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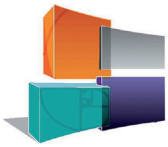

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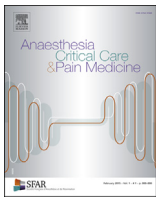

Original article

The effect of regional anaesthesia versus general anaesthesia on behavioural functions in children

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ABSTRACT

Purpose: The primary objective was to assess the effect of general anaesthesia versus regional anaesthesia in a single exposure before the age of 2 years on the development of long-term behavioural changes in children.

Methods: The study was conducted between January 2014 and March 2015. Medical records of eligible children were reviewed. Then, parents of children who were included in the study were contacted and asked to visit the Outpatient Department to fill the Eyberg Child Behaviour Inventory questionnaire to measure behavioural changes in children. Children who were exposed to regional or general anaesthesia for surgery between January 2002 and December 2006 were included. Data collected were age and weight at the time of the first anaesthesia exposure and surgery duration. Chi-square test, *t*-test and multivariate analysis were used.

Results: In total, 394 children were exposed to anaesthesia before the age of 2 years. Among the 168 patients who were exposed to general anaesthesia, 44 children (26.2%) developed behavioural abnormalities compared to 12 out of 226 patients (5.3%) who were exposed to regional anaesthesia (*P*-value < 0.0001). Exposure to anaesthesia before age of 2 years increases the risk of developing behavioural disorder when surgery is accompanied by general anaesthesia, younger age at time of exposure, and longer surgery duration (*P*-value < 0.0001, 0.001, 0.038 respectively).

Conclusion: Regional anaesthesia showed much lesser effect on children's behaviour compared to general anaesthesia. The incidence of behavioural disorder is increased with the use of general anaesthesia, younger age of the patient at time of exposure, and longer surgery duration.

1. Introduction

The use of anaesthesia in infants and children has raised a great concern regarding its safety and long-term consequences. Experimental research on animals showed that early exposure to anaesthesia is neurotoxic to the developing brain and can lead to long-term neuro-behavioural impairment [1–7]. However, there is controversy regarding the effect of anaesthesia exposure during childhood on developmental outcomes. Several studies assessed the effect of exposure to general anaesthesia before the age of 4 years on the development of behavioural and cognitive abnormalities in children. Some studies showed that general anaesthesia was associated with learning and developmental disorders [8–11]. However, a recent study did not find evidence that general anaesthesia increases the risk of adverse neurodevelopmental outcomes when compared to regional anaesthesia [12].

Given the limited number of studies that examined the influence of regional anaesthesia on behaviour and the controversial outcomes, it would be necessary to study its effect on children. Therefore, based on the significant changes in anaesthesia practice and the widespread use of regional anaesthesia in paediatric age group, the purpose of this study was to determine the effect of general anaesthesia vs. regional anaesthesia in a single exposure before the age of 2 years on the development of long-term behavioural changes in a birth cohort of children. The outcome

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measure was behavioural change assessed by the Eyberg Child Behaviour Inventory (ECBI) [13,14].

2. Materials and methods

The study was approved by the Institutional Review Board at Makassed General Hospital. It was conducted between January 2014 and March 2015. The medical records of children who were exposed to anaesthesia (regional or general) for surgery between January 2002 and December 2006 at Makassed General Hospital were reviewed. Children were divided into GA and RA groups. Exclusion criteria consisted of: children older than 2 years, surgery duration longer than 2 hours, multiple anaesthetic exposure, complicated neonatal course (respiratory distress and congenital anomalies), prematurity, admission to the neonatal intensive care unit, presence of any chronic disease (neurological, pulmonary, or cardiac diseases), and any complication during or after surgery. Then, parents of children who were included in the study were contacted and asked to visit the Outpatient Department (OPD) to fill the Eyberg Child Behaviour Inventory (ECBI) questionnaire. Parents who were not able to visit the OPD completed the questionnaire via phone calls.

2.1. Behavioural assessment

Behaviour problems were assessed based on Eyberg Child Behaviour Inventory (ECBI) questionnaire, which is a parent-rating validated tool that was used by several studies to measure behavioural changes in children [13–17]. Different daily habits such as eating and sleeping, attention and aggressiveness are some of the issues addressed by the ECBI questionnaire [14]. It is used for children between 2 and 17 years of age [15].

