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Neonatal Outcome with Magnesium Sulphate and Fentanyl as Adjuvants for Epidural Labour Analgesia: An Observational Study

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Abstract

Original Research Article

Introduction: The pain of childbirth is arguably the most severe pain most women endure in their lifetime. Since pain relief in labor has always been surrounded by myths and controversies, providing effective and safe analgesia during labor has remained an ongoing challenge. Neuraxial techniques are accepted as the gold standard for intrapartum labor analgesia. The study aimed to determine the neonatal outcome with magnesium sulfate and fentanyl as adjuvant for epidural labor analgesia. ***Methods:*** This prospective comparative study was conducted at the Department of Anaesthesia, Analgesia, Palliative and Intensive Care Medicine in collaboration with the obstetric department, Dhaka Medical College, Dhaka.Bangladesh. The study was carried out from October 2020 to March 2021. A total of 60 patients were assigned by computer-generated random table to one group (Group A) and another group (Group B). Group-A (n=30): Group-A received Fentanyl 25 micrograms as adjuvant to bupivacaine (0.5% plain bupivacaine 2.5 ml+25 microgram of fentanyl 0.005% 0.5 ml + 7 ml normal saline=10 ml) via epidural catheter. Group B received MgSO4 50 mg as an adjuvant to bupivacaine (0.5% plain bupivacaine 2.5 ml + 50 mg of MgSO4 10% 0.5 ml +7 ml normal saline=10 ml) via epidural catheter. Data were statistically described in terms of mean ± standard deviation (±SD), or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using the Student t-test for independent samples. For comparing categorical data, a Chi-square (x^2) test was performed. P values of less than 0.05 were considered statistically significant. F-value was determined by the Repeated measured ANOVA test where data were repeated more than one time. All statistical calculations were done using the computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 22 for Microsoft Windows. Informed written consent was taken from the participants and the local committee approved the research protocol. ***Result:*** The mean age of the parturient was (25.45±6.35) years in Group A and (26.63±5.21) years in Group B. Based on the parity most of the parturients were primipara. In Group A (83.34%) were primipara and in Group B (80%) were primipara. There was no statistically significant difference in the aspect of gestational age, cervical dilatation, and duration of the stage of labor between the two groups (p-value was > 0.05). There had been no significant difference in mean arterial pressure (MAP) of parturients, and in average Fetal HR between the two groups (p-value was > 0.05). Most parturients were delivered to the fetus by NVD, in Group A (76.6%) and Group B (73.26%) when the others were assisted by an instrument, in Group A (16.67%) and Group B (13.32%) and emergency LSCS were needed in Group-A (6.67%) and Group-B (13.32%). APGAR score was comparatively low (≤ 6) at 1 min in Group A (10%), while the Apgar score was very good in Group B at 1 min and 5 min. ***Conclusion:*** This study concluded that there had been no statistical difference between fentanyl and $MgSo_4$ as an adjuvant to bupivacaine in terms of MAP of parturients and FHR. However, $MgSo_4$ as an adjuvant showed better outcomes concerning the APGAR score of neonates.

Keywords: Magnesium Sulphate, Fentanyl, Epidural Analgesia, APGAR Score.

