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Title: Caesarean section in labour and neonatal morbidity after epidural analgesia or remifentanil-PCA in breech and twin deliveries
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INTRODUCTION	METHODS
A recent Cochrane review comparing remifentanil-PCA with alternative parenteral labor analgesic modalities noted that there is currently low-quality evidence to inform clinical practice regarding maternal and neonatal safety outcomes for remifentanil-PCA (maternal apnoea and respiratory depression as well as neonatal Apgar score) (1). Our group found no evidence of increased CS rate, serious maternal complications, operative vaginal delivery rate, non-reassuring fetal status during labor, and Apgar score of less than 7 at five minutes from birth with remifentanil-PCA compared to EA (2). However, it is unclear if data on labor outcomes associated with EA and remifentanil-PCA can be generalized to all groups of women in labor. This is especially true for vaginal breech and twin deliveries, where associated problems like prematurity, trauma, and hypoxia necessitate special anesthetic and obstetric considerations. When strict criteria are met before and during labor, planned vaginal delivery of singleton fetuses in breech presentation at term as well as twins with the first twin in cephalic presentation, remains a safe option. Nevertheless, comparative data on the potential impact of various forms of labor analgesia on the mode of delivery and neonatal complications in vaginal deliveries of singleton breech fetuses and twins remain scarce. The objective of the present study was to explore the associations between type of labor analgesia (EA vs. remifentanil-PCA) and CS in labor, maternal outcomes (postpartum hemorrhage and perineal trauma) as well as neonatal outcomes (low Apgar score, birth asphyxia and neonatal admission to intensive care unit (NICU)) in planned breech and twin vaginal births.	We analyzed the Slovenian National Perinatal Information System (NPIS) data from 2013 to 2021. We included planned vaginal breech and twin deliveries at the Department of Perinatology, University Medical Centre Ljubljana. The following criteria for trial of vaginal breech delivery have been followed throughout the study period: no contraindication to vaginal birth (e.g. placenta previa); estimated fetal weight at least 2500 g and not more than 4000 g; no hyperextension of the fetal head (i. e., an extension angle of greater than 90 degrees); frank or complete breech presentation (incomplete or footling breech presentations were considered contraindications); adequate maternal pelvis; absence of fetal anomaly that may cause dystocia; staff skilled in breech delivery and immediate availability of facilities for safe emergency cesarean delivery; and no cord presentation. In twins, vaginal delivery was recommended when the presenting twin was in cephalic presentation. In the present study, we included women who received either remifentanil-PCA or EA at $\geq 37^{+0}$ weeks for singleton breech deliveries or twin deliveries at $\geq 34^{+0}$ weeks. Only women with spontaneous onset of labor or induction of labor were included in the analysis. Women with planned (pre-labor) CS were excluded from the analysis. Decision on labor analgesia method (remifentanil-PCA or EA) was taken by women during labor after consulting with anesthesiologists, obstetricians and midwives. The pre-specified outcomes studied were rates of CS in labor, postpartum hemorrhage (defined as > 500 mL weighted blood loss and need for at least one unit of red blood cell transfusion), OASI (obstetric anal sphincter injury, i.e. 3rd or 4th degree perineal tears) rates, Apgar score of < 7 at 5 minutes after birth, birth asphyxia (diagnosed by attending neonatologist and classified as mild to moderate (ICD-10 code P21.1) or severe (ICD-10 code P21.0)), and neonatal intensive care unit (NICU) admission. The second twin’s Apgar score of < 7 at 5 minutes, birth asphyxia rates and NICU admission were analyzed for twin deliveries. We chose to focus on the second twin’s adverse neonatal outcomes, as labor complications after the birth of the first twin can potentially be attributed to the method of labor analgesia and given the higher risk of adverse outcomes for the second twin reported in most observational studies to date.

RESULTS and DISCUSSION
371 deliveries fulfilled the inclusion criteria; 127 term breech and 244 twin births. In term breech, there were no significant differences between the groups regarding maternal age, body-mass index, nulliparity, assisted conception, mode of onset of labor, gestational age at delivery, fetal birth weight, and fetal size. In twins at $\geq 34^{+0}$ weeks of gestation, the maternal body-mass index at delivery was significantly lower, and the proportion of nulliparous women was higher in the EA group. The birth weight of the first and second twins was statistically lower in the EA group. In both, breech and twin deliveries, there were no statistically significant nor clinically relevant differences between EA and remifentanil-PCA groups in terms of intrapartum CS rates, postpartum hemorrhage and OASI rates as well as in terms of low Apgar scores, birth asphyxia and NICU admission. In conclusion, data on the safety of different analgesic methods in breech and twin deliveries are limited to a few older retrospective studies; hence more recent studies are imperative to inform modern practice. In the present study, we analyzed data obtained from the Slovenian National Perinatal Information System and found that type of labor analgesia (EA vs. remifentanil-PCA) was not associated with a higher risk of intrapartum CS, postpartum hemorrhage, OASI, Apgar score of < 7 at 5 minutes after birth, birth asphyxia or NICU admission in breech and twin deliveries. Our findings suggest that the current use of EA and remifentanil-PCA is safe for pain relief in singleton breech and twin deliveries.
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