The ECBI is composed of 36 items having two scales: Intensity and Problem scales. The frequency of the behavioural problem is measured through the Intensity scale. Parents rate every element in the 36 items with a score ranging from 1 to 7, with 1 indicating that the problem never occurs and 7 showing that the problem always happens. The Problem scale measures parents' perception of the specific behaviour as a problem by rating the 36 behaviours as "no" or "yes" [15,16]. The Intensity score is the sum of the occurrence for the 36 behaviours, while the Problem score is the total number of behaviours answered by "yes" [13]. There are two clinical cutoff scores recommended by Eyberg and Ross; 127 for the Intensity scale and 11 for the Problem scale. Higher scores indicate that there is behavioural problem that may require treatment [13,15].

2.2. Data collection

Additional data were also collected such as: demographics, parental education level in addition to age and weight at the time of the first anaesthesia exposure. Anonymity and confidentiality of the collected data were ensured.

2.3. Statistical analysis

Statistical analysis was done using SPSS version 19 (SPSS, Chicago, IL, USA). Chi-square test and *t*-test (two-tailed) were used to assess any significant difference between the two groups. Multivariate analysis was performed since some parameters might be dependent. Data were reported as number of patients (percentage) or mean (standard deviation). *P*-values less than 0.05 were considered statistically significant. A sample size of 250 children in each group was needed to detect a 30% reduction in behavioural problems in the RA group with $\alpha = 0.05$ and power 85% [18].

3. Results

Between January 2002 and December 2006, 394 children had been exposed to anaesthesia for surgery before the age of 2 years at Makassed General Hospital. Of the 394 children, 226 patients were exposed to regional anaesthesia whereas 168 children had general anaesthesia (Fig. 1).

Patients' characteristics are showed in Table 1. Among the 168 patients who were exposed to general anaesthesia before age

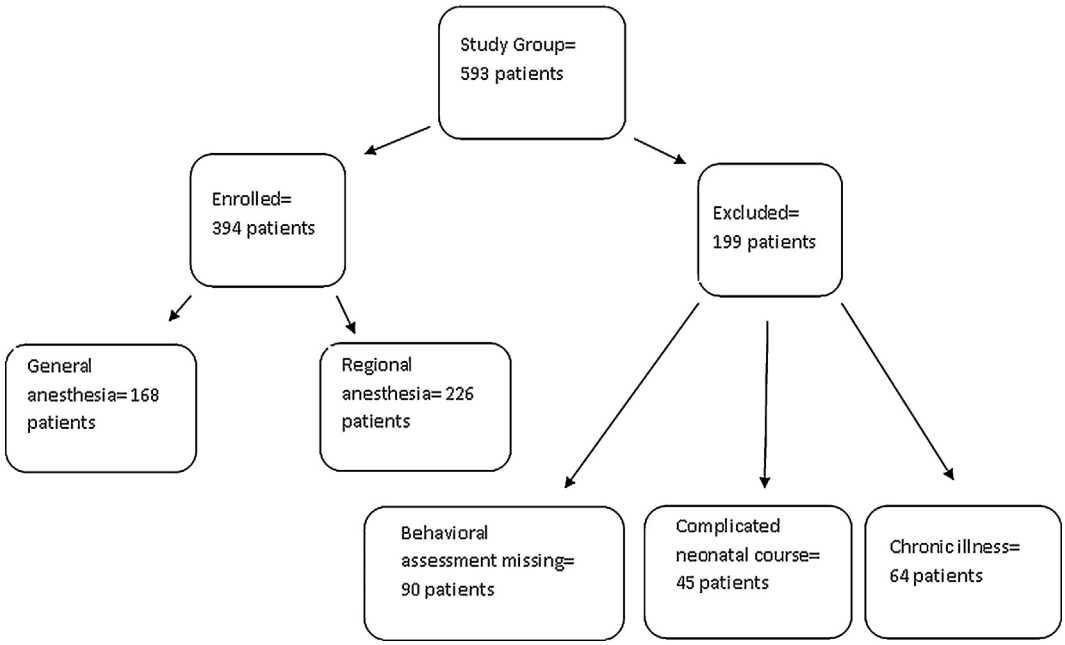

Fig. 1. Flowchart illustrating selection of patients.

