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Does the exposure to general anaesthesia in children affect long-term academic and cognitive performance?

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Spanish key words: anestesia; lactante; preescolar; inteligencia.

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Does the exposure to general anaesthesia in children affect long-term academic and cognitive performance?

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Abstract

Authors' conclusions: exposure to anaesthesia before the age of four years has a small association with academic or cognitive performance in adolescence. While more vulnerable groups of children may exist, the low overall difference in academic performance after childhood exposure to surgery is reassuring.

Reviewers' commentary: although this is a minimal and doubtful effect, this information should be taken into account when assessing toddlers for whom we are considering programmed surgery for indications that could be postponed.

Key words: anaesthesia; infant; child; intelligence.

¿La exposición a anestesia general en niños afecta el rendimiento académico y cognitivo a largo plazo?

Resumen

Conclusiones de los autores del estudio: la exposición anestésica a edades menores de cuatro años tiene un efecto pequeño sobre el rendimiento académico o inteligencia en la adolescencia. Aunque pueden existir grupos vulnerables con un riesgo mayor, la baja diferencia global en el rendimiento académico en niños expuestos a cirugía es tranquilizadora.

Comentario de los revisores: aunque se trata de un efecto mínimo y dudoso, es una información que debemos considerar cuando nos planteemos someter niños en edad preescolar a actos quirúrgicos programados que podrían ser aplazados.

Palabras clave: anestesia; lactante; preescolar; inteligencia.

STRUCTURED ABSTRACT

Objective: analysing the association between exposure to anaesthesia and surgery before age 4 years and long-term academic and cognitive performance.

Design: retrospective cohort study.

Setting: Study of national scope. Swedish population born between 1973 and 1993.

Study population: children that had a single exposure to anaesthesia for surgery before age 4 years and no subsequent hospitalizations until age 16 years. The total number of children that underwent surgery in the period under study was 121 498, of which 59 714 were excluded and 61 784 were

eligible, and finally 33 514 were included in the surgery cohort (SC). The control cohort (CC) consisted of 159 619 unexposed children matched 5:1 by sex, month of birth, county of residence at birth and maternal parity. Data were recovered from the Swedish Medical Birth Register and the Swedish Patient Register. Two more groups were analysed: patients with two or more surgeries (secondary cohort, 3640 patients) and patients in the SC that required in-hospital care for any reason between ages 4 and 16 years (tertiary cohort, 54 637 patients).

The exclusion criteria were patients born in or that eventually moved to counties without register coverage, that died before 16 years, at high risk of cognitive impairment by nature of the disease for which surgery was indicated, or with one of several predetermined diagnoses such as cancer or major malformation.

Outcome measurement: the primary outcome was academic performance, assessed by the mean school grades at age 16 years and intelligence test (IT) scores from the military conscription review. The means were normalised to allow for comparison and the final effect was calculated as the difference between the means of the two cohorts expressed as percentage unit change. The authors performed logistic regression to analyse the association of having grades below the 10th percentile, no recorded school grades at age 16 and no available IT scores with other covariates such as age at surgery, type of surgery or number of procedures.

Results: the mean school grades were 0.41% lower in the SC than in the CC (95% confidence interval [95 CI], -0.70 to -0.12). There was heterogeneity between the different types of surgery: -1.22% (95 CI, -1.87 to -0.57) for ENT surgery, or 0.93% (95 CI, 0.12 to 1.75) for urological surgery. There was no association between having grades below the 10th percentile and exposure (odds ratio [OR], 1.02; 95 CI, 0.98 to 1.07). In the secondary cohort, the mean school grades were -1.41% lower (95 CI, -2.31 to -0.50) in children with two procedures and -1.82% lower (95 CI, -3.49 to -0.15) in children with three, while in the tertiary cohort they were -0.87% lower (95 CI, -1.11 to -0.64). The mean IT score for the SC was 0.97% lower than for the CC (95 CI, -1.78 to -0.15).

The authors analysed other variables associated with academic achievement. Mean school grades showed a correlation with being male as opposed to female of -9.88 (95 CI, -10.1 to -9.69), with low versus high maternal educational level of -9.89 (95 CI, -10.2 to -9.61) and with being born in December versus January of -5.34 (95 CI, -5.80 to -4.89).

Conclusions: exposure to anaesthesia at age less than 4 years has a small effect on academic and cognitive performance in adolescence. There may be vulnerable groups that are at higher risk.

Conflicts of interest: the authors had no conflicts of interest.

Funding source: various grants from Swedish institutions.

COMMENTARY

Justification: data from animal model studies suggest that exposure to anaesthetic agents at early ages causes neuronal apoptosis and long-term learning and memory impairment.¹ Since millions of children require anaesthesia for surgical interventions every year, these findings have raised significant concern. At present, there is no conclusive evidence that confirms or refutes the potential neurotoxicity of anaesthetic agents on the developing human brain, which could lead to learning and cognitive impairments in the long term.^{2,3}

Validity/scientific rigour: this was a well-designed retrospective cohort study with a suitable study population and appropriately defined outcome measures, the latter of which were assessed independently within an adequate time frame. The cohort under study seems to be representative of the population, except for the assessment of IT scores, which were only measured in males. The analysis was performed correctly. However, while the authors strived to adjust for potential confounding factors, it is difficult to isolate the effects of anaesthesia from all other perioperative effects (underlying disease, school absences, etc). Similarly, children that underwent ENT surgeries had lower grades than children that underwent other types of surgery, but this could be due to underlying hearing and speech impairments. The researchers also made the effort to estimate the duration of anaesthesia, but did not take this factor into account in the assessment of its effects. It would have been interesting to learn whether longer duration of anaesthesia exposure was associated with a larger effect.

Clinical relevance: children exposed to anaesthesia had mean school grades that were 0.41% lower (and this difference was greater in children that underwent several surgeries) and a mean IT score that was 0.97% lower compared to unexposed children. These differences are minimal, with the lower bound of the confidence interval approximating the absence of difference, and far from the differences observed based on maternal educational level, sex, or month of birth. Observational studies conducted on smaller samples have found variable outcomes. However, one multicentre randomised controlled trial (RCT)⁴ did not find significant differences between the effects of regional and general anaesthesia. This recent RCT was designed to reduce the impact of confounding factors on the observed effect.

Applicability to clinical practice: the findings of the study are applicable in our area. Although the effect was minimum and is not corroborated by other studies, it is information that we need to take into account if we are considering subjecting preschool-aged children to scheduled surgical interventions that could be postponed. Since children considered high-risk were excluded from the study, we do not know whether the effect found would differ in this subset of children.

Conflicts of interest: the authors of the commentary have no conflicts of interest to declare.

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