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A review of randomized trials comparisons of epidural with parenteral forms of pain relief during labour and its impact on operative and cesarean delivery rate

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ABSTRACT

Objectives: The aim of this review was to summarise the available literature on different modalities of labour pain relief (epidural vs. parenteral) and to assess their impact on the rate of caesarean section deliveries and instrumental deliveries, and on the need to support the uterine contractile function.

Material and methods: The PubMed, Web of Science and Cochrane databases were reviewed to identify articles describing the effect of labour pain relief on the course of labour. This review includes 16 studies with 7150 patients.

Results: The analysis of the obtained data revealed that epidural analgesia (EA) or combined epidural and spinal anaesthesia (CESA) provided significantly better labour pain relief when compared with parenteral opioids. Conduction anaesthesia was not associated with an increase in the caesarean section delivery rate. Some authors concluded that conduction anaesthesia was associated with the need for assisted delivery.

Conclusions: Epidural analgesia is a well-recognised method of labour pain relief. It is associated with the parturient's higher satisfaction when compared to parenteral opioids. EA does not directly increase the caesarean section delivery rate, yet it can lead to instrumental deliveries (vacuum-assisted, obstetrics forceps) and a need to pharmacologically support the uterine contractile function. Further studies are required to evaluate the effect of EA on the course of labour, and methods of minimising its adverse effects.

Key words: epidural analgesia, labour, delivery, caesarean section, instrumental delivery

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INTRODUCTION

The International Association for the Study of Pain (IASP) defines pain as an unpleasant, subjective physical or emotional experience associated with actual or potential tissue damage [1]. Pain plays a protective-warning role and is a specific symptom of potential danger and releases a behavioural and reflexive body response aimed at limiting the results of such an injury [2]. As labour pain is not associated with any disease or trauma, it is physiological in nature and one of a kind. Its presence does not indicate any pathology, but the progression of labour itself. It differs from other forms of pain experienced by human beings. Its characteristic features include the completion of physiological pregnancy, a quick increase in intensity and frequency as well as an interrupted nature. The intensity of suffered pain varies among women in labour: some deliveries are rapid and the parturient does not experience any labour pain, while others describe their labour pain as the most intense a woman can experience in her entire life. Labour pain is managed not only to comfort the parturient, but also to beneficially influence the condition of the foetus and the course of the labour [3]. The standards of pain management during labour are described in the Ministry of Health Regulation of November 9th 2016 (Journal of Laws 2016, item 618, with subsequent amendments) [4].

The modern obstetric practice aims at presenting the pregnant woman and her partner with a comprehensive

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overview of the course of the labour, including the methods of pain management. Epidural analgesia is gaining popularity in obstetrics departments as a method of labour pain relief. Scientific research provides growing evidence that epidural analgesia (EA) is an effective method of labour pain management, yet it may prolong the total duration of labour and represent a risk for instrumental deliveries. Pregnant women and their relatives may acquire knowledge on analgesia from different sources and some of these data are incomplete or even untrue. Midwives, obstetricians and anaesthetists should, therefore, provide each pregnant woman with information on methods of labour pain relief, especially epidural analgesia. Many women may experience complete satisfaction from pain-free, dignified labour with only minimal professional support or with the use of the simplest methods such as verbal calming, respiratory exercises, relaxation, percutaneous nerve stimulation or the selection of a convenient body position. The physiological response of a parturient to labour pain has a significant influence on the condition of both herself and the foetus, as well as the progress of the labour. Pain itself is a strong impulse which activates the respiratory system, increasing the minute volume and oxygen consumption during contractions. Psychological factors such as anxiety or fear are not of negligible significance for the initiation of hyperventilation. The stress reaction stimulates the parturient's sympathetic system, which leads to the release of catecholamines, and an increase in arterial pressure and cardiac output. A stress-related adrenalin release results in the reduction of uterine contractile activity, concomitantly prolonging the duration of the labour. Noradrenaline, which is released with adrenalin, leads to the contraction of blood vessels due to the reduction of the uterine-placental blood flow, which, in turn, may result in foetal hypoxia and acidosis [5].

