ENT surgery	2.5	1.00-6.00	0.040
Sex	1.02	0.49-2.10	0.973
Volatile agents	1.36	0.64-2.90	0.426
Age	0.95	0.85-1.10	0.397

patients as compared with 10.4% (5/48) of non-African patients ($p = 0.007$); and postoperative vomiting in 1.2% of African patients as compared with 4.4% of non-African patients ($p = 0.074$).

Univariate analysis found ENT surgery, non-African race (Caucasian and Indian), and preoperative agitation to be associated with postoperative delirium. Analysis of the perioperative variables using a multivariable regression model found non-African race (odds ratio [OR] 3.67; 95% confidence interval [CI] 1.22–11.07; $p = 0.021$), significant preoperative agitation (OR 3.54; 95% CI 1.55–8.09; $p = 0.003$), and ENT surgery (OR 2.5; 95% CI 1.0–6.0; $p = 0.040$) to predict postoperative agitation (Table 1). No collinearity was detected.

For the outcome of postoperative vomiting only non-African race was predictive (OR 3.73; 95% CI 1.01–13.79; $p = 0.049$) while ENT surgery (OR 1.94, 95% CI 0.52–7.27; $p = 0.322$) and induction anxiety (OR 1.19, 95% CI 0.67–2.14, $p = 0.538$) were not predictive (Table 2). No collinearity was detected.

Discussion

Delirium

In the literature the reported incidence of postoperative delirium varies considerably based on the population group in which the study has been conducted, the scoring system used to quantify delirium, and the anaesthetic technique used.[19] Incidences range between 13% and 15%[20] with some as high as 28% depending on surgery type.[21] In our analysis the baseline incidence of postoperative delirium was 3.4%. Not only was there a significant difference in incidence between African patients and non-African patients (3.1% vs. 10.4%, $p = 0.007$) but the incidence in African patients lies at the lower range of what has been reported in the literature. The basis for this difference remains speculative but it is interesting to note that human migration out of Africa has led to the development of specific haplotype lineages with African populations having distinctly different HLA and human Toll-like receptor genetic haplotypes than non-African populations,[22] both of which can be associated with immune and allergy response although there is poor evidence linking immune mechanisms to PONV and emergence delirium.

The literature has shown both supporting[5,7] and contradicting evidence[8,9] for an association between preoperative agitation and postoperative delirium. In the analysis we found a strong association between significant preoperative agitation and postoperative delirium (OR 3.54 95% CI 1.55–8.09: $p = 0.003$). Therefore, we suggest that significant preoperative anxiety could be considered a risk factor for postoperative delirium and its identification may result in clinicians taking preventive measures

Table 2: Predictors for postoperative vomiting

Predictors	Odds ratio	95% confidence interval	*p*-value
Non-African race	3.73	1.01-13.79	0.049
Significant perioperative agitation	1.94	0.52-7.27	0.322
ENT surgery	1.19	0.67-2.14	0.538

against postoperative delirium.[19] These measures may include the use of intraoperative ketamine, opioids, propofol or an $\alpha 2$ agonist.[1]

Numerous studies have found the type of surgery, and in particular ENT surgery, to be a risk factor for postoperative delirium (Table 3). This is in keeping with the findings of Mousavi *et al.*, who reported that 42.2% of emergence delirium cases had undergone ENT surgery of some nature.[23]

Postoperative vomiting

For the outcome of postoperative vomiting we again found a difference in the incidence between African and non-African patients (1.2% vs. 4.4% respectively, $p = 0.074$) and on multivariate analysis only non-African race was a predictor of postoperative vomiting (OR 3.73; 95% CI 1.01–13.79; $p = 0.049$). The incidence of PONV in surgical patients receiving a general anaesthetic is 25–30%[24] and postoperative vomiting in children has a similar incidence (34%).[10] Race has been implicated as a risk factor for PONV in adults with Rodseth *et al.*[18] and Ugochukwu *et al.*[25] finding a significantly lower incidence of PONV in African adult patients. However, few studies have evaluated this in a paediatric population. Despite the fact that our population consisted of children, our incidence was also lower in African patients. It has been postulated that the hepatic P-450 cytochrome system and in particular its role in volatile metabolism affects the incidence of PONV with a higher risk in the CYP2E1 poor metaboliser phenotype.[26] This phenotype has not been identified in African patients residing in the province of our study. In keeping with the findings of Van den Bosch *et al.*,[16] we found no significant association between vomiting and significant preoperative anxiety.

Limitations

This study is necessarily limited by its retrospective nature. The assessment of emergence delirium poses significant challenges since pain is a prominent confounding factor. Scales such as the Cravero, Pediatric Anesthesia Emergence Delirium (PAED) and Watcha are commonly used. However, they are all unable to distinguish accurately between pain and delirium. Some scales, like the PAED scale, do not have a cut-off threshold with which to define emergence delirium, making it difficult to determine the true incidence of postoperative delirium. The Watcha scale has the advantage of being easy to use in clinical practice and may be more sensitive and specific than the other two scales.[27] However, the Watcha scale was not intended for use as a tool to measure preoperative anxiety.

Table 3: Incidences of postoperative agitation

Type of surgery	Incidence (%)
ENT	6.38
Orthopaedics	3.41
General	2.31
Eye	2.13

One of the limitations of the study is small sample size for non-African patients. There were 48 non-African patients included in the analysis for postoperative agitation, and 45 non-African patients included in the analysis for POV.

Postoperative vomiting that does not manifest in the recovery room may still be a problem in the ward. Only the incidence of postoperative vomiting in the post-anaesthesia care unit (PACU) was evaluated.

Conclusion

Postoperative delirium occurred in 3.4% of patients and postoperative vomiting in 1.4%. In African patients the incidence of both delirium and vomiting was lower than in non-African patients: 3.1% vs. 10.4%, $p = 0.007$ and 1.2% vs. 4.4%, $p = 0.074$ respectively. Predictors of postoperative delirium were non-African race, significant preoperative agitation, and ENT surgery. Only non-African race predicted postoperative vomiting, which correlates with the trend seen in adults, even though the finding was not statistically significant.

Ethics

This observational cohort study was granted full ethics approval from the University of KwaZulu-Natal Bio-medical Ethics Committee (REF: BE452/15), which is registered with the South African National Research Ethics Council.

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Disclosure

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