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Anaesthesia mode for caesarean section and mortality in very preterm infants: An epidemiologic study in the EPIPAGE cohort

V. Laudenbach,[a] F. J. Mercier,[b] J.-C. Rozé,[c] B. Larroque,[d] P.-Y. Ancel,[d] M. Kaminski,[d] G. Bréart,[d] P. Diemunsch,[e] D. Subtil,[f] C. Lejus,[g] J. Fresson,[h] C. Arnaud,[i] B. Rachet,[j] A. Burguet,[k] G. Cambonie[l], Epipage Study Group *

[a] *Department of Neonatology and Pediatric Intensive Care & EA 4309 NeoVasc Research Group, Rouen Institute for Biomedical Research, University of Rouen, Rouen, France*
[b] *Department of Anesthesiology, Assistance Publique – Hôpitaux de Paris, Antoine Béclère University Hospital, Clamart & University of Paris XI, France*
[c] *Department of Perinatalogy, University Hospital, Nantes, France*
[d] *INSERM U149, Epidemiological Research Unit on Perinatal and Women's Health, Villejuif, France*
[e] *Department of Anesthesiology, University Hospital, Strasbourg, France*
[f] *Department of Obstetrics and Gynecology, University Hospital, Lille, France*
[g] *Department of Anesthesiology, University Hospital, Nantes, France*
[h] *Department of Neonatology, University Hospital, Nancy, France*
[i] *INSERM U 558, Toulouse, France*
[j] *Department of Anesthesiology, University Hospital, Rouen, France*
[k] *Department of Neonatology, University Hospital, Dijon, France*
[l] *Department of Neonatology, University Hospital, Montpellier, France*

ABSTRACT

Background: Little is known about the influence of anaesthesia for caesarean section on outcome in very preterm infants.
Methods: A prospective, population-based, cohort study (the EPIPAGE cohort) included all births before 33 weeks in nine French regions in 1997. Of 2360 infants live-born between 27 and 32 weeks, 1338 were delivered by caesarean section with general anaesthesia (n = 711, 53.1%), spinal anaesthesia (n = 419, 31.3%), or epidural anaesthesia (n = 208, 15.6%). Neonatal mortality was compared among these three groups using bi- (according to gestational age and to anaesthetic technique) and multivariate analyses.
Results: Neonatal mortality was 10.1% with general anaesthesia, 12.2% with spinal anaesthesia and 7.7% with epidural anaesthesia. After adjustment for gestational age and characteristics of pregnancy, delivery and neonate, spinal anaesthesia was associated with a higher risk of neonatal death than general anaesthesia (adjusted odds ratio, 1.7; 95% confidence interval 1.1 to 2.6).

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Correspondence to: Vincent Laudenbach, M.D., Ph.D., Professor of Anesthesiology, Service de Pédiatrie Néonatale et Réanimation, CHU Charles Nicolle, 1 rue de Germont, 76031 Rouen Cedex, France.
E-mail address: vincent.laudenbach@chu-rouen.fr

* The EPIPAGE Study Group includes the following: B Larroque (national coordinator), PY Ancel, B Blondel, G Bréart, M Dehan, M Garel, M Kaminski, F Maillard, C du Mazaubrun, P Missy, K Supernant (INSERM U149, Paris, France); M Durand, J Matis, J Messer, A Treisser (Hôpital de Hautepierre, Strasbourg, France); A Burguet, L Abraham-Lerat, A Menget, P Roth, J-P Schaal, G Thiriez (University Hospital St Jacques, Besançon, France); C Lévêque, S Marret, L Marpeau (University Hospital Charles Nicolle, Rouen, France); P Boulot, J-C Picaud (University Hospital Arnaud de Villeneuve, Montpellier, France); A-M Donadio, B Ledésert (Regional Health Observatory of Montpellier, France); André, J. Fresson, JL Boutroy, JM Hascoët (University Regional Maternity, Nancy, France); C Arnaud, S Bourdet-Loubère, H Grandjean (INSERM U558, Toulouse, France); M Rolland (Children Hospital, Toulouse, France); C Leignel, P Lequien, V Pierrat, F Puech, D Subtil, P Truffert (University Hospital Jeanne de Flandre, Lille, France); G Boog, E Le Mauff, V Rouger-Bureau, J-C Rozé (University Mothers & Children Hospital, Nantes); P-Y Ancel, G Bréart, M Kaminski, C du Mazaubrun (INSERM U149, Paris, France), M Dehan, V Zupan (University Hospital Antoine Béclère, Clamart, France); M Vodovar, M Voyer (Institut de Puériculture, Paris, France).