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INTRODUCTION

Many pharmacological and non-pharmacological methods of labor analgesia have been adopted over the years. Of these, neuraxial or regional analgesia has become the most popular method. Possible regional anesthesia techniques include epidural analgesia, spinal analgesia (sometimes referred to as the intrathecal or subarachnoid space), or a combination of epidural and spinal analgesia. Approximately 60% of laboring women (2.4 million each year) choose regional analgesia for pain relief during labor [1]. The first reported case of regional anesthesia used in labor occurred in 1900 when a physician from Switzerland administered spinal cocaine to six of his patients. Two years later, spinal anesthesia was used for the first time for cesarean delivery in the U.S [2]. In the late 1960s, epidural analgesia became more accepted, especially among academic health centers and private hospitals. Epidural labor analgesia using local anesthetic solutions combined with an opioid is commonly used for the relief of labor pain. Low-concentration local anesthetic solutions with opioids have been shown to reduce motor block without compromising labor analgesia [3, 4]. However, the onset of analgesia can be delayed. There is some evidence that the addition of fentanyl or magnesium sulfate bolus at the initiation of labor epidural analgesia can improve the onset and quality of analgesia and decrease motor block [5- 7]. Sensory nerve roots within the epidural space can be blocked by using a low concentration of the local anesthetic solution. Extension of epidural local anesthetic agent is influenced by the volume of local anesthetic agent administered [8]. Magnesium has postsynaptic N-methyl D- aspartate (NMDA) calcium channel-blocking properties and has been used successfully to potentiate opioid analgesics and to treat neuropathic pain in animals [9]. The administration of magnesium sulfate in the perioperative period was associated with fewer analgesic requirements in the postoperative period [10]. Other studies examined different routes of magnesium administration such as the intravenous or the intrathecal route and were found to improve anaesthetic and analgesic quality [11]. Epidural magnesium was found to reduce the use of postoperative analgesia without increases in side effects [12, 13]. The addition of magnesium to spinal bupivacaine–fentanyl anesthesia improves the duration of spinal analgesia for labor without any side effects [14]. The addition of magnesium to epidurally administered bupivacaine and fentanyl in patients undergoing elective cesarean section with combined spinal-epidural anesthesia helped to improve the quality of postoperative analgesia [15]. Many adjuvants such as morphine, fentanyl, buprenorphine, clonidine, neostigmine, dexamethasone, and magnesium sulfate are used with local anesthetic agents. Commonly used adjuvant fentanyl has been shown to prolong the analgesic effects of local anesthetic agents such as bupivacaine when used epidurally but has some adverse effects such as pruritus, nausea, vomiting, bradycardia, and respiratory depression. Magnesium sulfate is an NMDA antagonist that is used as an adjuvant to local anesthetic agents, which can prolong the analgesic effect of local anesthetic agents such as bupivacaine. So, this study aimed to determine the neonatal outcome with magnesium sulfate and fentanyl as adjuvant for epidural labor analgesia.

OBJECTIVE

General Objective

- To determine the neonatal outcome with magnesium sulfate and fentanyl as adjuvant for epidural labor analgesia.

Specific Objectives

- To see the demographics of the respondents.
- To assess the labor characteristics of the study population.
- To analyze FHR and MAP (Mean Arterial Pressure) of parturients.

METHODS

This prospective comparative study was conducted at the Department of Anaesthesia, Analgesia, Palliative, and Intensive Care Medicine in collaboration with the obstetric department, Dhaka Medical College, Dhaka.Bangladesh. The study was carried out from October 2020 to March 2021. A total of 60 pregnant women with a full-term pregnancy, who requested epidural analgesia for labor was selected as the study population as per inclusion and exclusion criteria. A purposive sampling technique was used in this study. 60 patients were assigned by computer-generated random table to one group (Group A) and another group (Group B). Group-A (n=30): Group-A received Fentanyl 25 micrograms as adjuvant to bupivacaine (0.5% plain bupivacaine 2.5 ml+25 microgram of fentanyl 0.005% 0.5 ml + 7 ml normal saline=10 ml) via epidural catheter. Group B received MgSO4 50 mg as an adjuvant to bupivacaine (0.5% plain bupivacaine 2.5 ml + 50 mg of MgSO4 10% 0.5 ml +7 ml normal saline=10 ml) via epidural catheter. Intravenous fluid loading with 10- 15 ml /kg of Ringer's lactate solution was given. Patients were then placed in the sitting position, and local anesthesia infiltration of the skin and subcutaneous tissues was done at the level of L2–3 or L3–4 with 2–3 mL of lidocaine 0.5%. The mid-lumbar extradural space L2–L3/L3–L4 was identified by using a loss of resistance to air with an 18 G Tuohy needle and an epidural catheter (Perifix 18 G catheter; B. Braun, Melsungen, Germany) was inserted 4–5 cm into the epidural space in a cephalic direction and aspirated for detection of cerebrospinal fluid or blood in the space. Then the catheter was fixed and patients were repositioned with left uterine displacement. 3 mL of 2% lidocaine with 15 µg of epinephrine as a test dose was injected. In the absence of intravascular or intrathecal placement of the catheter, the study drug (In Group-A, 0.5% plain bupivacaine 2.5 ml+25 microgram of fentanyl 0.005% 0.5 ml + 7 ml normal saline=10 ml and in Group-B, 0.5% plain bupivacaine 2.5 ml + 50 mg of MgSO4 10% 0.5 ml +7 ml normal saline=10 ml) was injected 5 min after the test

