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Original Research Article

Effect of intrathecal midazolam on single dose morphine-bupivacaine co-mixture for spinal analgesia in labour

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ABSTRACT

Background: When spinal analgesia is used for relief of labour pain, a major challenge has been how to extend its duration without increasing the associated adverse effects. The aim of this study was to evaluate the effect of intra-thecal midazolam on pain relief by low dose bupivacaine and morphine mixture administered intrathecally to women in labour.
Methods: 160 labouring women, aged between 18 and 40 years gave consent and enrolled for this comparative study. The women were randomly allocated into two equal groups, MBM and BM. Group MBM received intrathecal 2.0 mg midazolam, 2.5 mg bupivacaine and 150 mcg morphine. Group BM received intra-thecal 2.5 mg bupivacaine and 150 mcg morphine. An epidural bolus dose of bupivacaine 10 mg plus fentanyl 25 mcg was given whenever rescue analgesia was needed. Foeto-maternal parameters, were assessed and recorded.
Results: Duration of effective spinal analgesia was significantly longer in group MBM than in group BM, p=0.0001. More participants in group BM had epidural rescue analgesia compared to group MBM, p=0.001. More participants in group MBM had adequate spinal analgesia till delivery compared to group BM, p=0.001. All the participants in both groups were able to ambulate without support after 30 minutes following the injection of spinal drugs. Nausea and vomiting occurred less commonly in group MBM than in BM, p=0.006.
Conclusions: Addition of midazolam to bupivacaine-morphine co-mixture significantly prolonged the duration of spinal analgesia without affecting ambulation or causing any considerable maternal or neonatal adverse effect.

Keywords: Labour, Intrathecal analgesia, Bupivacaine, Morphine, Midazolam

INTRODUCTION

Epidural services have become the gold standard for labour analgesia in many parts of the world but spinal analgesia is beginning to gain popularity especially in the developing countries.[1] However, owing to its comparatively short duration of action, a repeat dose or supplemental analgesia may be required. Addition of adjuvants to local anaesthetics administered intrathecally prolongs the duration of analgesia.[2] Such adjuvants include fentanyl, morphine, clonidine, dexmedetomidine and midazolam. Intra-thecal midazolam on its own is not known to provide significant labour analgesia. However, as an adjuvant, it has been shown to be a 'promising' option for decreasing labour pain.[2]

Its impact on intra-thecal bupivacaine and morphine mixture is yet to be sufficiently evaluated especially in our sub-region. Therefore, the aim of this study was to evaluate the effects of intra-thecal midazolam (2.0 mg) on intra-thecal labour analgesia from a mixture of bupivacaine (2.5 mg) and morphine (150 mcg).

METHODS

This randomized double-blind comparative study was conducted in the labour ward of University of Port Harcourt teaching hospital (UPTH), Port Harcourt. Nigeria from June 2017 to February 2018. All subjects enrolled in this research responded to an informed consent which has been approved by the local ethics committee on human research and the protocol has been found acceptable by them. The study participants were booked obstetric patients with no contraindication to vaginal delivery. Participants with term, singleton pregnancies with cephalic presentation, who were within the age range 18 to 40 years and American society of anesthesiologists (ASA) physical status I and II were included. Excluded from the study were those with dilatation of cervix more than 6cm, those with contraindication to regional anaesthesia/ analgesia or hypersensitivity to any of the study drugs. A sample size of 160 participants (80 participants per group) was used for the study based on a formula[3] for sample size determination and a 10% provision for attrition.

Participants were randomly allocated into two groups, MBM (midazolam-bupivacaine-morphine) or BM (bupivacaine-morphine) through sequentially numbered opaque sealed envelope **(**SNOSE) method.[4] Each received either intra-thecal midazolam 2.0 mg, hyperbaric bupivacaine 2.5 mg and morphine 150 mcg (group MBM, 80 participants) or intra-thecal bupivacaine 2.5 mg and morphine 150 mcg (group BM, 80 participants). A research assistant allocated each participant to a group by picking the envelopes and opening only after the participant's name was written on the appropriate envelope. The nurse on duty in the labour ward suite maintained the study code to facilitate accessibility should adverse reaction occur. The administration of the study solutions was done by the investigator. However, the research assistant prepared the solutions (each drug preparation was made 2 ml with sterile normal saline) and handed over to the investigator. The investigator and the patients were not aware of group drug assignment. The investigator also assessed and recorded the measured parameters.