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Conclusion: In this population-based study, spinal anaesthesia was associated with an increased risk of neonatal mortality in very preterm infants compared to general anaesthesia (and epidural anaesthesia), independently from gestational age and characteristics of the pregnancies, deliveries and neonates. Although this multivariate analysis does not prove a causal relationship, the results suggest it could exist, particularly if maternal haemodynamics are poorly controlled. With recent significant change in the conduct of spinal anaesthesia, further studies are needed to investigate potential harmful effects of anaesthesia on very preterm infants delivered by caesarean section.

Keywords: Caesarean section; Premature infants; Mortality; Anaesthesia; Obstetrical

Introduction

The risk of anaesthesia-related maternal death during caesarean section (CS) is lower with neuraxial than with general anaesthesia (GA) in retrospective studies.[1] Randomised trials with maternal mortality as a primary outcome are lacking, because the maternal mortality rate is so low.[2] The expert opinion of most obstetric anaesthesiologists is that neuraxial anaesthesia has many advantages over general anaesthesia, in terms of maternal blood loss, safety and postoperative pain control.[3,4] Nonetheless, a 2006 Cochrane review failed to show that major maternal outcomes were better with neuraxial than with general anaesthesia.[5] The main disadvantage of spinal anaesthesia (SA) is the risk of maternal hypotension with possible deleterious effects on uteroplacental perfusion and subsequent acute fetal distress.[3,5–7] The influence of maternal anaesthesia on neonatal variables has been studied in term and, to a lesser extent, in preterm newborns.[5,7–9] Significant differences have been found among anaesthesia modalities in umbilical acid-base measurements and early adaptation of infants to extrauterine life as assessed by the Apgar scores. A cohort study[8] and a large epidemiological study[9] showed an increased risk of fetal acidaemia after neuraxial anaesthesia as compared to GA and an even greater increase after SA compared to epidural anaesthesia (EA). Two meta-analyses comparing the influence on the newborn well-being of two or three different types of anaesthesia for CS yielded different conclusions.[5,7] Reynolds and Seed included 27 studies in their analysis and found that the use of SA was associated with significantly lower umbilical pH and higher base deficit than were both GA and EA.[7] On the other hand, Afolabi et al. looked at several measures of maternal and neonatal outcome in 16 prospective studies, but included only three studies comparing umbilical artery pH (and excluded base deficit) in SA and GA, and did not confirm the former results.[5] Until now, no difference in neonatal mortality has been demonstrated by any study.[9,10] In addition, the studies included in these two meta-analyses spanned from 1965 to 2005.[5,9] Over this important period of time, there have been significant changes in the practice of SA, yielding marked improvement in haemodynamic control.

Few studies have been done in very premature infants (VPIs), i.e. infants born before 33 weeks.[10] In recent epidemiological studies, the incidence of very premature birth was as high as 1.3 per 100 live births and stillbirths.[11,12] VPIs have high rates of mortality compared to term infants.[12] Therefore, we designed this study to assess the possible influence of maternal anaesthesia mode on the rate of neonatal mortality in VPIs delivered by CS.

Methods

The prospective population-based cohort study EPIPAGE (Etude éPIdémiologique sur les Petits Ages Gestationnels) included all births (live births and stillbirths) before 33 weeks that occurred in 1997 in nine (of 22) administrative French regions.[13] Among the 2360 live-born infants delivered between 27 and 32 weeks in 158 maternity hospitals, 1440 (61%) were delivered by CS. The present work is a secondary analysis of the EPIPAGE database, focusing only on babies born by CS. We aimed to test the hypothesis that there would be a statistical association between mode of anaesthesia used for CS and mortality among very preterm infants. We excluded infants for whom the mode of anaesthesia was not known ($n = 51$) or for whom several modes were used in combination or successively ($n = 51$). This left 1338 infants born to 1128 mothers, 711 under GA (53.1%), 419 under SA (31.3%) and 208 under EA (15.6%).

The EPIPAGE cohort study involved prospective collection of 1350 items on the mothers, pregnancies, deliveries, infants, neonatal resuscitation procedures, other treatments, and obstetrics and neonatology units to which the mothers and infants were admitted, with the goal of further characterizing short- and long-term outcomes in VPIs.[13] Data on pregnancy and delivery were collected during the maternity hospital stay by midwives, who were aware of the anaesthesia mode, while data on infants during the neonatal intensive care unit (ICU) stay were collected by neonatologists. In the present study, we paid special attention to the characteristics of pregnancies, deliveries, and infants previously reported to be associated with neonatal mortality.