dose. The time of the injection of the study drug was considered as T =0 and assessments were done accordingly. Fetal heart rate was monitored at 30-minute intervals till delivery. Fetal heart rate was continuously recorded on a cardiotocograph (Hewlett–Packard 80300A, Hewlett Packard, Palo Alto, CA), and was monitored by obstetricians who were blinded to group allocation and rechecked postpartum for detection of fetal heart rate abnormalities. The analysis compared tracings obtained at least 30 min before epidural and recorded during epidural analgesia. Fetal conditions were managed according to the situation by oxygen, left or right lateral uterine displacement, ephedrine if needed; cessation of oxytocin, and possible tocolytic treatment. Fetal outcome was checked by APGAR score at 1 min & 5 min. Data were statistically described in terms of mean ± standard deviation (±SD), or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using the Student t-test for independent samples. For comparing categorical data, a Chi-square (x^2) test was performed. P values of less than 0.05 were considered statistically significant. F-value was determined by the Repeated measured ANOVA test where data were repeated more than one time. All statistical calculations were done using the computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 22 for Microsoft Windows. Informed written consent was taken from the participants and the local committee approved the research protocol.

Inclusion Criteria

- Patient with full-term pregnancy with vertex presentation and in active labor with a cervical dilatation of 3-5 cm.
- Patients having normal fetal heart rate pattern (CTG) before the time of induction.
- Patients who had given consent to participate in the study.

Exclusion Criteria

- Patients who had cervical dilatation >5 cm before epidural catheter insertion.
- Patient with anticoagulant therapy, preterm labor, breech presentation, obstructed labor, infection at the local site of catheter placement, and anatomical deformity of the spine.
- Patients with BMI > 35 kg/m^2.
- Patients who did not want to participate in the study.

RESULTS

Table 1: Distributions of parturient according to demographics and labor characteristics (N=60)

Characteristics		Group A (n=30)	Group B (n=30)	p-value
Mean age(year)		25.45±6.35	26.63±5.21	0.234^{NS}
BMI (kg/m^2)		22.23±4.88	23.52±4.21	0.186^{NS}
Parity	Primipara	25(83.34%)	24(80.00%)	0.132^{NS}
	Multipara	5(16.67%)	6(20.00%)	0.146^{NS}
Gestational age (weeks)		39.5±2.5	40±1.5	0.153^{NS}
Cervical dilatation (cm)		3.5±0.5	3.8±0.8	0.142^{NS}
Duration of the stage (min)	1st	237.96±57.87	244.63±62.42	0.240^{NS}
	2nd	98.23±27.74	89.78±29.76	0.189^{NS}

Values are expressed as Mean±SD and within parenthesis percentage (%) over the column in total. Pearson chi-squared Test (χ^2) was performed. NS: Statistically not significant.

The mean age of the parturient was (25.45±6.35) years in Group A and (26.63±5.21) years in Group B. Based on the parity most of the parturients were primi gravida. In Group-A (83.34%) were primi gravida and in Group-B (80%) were primi gravida. There was no statistically significant difference in the aspect of gestational age, cervical dilatation, and duration of the stage of labor between the two groups (p-value was > 0.05). [Table 1]

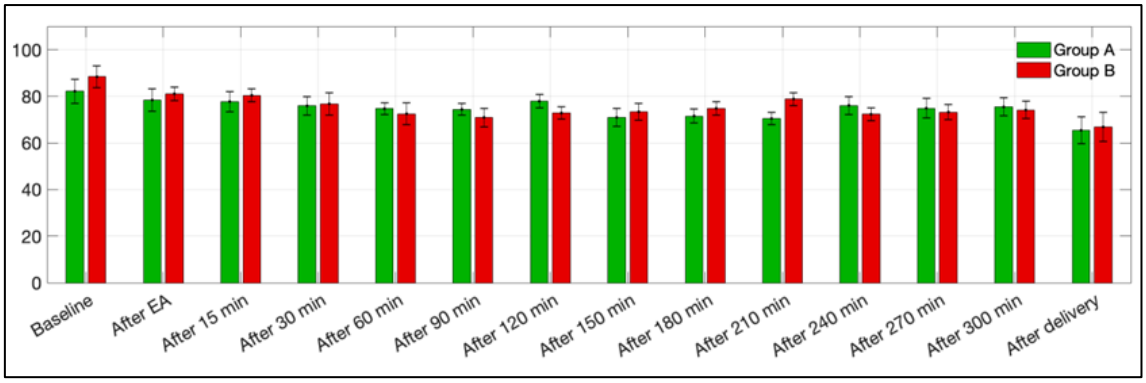

Figure 1: Distributions of parturient according to Mean arterial pressure (N=60)