Table 1
Patients characteristics by group.

	Regional anaesthesia ($n = 226$)	General anaesthesia ($n = 168$)	*P*-value
Gender			0.947
Male	181 (80.1%)	135 (80.4%)	
Female	45 (19.9%)	33 (19.6%)	
Mother education			0.488
School	89 (39.4%)	72 (42.9%)	
University	137 (60.6%)	96 (57.1%)	
Father education			0.228
School	69 (30.5%)	61 (36.3%)	
University	157 (69.5%)	107 (63.7%)	
Age at exposure	108 (47.8%)	71 (42.3%)	0.276
< 1 year	118 (52.2%)	97 (57.7%)	
1–2 years			
Weight			0.533
≤ 10 kg	104 (46.0%)	72 (42.9%)	
> 10 kg	122 (54.0%)	96 (57.1%)	
Surgery duration			0.526
< 1 hour	135 (59.7%)	95 (56.5%)	
1–2 hours	91 (40.3%)	73 (43.5%)	
ECBI			< 0.0001
Normal behaviour	214 (94.7%)	124 (73.8%)	
Behavioural abnormality	12 (5.3%)	44 (26.2%)	

2 years, 44 children (26.2%) developed behavioural abnormalities compared to 12 patients (5.3%) who were exposed to regional anaesthesia (*P*-value < 0.0001). There is no statistically significant difference between the two groups with respect to gender, mothers and fathers' educational level, age and weight at time of exposure as well as surgery duration (Table 1).

Taking together the two study groups, 179 children were younger than 1 year and 215 children were between 1 and 2 years. Of those children, 20.1% and 9.3%, respectively, developed behavioural abnormalities (*P*-value = 0.002). In addition, at the time of their exposure to anaesthesia whether regional or general, 176 patients weighed ≤ 10 kg and 218 patients had a weight more than 10 kg. Of those children, 18.8% and 10.6%, respectively, developed behavioural abnormalities (*P*-value = 0.020) (Table 2). The surgical duration for 230 children in both study groups was below one hour while 164 children had surgery duration between 1 and 2 hours. 24 patients (10.4%) of the 164 children who had surgeries lasting between 1 and 2 hours developed behavioural abnormalities (*P*-value = 0.011) (Table 2).

The results of multivariate analysis with behavioural abnormalities as the dependent variable were presented in Table 3. Exposure to anaesthesia before age of 2 years increases risk of developing behavioural disorder when surgery is accompanied by general anaesthesia, younger age at time of exposure, and longer surgery duration (*P*-value < 0.0001, 0.001, 0.038 respectively). The risk is lower with the use of regional anaesthesia.

4. Discussion

The results of the present study revealed that children who were exposed to RA before the age of 2 years had lower risk of developing behaviour problems in comparison with children who were exposed to GA.

Even though conflicting results exist in literature, three significant risk factors were worth being discussed, as they were associated with the development of behavioural disorders as revealed by multivariate analysis.

The first factor was the type of anaesthesia used. The risk of behavioural disorders development increased significantly with general anaesthesia in comparison to regional anaesthesia since 26.2% of GA patients developed behavioural disorders in comparison to only 5.3% of RA patients. Many studies examined the

Table 2
ECBI rates in relation to patients and surgery characteristics.

	Normal behaviour ($n = 338$)	Behavioural abnormality ($n = 56$)	*P*-value
Gender			0.741
Male	272 (86.1%)	44 (13.9%)	
Female	66 (84.6%)	12 (15.4%)	
Mother education			0.580
School	140 (87.0%)	21 (13.0%)	
University	198 (85.0%)	35 (15.0%)	
Father education			0.884
School	112 (86.2%)	18 (13.8%)	
University	226 (85.6%)	38 (14.4%)	
Age at exposure			0.002
< 1 year	143 (79.9%)	36 (20.1%)	
1–2 years	195 (90.7%)	20 (9.3%)	
Weight			0.020
≤ 10 kg	143 (81.3%)	33 (18.8%)	
> 10 kg	195 (89.4%)	23 (10.6%)	
Surgery duration			0.011
< 1 hour	206 (89.6%)	24 (10.4%)	
1–2 hours	132 (80.5%)	32 (19.5%)	

Table 3
Results of multivariate analysis with behavioural abnormalities as the dependent variable.