Procedure

Each parturient was assessed and the medical records reviewed before commencement of procedure. The obstetric team examined the participants and confirmed cephalic presentation and cervical dilatation of 4-6 cm, foetal heart rate regularity, and uterine contraction. Participants were educated on how to use visual analogue scale (VAS) for pain assessment. They were counselled for the procedure and informed consent obtained. Baseline vital signs such as maternal pulse rate, non-invasive blood pressure, respiratory rate, arterial oxygen saturation, and the foetal heart rate, the frequency and duration of uterine contraction (using cardiotocograph-BD4000XS Huntleigh USA) were checked and recorded.

Intravenous access was secured with a 16-gauge cannula and the participants were preloaded with 500 ml of warmed 0.9% saline before the institution of the block at cervical dilatation of 4-6 cm. The researcher wore a face mask, scrubbed, gowned and gloved to ensure asepsis.

The participant was supported in the sitting position, the lower back cleaned with povidone iodine and draped before the administration of the study solution. The L3/L4 inter-spinal space was identified and the skin over the area infiltrated with 2 ml of 1% plain lidocaine. An 18-gauge Tuohy epidural needle was passed into the epidural space after which a spinal needle was inserted through the epidural needle until free back flow of cerebrospinal fluid was visualized and the intra-thecal drug dose heavy bupivacaine (AstraZeneca) and morphine (Martindale), plus or minus midazolam (Martindale), depending on the group was administered. After withdrawal of the spinal needle, the epidural catheter was threaded 3-5 cm into the epidural space and the epidural needle was removed. A sterile dressing was placed over the skin puncture site and adhesive tape applied to secure the catheter in place along the patient's back. The participants were returned to the supine position with left uterine displacement The participants were given additional analgesia through the epidural catheter when they needed it.

Maternal haemodynamic parameters were recorded at 5 minutes intervals during and after the procedure for the first 15 minutes, then every 15 minutes using multi parameter monitor (DASH 3000/4000, USA) Hypotension in this study was defined as systolic blood pressure (SBP) < 100 mmHg or a 20% decrease from base line, and bradycardia was heart rate less than 60 beats/min and oxygen de-saturation was SpO_2 less than 94%.[5] The level of sensory block was assessed using cotton wool soaked in ethyl alcohol (methylated spirit), on both sides of the body at 5 minutes interval for the first 15 minutes, then every 15 minutes until the maximum dermatomal level of sensory block was noted and recorded. Motor block was assessed using Bromage score at 5 minutes interval for the first 15 minutes, and then 15 minutes (able to raise the leg with extended knee above the bed=1, able to flex the knees=2, able to move feet only=3, no movement in legs or feet=4). Pain intensity was rated by the parturient using a 10cm VAS (already explained to patients) with 0= no pain, and 10= worst pain imaginable. Pain score was assessed immediately after uterine contraction. Pain score was approximated to a whole number and recorded just before the procedure, then at 5 minutes interval for the first 15 minutes, then every 15 minutes for the first hour, then, half-hourly until after activation of epidural analgesia; and thereafter before each bolus epidural dose. A supplemental analgesia comprising epidural 10 ml boluses of 0.1% plain bupivacaine (duracaine, myungmoon pharm) with 25 mcg of fentanyl (panapharma) was administered to those whose analgesia

wore off. The pain score and duration of analgesia before the supplemental analgesia were recorded.

The onset of effective analgesia was defined as the time from intra-thecal injection to the time the VAS mark ≤ 3 cm (mild pain) was attained. The duration of effective analgesia was defined as the time from the onset of effective analgesia to the time the parturient requested additional analgesia or VAS mark >4 cm. The ability to ambulate was assessed from 30 minutes following intra-thecal injection and parturient having achieved Bromage score of 1. The ability to walk with or without assistance was done by assisting/encouraging patient out of the bed, and repeated at 30 minutes interval. The effect was categorized as "no effect" (no numbness in the legs, able to ambulate), "mild effect" (numbness in the legs but able to ambulate without support), "moderate effect" (numbness in the legs but able to ambulate with support), "severe effect" (inability to ambulate). Neonatal outcome such as APGAR (appearance, pulse, grimace, activity, and respiration) score in the 1st, 5th and 10th minutes, and the need for use of naloxone in neonatal resuscitation was ascertained from the attending paediatrician and recorded. Immediately after delivery, the umbilical cord arterial blood was aspirated with 2 ml heparinized syringe with 23-G needle. The pH was determined using a pH metre (IQ scientific instruments, Minilab Model IQ 125 USA) and recorded. Obstetric outcome, such as vaginal delivery and Caesarean section were noted. Complications such as maternal respiratory depression, nausea, vomiting, pruritus, hypotension, and bradycardia were recorded.