Values of the Mean arterial pressure of the parturient at baseline, after epidural drug administration, at different time intervals, and after delivery. There had been no significant difference in mean arterial pressure (MAP) between the two groups (p-value was > 0.05). [Figure 1]

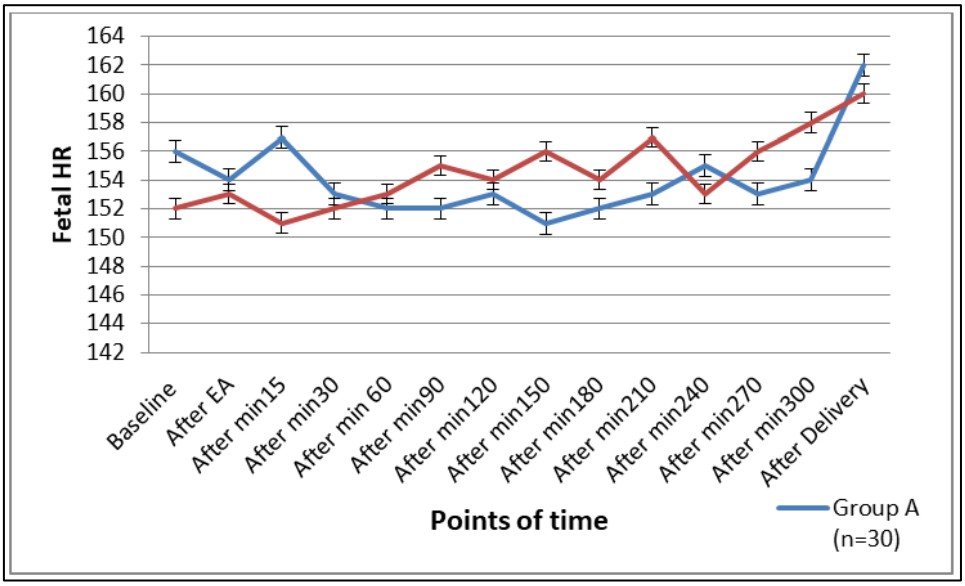

Figure 2: Trends in Fetal Heart Rate. (N=60)

Values of the fetal heart rate at baseline, after epidural drug administration, at different time intervals, and after delivery. There had been no significant difference in average Fetal HR between the two groups (p-value was > 0.05). [Figure 2]

Table 2: Distributions of parturient according to Modes of delivery and outcome of the fetus (N=60)

Characteristics		**Group A (n=30)**	**Group B (n=30)**
Modes of delivery	NVD	23(76.6%)	22(73.26%)
	Instrumental delivery	5(16.67%)	4(13.32%)
	Emergency LSCS	2(6.67%)	4(13.32%)
APGAR score	At 1 min ≤6	3(10%)	0
	At 5 min ≤6	1(3.34%)	0

Most parturients were delivered to the fetus by NVD, in Group A (76.6%) and Group B (73.26%) when the others were assisted by an instrument, in Group A (16.67%) and Group B (13.32%) and emergency LSCS were needed in Group-A (6.67%) and Group-B (13.32%). APGAR score was comparatively low (≤ 6) at 1 min in Group A (10%), while the Apgar score was very good in Group B at 1 min and 5 min. [Table 2]