Medical indications for the introduction of labour pain relief methods include subjective pain intolerance, parturient request, and certain respiratory conditions (e.g. bronchial asthma), cardiovascular diseases (heart defect, arterial hypertension), renal diseases and diabetes [6]. The method of pain management is selected according to the type of labour initiation (spontaneous or induced) as well as the type of medical intervention (episiotomy, vacuum-assisted vaginal delivery, forceps delivery) [7].

An increase in the caesarean section delivery rate was observed in the last few decades [8]. A similar trend was observed in Polish hospitals, where it reached from 23.6% up to 77.9% in 2014 [9]. Thus, it significantly exceeded the rate recommended by the WHO till 2014, i.e. 10–15% [10]. According to the report issued by the OECD, the highest caesarean section delivery rate is noted in Poland (36.2%) [11]. Caesarean section delivery increases the maternal and foetal mortality rates, as well as the rate of perinatal complications [12]. Some authors associated the increase in the caesarean section delivery rate with the use of epidural analgesia, yet this was mostly a result of faulty research design (retrospective studies instead of randomised trials), small study populations and the enrolment of both nulliparous and multiparous women, who present significantly different indications for caesarean sections [13]. The caesarean section delivery rate is also influenced by the level of anxiety and labour pain. Therefore, epidural analgesia should be considered in every parturient with tokophobia, which should effectively reduce the caesarean section delivery rate [12].

Objectives

The aim of this review was to summarise the available literature on different modalities of labour pain relief (epidural vs. parenteral) and to assess their impact on the rate of caesarean section deliveries and instrumental deliveries, and on the need to support the uterine contractile function.

MATERIAL AND METHODS

Search strategy

The PubMed, Web of Science and Cochrane databases were reviewed using the following keywords: caesarean section, epidural, parenteral analgesia, pain relief, labour, caesarean section delivery rate and instrumental delivery to identify articles describing the effect of labour pain relief on the course of labour. The search was limited to full-text articles published in Polish or English. Single key words as well as their combinationsusing AND and/or OR operators were used. The number of obtained results was reduced as subsequent abstracts were analysed and a new database was created for review. The analysis included the references provided with each article. As a result, 16 full-text articles concerning randomised trials were selected. If there was more than one article by the same author concerning the same clinical problem, only the most recent study was selected. This review includes 16 studies with 7150 patients (Fig. 1).

Study selection

This review includes randomised trials describing the impact that different methods of labour analgesia have on the course of labour. The exclusion criteria were:

- opinions and case studies, as well as articles published in languages other than Polish or English;
- studies with less than 20 participants;
- surveys conducted to ascertain maternal opinions of various methods of pain relief during labour;
- studies with missing data which were crucial for the review.

Data extraction

The reviewers independently assessed the articles that had been selected using a standardised chart (Tab. 1) to

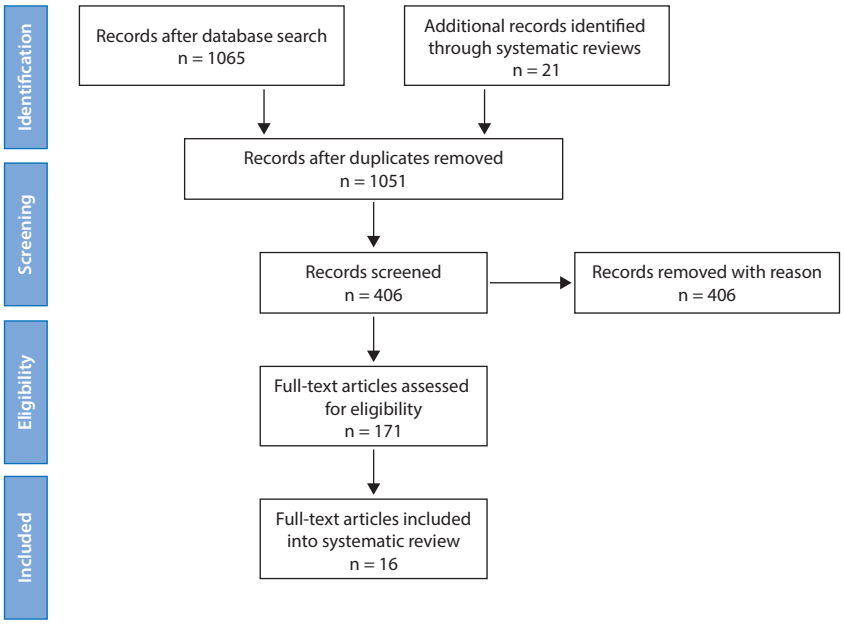

Figure 1. Scheme for articles qualified for a systematic review

register the required data. These data included the name of the first author, publication year, number of participants, a method of analgesia and results. The quality of each study was assessed based on the following criteria:

- description of the study inclusion/exclusion criteria;
- a detailed description of pain management during labour;
- number of study participants;
- use of standardised tools for pain level assessment;
- description of factors influencing the final number of participants and methods of allocation to the study group.

