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Neurodevelopmental outcomes of neonates undergoing surgery under general anesthesia for malrotation of intestines

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ABSTRACT

Background: It is difficult to differentiate between the potential adverse effects of general anesthesia (GA) on the developing brain and the role of associated co-morbidities and syndromes that can adversely affect neurodevelopmental outcomes in neonates undergoing GA. Neonates with malrotation of the intestines without volvulus usually do not have co-morbidities or syndromes. In addition, majority of them recover very well after surgery and are discharged home within a few days. Neonates with malrotation are a clean cohort of babies to study the role of a single episode of GA on the developing brain.

Aims: The study aimed to evaluate the neurodevelopmental outcomes of neonates undergoing GA for malrotation surgery.

Study design: Retrospective review of neonates born at gestational age of ≥ 32 weeks undergoing laparotomy for malrotation.

Outcome measures: Neurodevelopment in the study cohort at the age of one year.

Results: 33 eligible infants were identified from the departmental database. All 33 survived and were assessed using the Griffiths Mental Development Scales (GMDS) at one year. Mean general quotient (GQ) of the study population was 98 (SD 7.33) which was similar to the population norms (100.2, SD 12.8); p value 0.10. None of the infants developed cerebral palsy, tone abnormality, sensorineural deafness or blindness. There was no significant difference in the centiles at birth versus one year for weight and length (p values 0.454 and 0.178 respectively). Reassuringly, the head circumference centiles at one year showed a trend towards higher values (p value: 0.0735).

Conclusion: One year developmental outcomes of neonates undergoing surgery under GA for malrotation were similar to population norms.

1. Introduction

In recent years, animal studies have suggested that the commonly used general anesthetic agents are neurotoxic to the developing brain and can cause adverse effects on cognition and behaviour [1,2]. Observational studies in human children have also suggested that exposure to general anesthesia in children younger than 4 years may be associated with developmental and behavioural disorders such as language and mathematical learning disabilities or abstract reasoning deficits [3–7]. However, the study population included serious conditions such as congenital heart disease, esophageal atresia, necrotizing enterocolitis, gastroschisis etc. [7,8]. These infants are at high risk of adverse events such as infection, hypotension, hypoxia, acidosis, hypoglycemia, hypocarbia and electrolyte disturbances in the perioperative period, all of which are known to result in adverse neurological problems [9]. In addition, the presence of associated anomalies and syndromes can also influence the neurodevelopmental outcomes.

To test the effects of general anesthesia on neurodevelopmental outcomes, it is important to avoid such confounding factors. Malrotation of intestines is one such condition that lends itself to study the long-term effects of a single episode of general anesthesia in the neonatal period. This is because malrotation usually presents in the neonatal period and is not associated with other comorbidities in majority of the instances. Early identification and prompt surgical

Abbreviations: UGI, upper gastrointestinal; GA, general anesthesia; GMDS, Griffiths mental development scales; GQ, general quotient; ND, neurodevelopment; SD, standard deviation; MASK, Mayo Anesthesia Safety in Kids; PANDA, pediatric anesthesia neurodevelopment assessment; GAS, general anaesthesia and awake-regional anaesthesia in infancy

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intervention with Ladd procedure results in correction of this anomaly, with recurrences being unusual [10]. In our experience, post-operative complications are rare and the length of stay in hospital is usually minimal if malrotation is diagnosed and treated in a timely fashion before the onset of volvulus. Hence, we aimed to evaluate the neurodevelopmental outcomes of neonates with malrotation.

2. Ethics approval

The conduct of this retrospective study was approved by the Institutional Clinical Audit Committee.

3. Methods

All full term and moderate to late preterm infants (≥ 32 weeks at birth) undergoing laparotomy for malrotation under general anesthesia (years 2005–2014) were included in this study. The diagnosis of malrotation was based on upper GI contrast study in all patients. It is the standard modality of investigation in our unit. The final confirmation of diagnosis was done at laparotomy. Infants with dysmorphic features and genetic anomalies were excluded.

General anesthesia was defined as the use of intravenous or inhalational agents to achieve amnesia, analgesia, muscle paralysis, and sedation. Intra-operatively vital parameters such temperature, heart rate, respiratory rate, pulse oximeter saturation and end tidal carbon dioxide ($etCO_2$) were continuously monitored. Regular blood gas analyses were performed as per the needs of the infant during the intra-operative period. If arterial access was present, blood pressure was monitored continuously; if arterial access was not present, non-invasive blood pressure (BP) was recorded intra-operatively every 10 min during surgery. The infants were closely monitored in the postoperative period with regular blood gas analyses (arterial or capillary) and all the other vital parameters.

Hypotension was defined as mean BP below the 10th percentile for age [11]. Mild hypocapnia was defined as CO_2 = 34–25 mm Hg, moderate hypocapnia was defined as CO_2 = 25–20 mm Hg and severe as CO_2 < 20 mm Hg [12]. Since the majority of the blood gas analyses were from capillary sample, normal lactate level was defined as 2.6 (SD 0.7) mmol/L [13].