Statistical analysis

The data collected from the study were analysed using the statistical package for social sciences, version 20 (IBM© Armonk, New York). The data were presented in tabular and chart forms as appropriate. Qualitative variables (e.g. demographic characteristics) were expressed as proportions and frequencies, quantitative variables were summarized using means and standard deviations. Differences in proportions were compared using Chi square or Fisher's exact test. Quantitative variables were compared with the use of either student t test or Mann Whitney U test. A p value of less than 0.05 was considered significant.

RESULTS

Only 154 (96.3%) of the 160 enrolled participants completed the study. Coincidentally, 77 participants completed the study in each group, MBM and BM. Therefore, data from the 154 participants were analyzed. There was no significant difference in the mean maternal age, weight, height, BMI and gestational age between the two groups (p>0.05) (Table 1). The mean time of onset of effective spinal analgesia was significantly longer in group MBM than in group BM, p=0.024 (Table 2). The time to attain maximum level of sensory block was also significantly longer in group MBM compared to the BM group, p=0.007.

Table 1: Comparison of patient characteristics and gestational age.

Variables	Group A (MBM) Mean±SD	Group B (MB) Mean±SD	T value	P value
Age in years	30.25 ±4.56	31.25 ±4.24	-1.410	0.161
Weight in kg	67.35±5.50	68.06±4.31	-0.898	0.371
Height in meters	1.64±0.05	1.64±0.04	0.714	0.476
BMI in Kg/m^2	25.00±1.51	25.47±1.50	-1.920	0.057
Gestational age in weeks	38.96±0.80	39.04±0.83	-0.591	0.555

Table 2: Comparison of mean time of onset of effective analgesia and mean time to attain maximum level of sensory block among the study groups.

Variables	Group A (MBM) Mean±SD	Group B (MB) Mean±SD	T value	P value
Time of onset of effective analgesia (min)	4.87±0.98	4.49±1.07	2.278	0.024
Time to attain maximum level of analgesia (min)	8.81±0.87	8.43±0.85	2.711	0.007

The mean duration of effective spinal analgesia was significantly longer in the MBM group than in the BM group, p=0.0001 (Table 3). It also shows that the mean doses of epidural bupivacaine and fentanyl administered were significantly less in the MBM group than in the BM group, p=0.012. There was no difference in the Bromage score in the two groups. All the participants had modified Bromage score of 1. There was also no difference in the ability to ambulate from 30 minutes after the injection of the spinal drugs in the two groups. All the participants were able to ambulate without support after 30 minutes following the injection of spinal drugs. There was no significant difference in the median APGAR scores in the 1st (p=0.296), 5th (p=0.736) and 10th (p=0.156) minutes.

Table 3: Comparison of mean duration of effective spinal analgesia and mean dose of epidural drugs used among the study groups.

Variables	Group A (MBM) Mean±SD	Group B (MB) Mean±SD	T value	P value
Duration of effective analgesia (min)	303.05±33.11	222.40±24.70	17.132	0.0001
Bupivacaine (mg)	11.50±4.89	16.75±8.29	-2.609	0.012
Fentanyl (mcg)	28.75±1.23	41.88±20.71	-2.609	0.012

Table 4: Comparison of mean duration of labour among groups in the study.

Variable	Group A (MBM) Mean±SD	Group B (MB) Mean±SD	T value	P value
Duration of labor before spinal injection (min)	441.47±86.77	421.10±95.81	1.382	0.169
Duration of labor after spinal injection (min)	325.99±66.02	288.82±76.20	3.235	0.001
Total duration of labor (min)	763.18±110.72	712.65±136.41	2.524	0.013

Concerning the mean umbilical cord arterial pH in the two groups, there was no significant difference in mean values in the MBM group (7.25±0.02) compared to the BM group (7.24±0.23), p=0.150. There was no significant difference in the mean duration of labour before spinal injection between MBM and BM groups p=0.169 (Table 4). However, the mean duration of labour after spinal analgesia until delivery or decision for Caesarean section was significantly longer in group MBM compared to group BM, p=0.001. The mode of delivery in the study groups is depicted in (Figure 1).