Parameters selected	Odds ratio (OR)	95% confidence interval	*P*-value
Anaesthesia type	7.512	3.717–15.184	< 0.0001
Age at exposure (yrs)	0.350	0.186–0.660	0.001
Surgery duration	0.919	1.036–3.555	0.038

influence of anaesthetic exposure on behaviour and learning disabilities [19]. Bong et al. found that the odds of developing learning disability by age 12 years was about 4 times higher in infants exposed to GA than those unexposed [8]. DiMaggio et al. compared children who had hernia repair before the age of 3 years to children who did not have surgery. The study concluded that children who underwent hernia repair had double the risk of being diagnosed with developmental or behavioural problems [20]. Another study by DiMaggio et al. showed that the risk of developing behaviour and developmental disorders is 60% more in children who underwent surgery before age of 3 compared to siblings who did not have surgery [21]. Ing et al. concluded that children who had a single anaesthetic exposure before the age of 3 had a higher risk of having receptive language deficiency at the age of ten. However, there was no significant effect on behavioural changes [9]. Davidson et al. showed evidence of equivalence between exposure to less than one hour GA and RA with respect to composite cognitive, motor, language and behaviour scores at 2 years of age [12]. Another study by Sun et al. concluded that there were no statistically significant differences in IQ scores in later childhood when comparing children with a single anaesthetic exposure before the age of 36 months with their healthy siblings who were not exposed to anaesthesia [22].

The second factor was anaesthesia duration. The risk of behavioural disorders significantly increased with longer exposure to anaesthesia. Although cognitive (learning) decline was not included in our study as a primary or secondary objective; yet, some published studies suggest that there is a significant relation between duration of exposure and cognitive decline. A study by Wilder et al. revealed that the risk of learning disabilities increased for longer anaesthesia duration [23]. Block et al. concluded that the longer the anaesthesia duration the lower the children's scores on academic achievement tests though other factors might have contributed to the results [24].

A third factor was age at exposure. This study showed significant increase in the risk of developing behavioural disorders as patient's age decreased at time of exposure to anaesthesia. These results are similar to the findings of a previous study, which demonstrated that the risk of developing behavioural disorders increased with exposure to anaesthesia at younger ages, mainly below the age of 6 months [18]. Kalkman et al. compared children who were exposed to anaesthesia before and after the age of 2 years. They found non-significant increase in behaviour disturbance in the group who were exposed before the age of 2 years [25].

The present study examined the effect of a single anaesthetic exposure on behaviour. Nevertheless, several studies assessed the effect of multiple anaesthetic exposures during childhood on behaviour and learning. Wilder at al compared multiple to single anaesthetic exposure and revealed that multiple exposures before the age of four years significantly increased the risk of having learning disabilities [23]. Similarly, other studies concluded that repeated exposure to anaesthesia before the age of two was a risk for developing learning disabilities and attention deficit hyperactivity disorder [10,11]. The total duration of anaesthesia can be viewed as a surrogate of the anaesthetic procedures; hence, supporting the findings of this study that increased duration of anaesthesia increases the risk of developing behaviour disorder.

The study has some limitations. It was retrospective single-centre study. Moreover, the children who were included in this study have varied socioeconomic status, resided in diverse communities and attended different schools. These factors might have an effect on the outcome.

In conclusion, this study showed that regional anaesthesia had lesser effect on children's behaviour in comparison to general anaesthesia. The incidence of behavioural disorder is increased when anaesthesia and surgery were accompanied by use of general anaesthesia, younger age of the patient at time of exposure, and longer duration of surgery.

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Ethical statement

The study was approved by the Institutional Review Board at Makassed General Hospital prior to study initiation.

The collected data were kept confidential.

Disclosure of interest

The authors declare that they have no competing interest.

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