3.1. Neurodevelopmental assessment

All neonates in Western Australia who undergo general anesthesia for surgical procedures are routinely enrolled in a formal developmental follow up program and are seen at 4, 8, and 12 months' corrected age. At the 12-month visit, development is formally assessed using the Griffiths Mental Development Scales [14,15]. The Griffiths Mental Development Scales assess development in 5 separate areas: locomotor, personal and social, hearing and speech, eye and hand coordination, and performance. The locomotor sub-scale measures the earliest motor milestones as the child moves from horizontal to vertical and becomes mobile. The personal-social sub-scale assesses early adaptive behaviour using interaction with the environment and skill in dressing and feeding as well as pointing out body parts as the child approaches 2 years of age. This sub-scale uses caregiver reports. The hearing and language sub-scale measures the earliest forms of expressive language such as babbling, the development of words with meaning, and receptive speech through the ability to follow commands and identify objects. The eye-hand co-ordination sub-scale measures the development of hand grasp, fine motor and visual abilities. The performance sub-scale measures fine motor manipulative skill as well as visual spatial orientation [16]. The 5 subscales are assessed and scored separately and then combined to provide an overall general quotient (GQ) reflecting the child's developmental performance level relative to the general population. The normal population mean score is 100.2 with a SD of 12.8 [16,17]. 80% of the Griffiths assessments were conducted by a single developmental pediatrician (J.M.). For our study, the main outcomes of interest were Griffiths scores, sub-optimal developmental outcome (GQ < 75), cerebral palsy, blindness (visual acuity of < 6/60 in the better eye), or sensorineural deafness requiring hearing aids. Cerebral Palsy was defined as abnormal muscle tone and a Gross Motor Function Classification System (GMFCS) level ≥ 1 [18]. Other outcomes of interest were mild developmental delay (GQ 76–88), and physical growth at 1 year of age.

3.2. Statistical analysis

Statistical analysis was performed using Stata 12.0 (StataCorp LP 4905 Lakeway Drive, College Station, Texas 77845-4512, USA). Mean and SD values were calculated for normally distributed data. Median, IQR, and range values were calculated for continuous data with non-normal distribution. The mean GQ of the study sample was compared with the published healthy population mean (100.2, SD 12.8) using the *t*-test, and the magnitude of this difference was evaluated using Cohen d, where d is the difference between the study and population means divided by the population SD. A d of 0.2 is considered a small effect; 0.5, a medium effect; and 0.8, a large effect size [19]. The physical growth parameters (centiles) at birth versus one year were compared using the Wilcoxon matched pairs rank sum test.

4. Results

After excluding three neonates with dysmorphic features and genetic anomalies (22q13 deletion, Mowat-Wilson syndrome), the final study population comprised of 33 patients (Fig. 1). There were 21 males (67%) and 12 females (33%); the difference was not statistically significant (p = 0.059). The study population was uniform with respect to their birth weight, gestational age and birth length. There were two growth restricted infants (6%) and the remaining 31 infants (94%) were not growth restricted. The difference was statistically significant (p = 0.0001). Clinical details of the study population are given in Table 1.

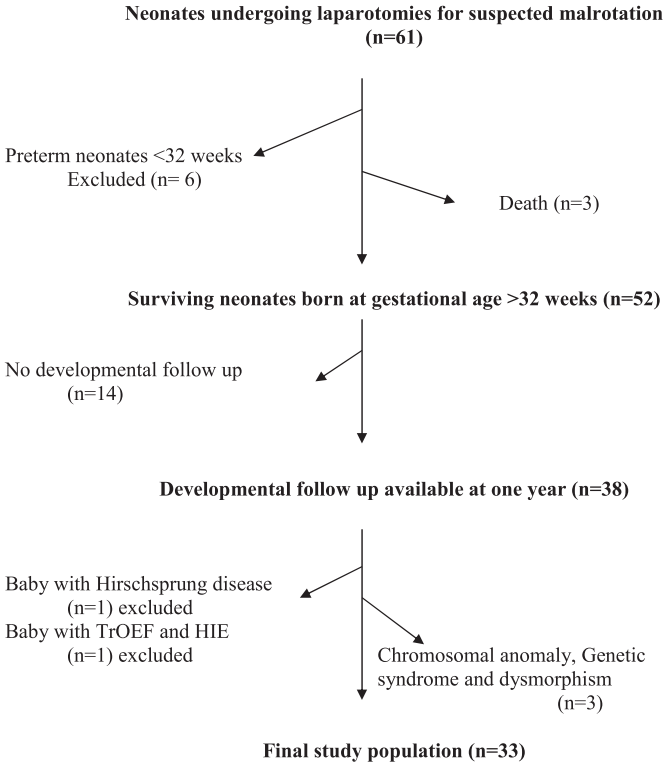

Fig. 1. Study flow diagram.