RESULTS

The analysis of obtained data revealed that epidural analgesia (EA) or combined epidural and spinal anaesthesia (CESA) provided significantly better labour pain relief [13–22] when compared with parenteral opioids. Most authors indicate that epidural analgesia prolongs the first and/or the second labour stages [13, 15, 17, 19, 23–27]. Conduction anaesthesia was not associated with an increase in the caesarean section delivery rate [13, 14, 16–18, 20–22, 24–26, 27]. It was only Thorp et al. and Ramin et al. who observed a significant increase in the caesarean section delivery rate after epidural analgesia ($p < 0.05$ and $p = 0.002$, respectively). Some authors concluded that conduction anaesthesia was associated with the need for forceps or vacuum-assisted delivery [13, 15, 19, 26, 27]. Howell et al. studied the effect of epidural analgesia on long-term back pain, yet no association was found between such a procedure and chronic back pain.

DISCUSSION

The analysis revealed the superiority of EA/CESA over other methods of labour pain relief. However, conduction anaesthesia increased the need for forceps/vacuum-assisted delivery [13, 15, 19, 26, 27], which may prove that conduction anaesthesia plays a role in the dynamics of the second stage of delivery. Despite the fact that most authors indicated the prolongation of labour, there are some contradicting trials. Rogers et al. studied the effect of early and delayed EA on the labour duration and the caesarean section delivery rate. They found that early EA was not associated with the prolongation of labour and did not increase the number of performed caesarean sections. The total labour duration was shorter in comparison with the control group ($p = 0.04$) [29]. Gupta et al. did not observe the influence of EA on either the prolongation of labour ($0 > 0.05$), the instrumental delivery rate or the caesarean section delivery rate [30]. A retrospective study performed by Fogel et al. revealed that women who requested EA more frequently experienced abnormalities during physiological labour, which was associated with more severe pain. Labour complications could have an influence on the level of experienced pain. It was the lack of progress in labour, not EA, which increased the caesarean section delivery rate [31]. Naik et al. studied the influence of early vs. delayed conduction anaesthesia on the duration of the first stage of delivery. They showed that early EA (cervix dilation up to approx. 3 cm) was associated with a shorter time to full cervix dilation ($p = 0.0001$ for nulliparous and $p = 0.003$ for multiparous). The caesarean section delivery rate was 6% in both groups (early vs. delayed EA) [32]. The satisfaction level in women who had early EA was higher than in the other group.

Table 1. A summary of the available literature on the use of various methods to relieve the pain of delivery (epidural vs parenteral)

