



Original Contribution

Effect of one anesthetic exposure on long-term behavioral changes in children[☆]



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Abstract

Study Objective: To determine the association between one anesthetic exposure and behavioral outcome at age 10 to 12 years.

Design: Retrospective comparative study.

Setting: University-affiliated pediatrics department.

Measurements: The medical records of children who underwent anesthesia between January 2004 and December 2005 at our institution were reviewed. The records of 292 children were included in the study group and 300 children in the control group. The study group involved children who had one anesthetic exposure before age of 4 years and the control group had children who were not exposed to anesthesia. The primary outcome was behavioral change as assessed by the Eyberg Child Behavior Inventory (ECBI) questionnaire.

Main Results: The rate of behavioral abnormalities before the age of 11 years was 28.4% in the study group ($P < 0.001$) and 5.7% in the control group. The risk of developing behavioral abnormalities was prominent in children being exposed to surgery versus those exposed during a diagnostic procedure (32.4% vs 4.8%; $P < 0.0001$). Eighty-three point nine percent of the children who were exposed to longer duration anesthesia (more than 3 hrs) had behavioral abnormalities ($P < 0.0001$), while 48.8% of children who received anesthesia at younger ages (0 - 6 mos) had behavioral abnormalities ($P < 0.0001$). Exposure to multiple anesthetic agents versus one anesthetic agent was a significant risk factor for development of behavioral abnormalities ($P < 0.0001$).

Conclusion: The incidence of behavioral abnormalities increased when anesthesia and surgery were accompanied by younger age, longer duration of surgery, and use of multiple anesthetic agents.

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1. Introduction

Experimental studies showed that anesthetic exposure may produce neural damage and apoptosis leading to cognitive impairment [1–6]. These results have raised concern about the long-term effect of early anesthetic exposure in children [7]. (See Fig. 1.)

Studies were conducted to assess changes in neurocognitive development and behavior after surgery and anesthesia in children [8,9]. Various factors associated with the risks that occur after pediatric anesthetic exposure were examined. These factors included the number of anesthetic exposures (single vs multiple), dose of anesthetic agents, type of agents, and age of first exposure [9]. However, different results have been obtained with respect to the studied risk factors, development of learning disabilities, and behavioral abnormalities [10–14].

There are inconsistent results about the long-term effect of anesthetic exposure on children's behavior [9]. The purpose of this study was to determine the effect of commonly used anesthetic agents in a single exposure before the age of 4 years on the development of long-term behavioral changes in a birth cohort of children. The primary outcome was behavioral change as assessed by the Eyberg Child Behavior Inventory (ECBI) [15,16].

2. Materials and methods

2.1. Data collection

The study was approved by the Institutional Review Board at Makassed General Hospital. It was a comparative study consisting of two groups (study and control) and was conducted between October 2012 and March 2013. The medical records of children who underwent anesthesia for

surgery or a diagnostic procedure between January 2004 and December 2005 at Makassed General Hospital were reviewed. Children were included in the study group if they had one anesthetic exposure before the age of 4 years, if they underwent behavioral assessment at age 8–13 years, and their parents gave written, informed consent. Children in the control group had the same inclusion criteria except that they had had no exposure to anesthesia. They were selected from the same institution and they were healthy, without developmental disorders. Exclusion criteria for both groups were prematurity and a complicated neonatal course [born premature, weighing < 2500 g, or admitted to the intensive care nursery (ICN) for any reason], presence of any chronic disease (congenital abnormalities, cardiac diseases, chronic lung diseases, neurological diseases), and any complication during or after surgery.

Children in the study group were identified for the following: surgery or diagnostic procedure (bronchoscopy, gastrointestinal endoscopy, colonoscopy), urgency, total duration of anesthesia, age and weight at the time of the first anesthetic exposure, and number of anesthetic agents (fentanyl, propofol, sevoflurane, nitrous oxide, atracurium, midazolam). Data on gender and parents' educational level were also collected for both groups.

2.2. Behavioral assessment

Behavioral change was assessed by ECBI questionnaire, which was distributed to parents of children in both groups. The ECBI has been validated and used by several studies as a tool to assess behavioral problems in children [15,17,18], and was a concise measure of childhood behavioral problems [19]. Some of the problems it addresses include eating and sleeping habits, aggressiveness, and attention [16]. The ECBI consists of 36 items rated by parents. It has two scales: Intensity and Problem scales. The Intensity scale assesses the frequency of the behavioral problem. Parents are

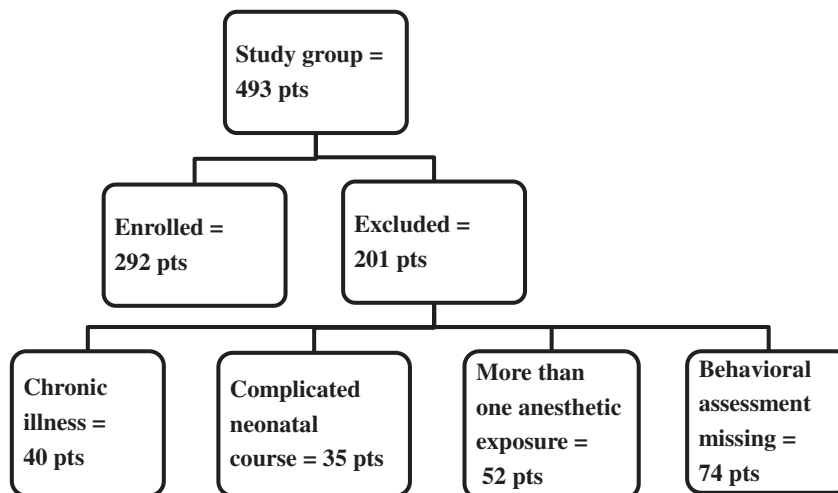


Fig. 1 Flowchart illustrating selection of patients. Pts = patients.

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