DISCUSSION

Epidural labor analgesia is the gold standard technique to relieve labor pain during the childbirth of a parturient. Currently, many adjuvants are used with local anesthetic agents. Of them, fentanyl and magnesium sulfate are used with local anesthetic agents to provide faster onset and longer duration of analgesia of local anesthetic agents such as bupivacaine without any

significant adverse effects. This study demonstrated the additive adjuvant effect on neonates of epidural administration of magnesium sulfate & fentanyl to bupivacaine during labor analgesia. The demographics and labor characteristics of the patients were well-matched between the two groups. The mean age of the parturient was (25.45 ± 6.35) years in Group- A and (26.63 ± 5.21) years in Group B. Based on the parity most of the parturients were primipara. In Group A (83.34%) were primipara and in Group B (80%) were primipara. There was no statistically significant difference in the aspect of gestational age, cervical dilatation, and duration of the stage of labor between the two groups (p-value was > 0.05). The Mean Arterial Pressure of the parturient was not statistically significant between the two groups (p-value was > 0.05). Our present study demonstrated that there was no statistically significant difference in average Fetal HR between the two groups (p-value was > 0.05) at baseline, after study drug administration, at different time intervals, and after delivery. A study of combined spinal- epidural and traditional epidural analgesia on uterine basal tone and its association with the occurrence of fetal heart rate abnormalities found that fetal heart rate abnormalities were statistically significant in between two groups (p-value was <0.01) related to the higher probability of uterine hypertonus in combined spinal-epidural compared to traditional epidural analgesia [16]. Most of the parturients were delivered to the fetus by NVD, in Group A (76.6%) and Group B (73.26%) while the others were assisted by an instrument, in Group-A (16.67%) and Group B (13.32%). Emergency LSCS were needed in Group A (6.67%) and in Group B (13.32%) which was comparable between the two groups. According to a study by Liu *et al.*, epidural analgesia using low-concentration infusions of bupivacaine is unlikely to increase the risk of a cesarean section but may increase the risk of instrumental vaginal delivery. Although women receiving epidural analgesia had a longer second stage of labor, they had better pain relief (Liu, E.H.C. and Sia, A.T.H., 2004) [17]. APGAR score was comparatively low (≤ 6) at 1 min in Group A (10%) but it is not specific to epidural fentanyl. The APGAR score was very good in Group B at 1 min and 5 min. Findings of a similar study done by Kesavan, R., Rajan, S., and Kumar, L. (2018) demonstrated that following lumbar epidural analgesia with intermittent boluses of 0.1% bupivacaine with fentanyl, 58.3% of parturients were delivered normally, 23.3% had an instrumental vaginal delivery, and 18.3% were required cesarean section that was similar to our study. It was found that the 1-min Apgar score was >7 in (80%) and Apgar score was <7 in (20%) neonates [18]. Leighton, B.L. and Halpern, S.H. (2002) described that fetal oxygenation is not affected by the analgesic method; however, neonates whose mothers received intravenous or intramuscular opioids rather than epidural analgesia require more naloxone and have lower Apgar scores. Epidural analgesia does not affect the rates of cesarean delivery, obstetrically indicated instrumented vaginal delivery, neonatal sepsis, or new-onset back pain [19].

Limitations of the Study

The study was conducted in a single hospital with a small sample size due to the COVID-19 pandemic situation. Moreover, there was a chance of bias because drug administration and data collection were done by the researcher. So, the results may not represent the whole community.

CONCLUSION

This study concluded that there had been no statistical difference between fentanyl and $MgSo_4$ as an adjuvant to bupivacaine in terms of MAP of parturients and FHR. However, $MgSo_4$ as an adjuvant showed better outcomes concerning the APGAR score of neonates.

FUNDING: No funding sources

CONFLICT OF INTEREST: None declared

ETHICAL APPROVAL: The study was approved by the Institutional Ethics Committee

RECOMMENDATION

Dose titration of Magnesium sulfate & Fentanyl in epidural labor analgesia in multiple centers can be carried out. Furthermore, studies should be conducted involving multiple centers and with a larger sample size in this context.