Author	Year	Study design	Participants	Analgesic treatment	Outcomes
Philipsen T et al. [14]	1989	Randomized prospective study	112	**Epidural** (0.375% bupivacaine 1 ml/10 kg body weight) **vs** **Pethidine IM** (75 mg; repeated if requested); All pts were offered 50% nitrous oxide. 85% in epidural group vs 86% in Pethidine group had a pudendal block	Pain ratings in the epidural group were significantly lower than in the pethidine group in the first stage of labour; 9/57 pts in the epidural group used nitrous oxide vs 29/54 pts in the pethidine group. Cesarean section was not significantly higher than in thaepethidine group
Thorp JA et al. [15]	1993	Randomized controlled prospective trial	93	**Epidural** (0.25% bupivacaine infusion) **vs** **Pethidine IV** (75 mg) and promethazine (25 mg) every 90 min as required	Epidural analgesia resulted in a significant prolongation in the first and second stages of labour and a significant increase in the frequency of Cesarean section ($p < 0.05$)
Ramin SM [16]	1995	Randomised trial	869	**Epidural** (3 ml boluses of 0.25% bupivacaine until T-10 sensory block was achieved followed with 0.125% bupivacaine infusion + 2 µg/ml fentanyl at 8–10 ml/hr) **vs** **Meperidine IV** bolus (50 mg) + 25 mg promethazine followed with 50 mg meperidine bolus on request to a maximum 200 mg in 4 hours	Cesarean section rate was higher in the epidural group ($p = 0.002$). The duration of labour was prolonged in the epidural group ($p = 0.001$). Low forceps deliveries were more frequent in the epidural group. Epidural analgesia provided better pain relief compared to parenteral meperidine ($p < 0.001$)
Bofill JA et al. [17]	1997	Randomized trial	100	**Epidural** (0.25% bupivacaine **±?** 50–100 µg fentanyl until sensory analgesia achieved; continuous infusion of 0.125% bupivacaine + 1.5 µg/ml fentanyl) **vs** **Butorphanol** (1–2 mg IV)	There were no significant differences between the lengths of the first or second stages of labour. 8% of deliveries in the epidural group and 6% in the narcotic group ended in Cesarean section
Clark A et al [18]	1998	Randomized prospective trial	318	**Epidural** (bolus with 0.25% + 50 µg fentanyl over 30 min. period, followed with continuous infusion 0.125% bupivacaine + 1 µg/ml fentanyl) **vs.** **Meperidine IV** (50–75 mg every 90 min as needed)	Patients in the epidural group were 3 times more likely to have an active phase duration ≥ 8 hours and were 10 times more likely to require ≥ 2 hours in the second stage of labour than those in the opioid group. There were no significant differences in Cesarean delivery rates (7.7% in the opioid group and 8.8% in the epidural group)
Gambling DR et al. [19]	1998	Randomized trial	1223	**CSE** (bolus of 10 µg sufentanil into subarachnoid space; then through epidural catheter bolus of 0.25% bupivacaine was injected followed with 0.125% bupivacaine + 2 µg/ml fentanyl continuous infusion) **vs.** **Meperidine IV** (50 mg) + promethazine (25 mg), followed with meperidine on request every hour to maximum 200 mg	Parturients in CSE group were more likely to be nulliparous and the duration of labour was significantly longer in both stages ($p < 0.0002$). Emergency Cesarean section was performed in 9/616 patients in the CSE group and in 0/607 in meperidine group
Loughnan BA et al. [20]	2000	Randomized controlled study	802*	**Epidural** (10–15 ml bolus of 0.25% bupivacaine followed with 0.125% bupivacaine continuous infusion) **vs.** **Pethidine IM** (100 mg every 2 hours repeated up to 300 mg)	The epidural group showed better pain relief during the first and second stages of labour. Cesarean section rates were similar in both groups

Table 1 (cont.). A summary of the available literature on the use of various methods to relieve the pain of delivery (epidural vs parenteral)

Lucas MJ et al. [21]	2001	Randomized trial	738	**Epidural** (0.25% bupivacaine boluses until sensory analgesia achieved followed with a continuous infusion of 0.125% bupivacaine + 2 µg/ml fentanyl) **vs.** **Meperidine IV** bolus (50 mg) + 25 mg promethazine followed with PCA infusion up to 15 mg meperidine every 10 minutes	Epidural analgesia was associated with a significantly prolonged second stage of labour and an increase in forceps deliveries. Cesarean delivery rates were similar. Pain relief was superior with the epidural method
Howell CJ et al. [22]	2001	Randomized controlled study	369	**Epidural** (10 ml bolus 0.25% bupivacaine, followed with boluses of 5–10 ml 0.25% bupivacaine, as required) **vs.** **Pethidine IV** (50–100 mg) — repeated according to standard midwifery practice. Entonox remained freely available to both groups	There was no significant difference in the length of the first stage; the length of the second stage was significantly increased in the epidural group. The rate of instrumental delivery was higher in the epidural group (30%) than in the non-epidural group (19%): p = 0.03. There was no difference in caesarean section rate. There was no evidence to support the suggestion of a direct association between the use of epidural anaesthesia in labour and the incidence of long-term backache
Dickinson JE et al. [23]	2002	Prospective randomised controlled clinical trial	992**	**CSE** (spinal block with 25 µg of fentanyl and 2 mg bupivacaine, 6 ml bolus of 0.125% bupivacaine through the epidural catheter followed with patient controlled epidural with 0.1% bupivacaine and 2 µg of pethidine) **vs.** **Pethidine IM**, nitrous oxide inhalation and TENS (Continuous midwifery support group, CMS)	The duration of labour was shorter in CMS group compared with epidural group (p = 0.039): the median duration of the first stage was 8.9 hours vs 9.5 hours (p = 0.069), and the median duration of the second stage was 1.33 hours vs 1.48 hours (p = 0.034). There was no significant difference in the caesarean section rates. The need for any operative delivery was significantly lower in CMS (p = 0.019)
Sharma SK et al. [13]	2002	Randomised study	449***	**Epidural** (initiated with 0.25% bupivacaine, maintained with 0.0625% bupivacaine + fentanyl 2 µg/ml at 6 ml/h with 5 ml bolus doses every 15 min as needed using a patient-controlled pump) **vs.** **Meperidine IV** (50 mg) + 25 mg promethazine as an initial bolus followed with 15 mg meperidine every 10 min as needed (patient controlled pump); additional 25 mg doses were administered not to exceed 100 mg in 2 hours	Epidural analgesia was significantly associated with prolongation of the first (p = 0.03) and second (p = 0.008) stages of labour, need for augmentation of labour with oxytocin (p = 0.01). 12% of women receiving epidural analgesia had forceps deliveries compared with 3% in the parenteral analgesia group (p < 0.001). The overall cesarean rates for epidural analgesia and intravenous meperidine analgesia were 7% and 9% (p = 0.61), respectively
Head BB et al. [24]	2002	Randomised trial	116****	**Epidural** (3 ml test bolus of 0.25% bupivacaine, then incremental bolus doses of 3–5 ml 0.25% bupivacaine to obtain sensory analgesia, followed with a continuous infusion of 0.125% bupivacaine + 2 µg fentanyl — 10 ml/hr **vs.** **Meperidine IV** (PCA) 10 mg and lockout interval of 10 minutes. Maximum dose of 240 mg in 6 hours + IV promethazine 25 mg every 4 hours	Epidural analgesia provided significantly better pain relief. The cesarean delivery rates in the epidural group (18%) and the PCA group (12%) were similar (p = 0.35)

Table 1 (cont.). A summary of the available literature on the use of various methods to relieve the pain of delivery (epidural vs parenteral)

Jain S et al. [25]	2003	Randomized study	128	**Epidural** (test dose 0.25% bupivacaine with adrenaline 1:200 000; followed with 10 ml bolus 0.25% bupivacaine + 30 µg fentanyl, repeated after 2 hours if needed; if fentanyl was reduced to 15 **ug** or anagesia was insufficient: a continuous infusion of 0.1% bupivacaine + 1 µg/ml fentanyl was commenced at 10 ml/hour) **vs.** **Meperidine IM** (50–100 mg) every 4 hours **Tramadol IM** (1 mg/kg body weight, to a total limit 200 mg in 24 hours)	Epidural caused a significant prolongation of first ($p < 0.05$) and second ($p < 0.01$) stage of labour with an increased number of operative deliveries (27% in the epidural, 7.6% in the meperidine, and 11.4% in the tramadol groups; $p < 0.05$). The analgesic efficacy and maternal satisfaction were better with epidural analgesia than with opioids
Long J et al. [26]	2003	Randomised study	80*****	**CSE** (spinal administration of 2.5 mg ropivacaine + 5 **ug** fentanyl; then epidural infusion 0.1% ropivacaine + 1.5 µg/ml fentanyl — background infusion 4 ml/hour and 4 ml patient-controlled boluses (lockout time 15 min) **vs.** **Tramadol IV** (1 mg/kg body weight bolus followed with backgroud infusion of 2 ml/hour of 0.75% tramadol; PCA dose 2 ml if needed, to a total dose of 400 mg)	The analgesic efficacy was better in the CSE group compared with the tramadol group ($p < 0.05$). The cesarean delivery rate was significantly higher in the control group (no analgesia) — $p < 0.01$, but did not differ between CSE and tramadol groups
Douma MR [27]	2011	Randomised study	20	**Epidural** (0.2% ropivacaine 12,5 ml loading dose followed with a continuous infusion of 0.1% ropivacaine + sufentanil 0.5 µg/ml at 10 ml/hr) **vs.** **Remifentanil PCA** (40 µg loading dose and boluses of 40 µg with a 2-minute lockout time; maximum dose limit of 1200 µg/hr)	There were no differences in average instrumental or cesarean delivery rates between the groups. In the epidural group, there was a significant decrease in pain scores ($p < 0.05$ 2 hr after pain treatment initiation; $p < 0.01$ 1 and 3 hr after pain treatment initiation)
Freeman LM [28]	2015	Randomised trial	1136	**Epidural** (ropivacaine/sufentanil; bupivacaine/sufentanil; levobupivacaine/sufentanil; bupivacaine/fentanyl) **vs.** **Remifentanil** (solution 20 **ug**/ml) 30 µg delivered on request (PCA) with a 3 min. lockout time (the dose could be increased to 40 µg — in case of insufficient pain relief or decreased to 20 µg in case of excessive side effects)	Cesarean section rate was the same in both groups (15%). Satisfaction scores were significantly lower in the remifentanil group ($p < 0.001$). Pain relief scores were significantly higher in the epidural group ($p < 0.001$)