REFERENCES

1. Schrock, S. D., & Harraway-Smith, C. (2012). Labor analgesia. *American Family Physician*, *85*(5), pp.447-454.
2. Gogarten, W., & Van-Aken, H. (2000). A century of regional analgesia in obstetrics. *Anesthesia & Analgesia*, *91*(4), pp.773-775.
3. Halpern, S. H., & Carvalho, B. (2009). Patient-controlled epidural analgesia for labor. *Anesthesia & Analgesia*, *108*(3), pp.921-928.
4. Abrahams, M., Higgins, P., Whyte, P., Breen, P., Muttu, S., & Gardiner, J. (1999). Intact proprioception and control of labour painduring epidural analgesia. *Acta anaesthesiologica scandinavica*, *43*(1), 46-50.
5. Bang, E. C., Lee, H. S., Kang, Y. I., Cho, K. S., Kim, S. Y., & Park, H. (2012). Onset of labor epidural analgesia with ropivacaine and a varying dose of fentanyl: a randomized controlled trial. *International journal of obstetric anesthesia*, *21*(1), 45-50.
6. Celleno, D., & Capogna, G. (1988). Epidural fentanyl plus bupivacaine 0.125 per cent for labour: analgesic effects. *Canadian journal of anaesthesia*, *35*, 375-378.
7. Chestnut, D. H. (1991). Epidural anesthesia and instrumental vaginal delivery. *The Journal of the*

American Society of Anesthesiologists, *74*(5), 805-808.

8. Fink, B. (1992). Toward the mathematization of spinal anesthesia. *Regional Anesthesia and Pain Medicine*, *17*(5), 263-273.
9. Begon, S., Pickering, G., Eschalier, A., & Dubray, C. (2002). Magnesium increases morphine analgesic effect in different experimental models of pain. *The Journal of the American Society of Anesthesiologists*, *96*(3), 627-632.
10. Tramer, M. R., Schneider, J., Marti, R. A., & Rifat, K. (1996). Role of magnesium sulfate in postoperative analgesia. *The Journal of the American Society of Anesthesiologists*, *84*(2), 340-347.
11. Seyhan, T. O., Tugrul, M., Sungur, M. O., Kayacan, S., Telci, L., Pembeci, K., & Akpir, K. (2006). Effects of three different dose regimens of magnesium on propofol requirements, haemodynamic variables and postoperative pain relief in gynaecological surgery. *British journal of anaesthesia*, *96*(2), 247-252.
12. Özalevli, M., Cetin, T. O., Unlugenc, H. A. K. K. I., Guler, T., & Isik, G. (2005). The effect of adding intrathecal magnesium sulphate to bupivacaine–fentanyl spinal anaesthesia. *Acta anaesthesiologica scandinavica*, *49*(10), 1514-1519.
13. Bilir, A. Y. T. E. N., Gulec, S., Erkan, A., & Ozcelik, A. B. D. U. R. R. A. H. M. A. N. (2007). Epidural magnesium reduces postoperative analgesic requirement. *British journal of anaesthesia*, *98*(4), 519-523.
14. Lysakowski, C., Dumont, L., Czarnetzki, C., & Tramèr, M. R. (2007). Magnesium as an adjuvant to postoperative analgesia: a systematic review of randomized trials. *Anesthesia & Analgesia*, *104*(6), 1532-1539.
15. Ghrab, B. E., Maatoug, M., Kallel, N., Khemakhem, K., Chaari, M., Kolsi, K., & Karoui, A. (2009, May). L'adjonction de sulfate de magnésium à la morphine en intrathécal améliore-t-elle l'analgésie après césarienne?. In *Annales francaises d'anesthesie et de reanimation* (Vol. 28, No. 5, pp. 454-459). Elsevier Masson.
16. Abrão, K. C., Francisco, R. P. V., Cicarelli, D. D., & Zugaib, M. (2009). Elevation of uterine basal tone and fetal heart rate abnormalities after labor analgesia: a randomized controlled trial. *Obstetrics & Gynecology*, *113*(6), 1374-1375.
17. Liu, E. H. C., & Sia, A. T. H. (2004). Rates of caesarean section and instrumental vaginal delivery in nulliparous women after low concentration epidural infusions or opioid analgesia: systematic review. *Bmj*, *328*(7453), 1410.
18. Kesavan, R., Rajan, S., & Kumar, L. (2018). Effect and safety of labor epidural analgesia with intermittent boluses of 0.1% bupivacaine with fentanyl on fetal and maternal outcomes and wellbeing. *Anesthesia, essays and researches*, *12*(4), 769.
19. Leighton, B. L., & Halpern, S. H. (2002). Epidural analgesia: effects on labor progress and maternal and neonatal outcome. *Seminars in perinatology*, 26(2), pp. 122-135.