*608 had epidural/parenteral narcotic; the remaining group did not require any analgesia or received nitrous oxide (Entonox)
**493 patients were assigned to an epidural group, but 136 did not receive an epidural
***Out of 226 in epidural group 214 followed protocol, in intravenous group protocol was followed in 207 participants (out of 233)
****7 women did not receive their allocated treatment
*****30 randomly assigned women did not receive any analgesia at all

On the other hand, however, Ohel et al. observed that early EA (performed after the first request expressed by the parturient) did not result in an increase in the caesarean section delivery rate or the assisted delivery rate, and moreover, led to a shortening of the first stage of delivery and an increase in parturients' satisfaction [33].

Thorpe et al. and Ramin et al. showed that conduction anaesthesia led to an increase in the caesarean section delivery rate. A similar conclusion was drawn by Kaul et al. as they observed a higher incidence of forceps/vacuum-assisted deliveries and caesarean sections. However, they also showed that it resulted from straightforward causality, as women whose labour lasted longer and was more painful more frequently decided to have EA performed [34]. The increase in the caesarean section delivery rate was also observed in the study conducted by Lieberman et al. in 1996. The two former trials were retrospective in nature, easily burdened by bias [35]. Some authors established a relationship between EA and an increase in the instrumental delivery rate [13, 16, 21–23]. In a 1977 study, Hoult et al. stated that conduction anaesthesia led to an increased frequency of forceps and vacuum-assisted deliveries (the incidence was 70% in nulliparous and 40% in multiparous) [36]. Initially, EA was only performed in women with obstetric complications, which made instrumental deliveries more probable. One of the methods to avoid such a high rate of forceps/vacuum-assisted deliveries could have been the reduction of local anaesthetics the concentration and control of the delivery rate so that the sense of feeling returns during the second stage of delivery [36, 37]. The retrospective trial published in 1999 by Yancey et al., which included 9637 women compared over 20-month-long periods before and after the introduction of the EA on request strategy, in turn, proved not to increase the instrumental and caesarean section delivery rates [38].

There are some limitations associated with the above-mentioned analysis — various scales (e.g. for pain assessment) were used by different authors, different patient groups were included in the trials (nulliparous and multiparous), and data were presented in a way which precluded their comparison. Another limitation was the large group of women who, despite being assigned to the parenteral opioid group, decided to have EA. It would be immoral to deny them such a possibility, yet it could have an effect on the final conclusions.

CONCLUSIONS

Epidural analgesia is a well-recognised method of labour pain relief. It is associated with the parturient's higher satisfaction when compared to parenteral opioids. EA does not directly increase the caesarean section delivery rate, yet it can lead to instrumental deliveries and the need to support the uterine contractile function. They, in turn, result in mechanical and mental trauma, which influence the level of satisfaction the patient experiences during labour. The course of EA should be supervised by experienced personnel who understand its nature and the reasons behind its use. Further studies are required to evaluate the effect of EA on the course of labour, and methods of minimising its adverse effects.

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