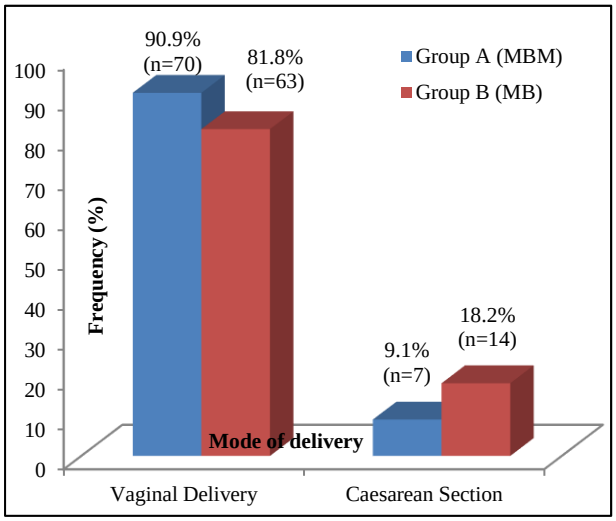

Figure 1: Distribution of mode of delivery among the study groups.

The differences in proportions of the participants that had vaginal or caesarean deliveries were not statistically significant (p=0.100). Pruritus occurred in 44.2% of the participants in group MBM, while 49.4% of participants in group BM complained of it, p=0.518. The incidence of nausea was significantly higher in BM group where 18 (23.4%) of the participants had it than in the MBM group where only 5 (6.5%) experienced it, p=0.003. Significantly also, none of the participants in MBM group vomited, while 8 (10.4%) participants in BM group vomited, p=0.006. All the participants had haemodynamic and respiratory stability within the study period. The distribution of side effects after labour among the groups in the study as depicted in (Figure 2). The proportions of participants that had pruritus and vomiting were significantly less in group MBM than in group BM. (p=0.004). No incidence of post dural puncture headache (PDPH) was recorded in both groups.

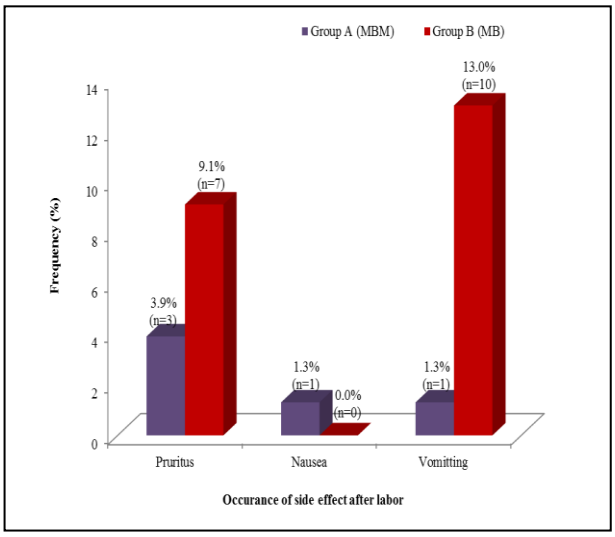

Figure 2: Distribution of side effects after labour among groups in the study.

DISCUSSION

This study showed that adding a low dose of midazolam to low dose bupivacaine-morphine co-mixture and administering the combination intrathecally, produced a significantly prolonged duration of pain relief compared to what can be obtained when bupivacaine and morphine combination was used in labouring women. The addition did not also affect the ability of the women to ambulate. Although the duration of effective analgesia was not sufficient for some of the participants throughout the

labour, more women in MBM group had sufficient analgesia. There were fewer requests for rescue epidural analgesia in MBM group than in BM group. In this study pain relief was considered adequate and effective when the VAS (pain score) was reduced to ≤4 cm after the intra-thecal injection similar to the scoring used in another study.[6] This ability of midazolam- bupivacaine-morphine combination to provide higher percentage of participants with adequate analgesia at a median cervical dilatation of 5cm in this study proves the sufficiency of the single dose spinal regime for labour analgesia. Most of the participants in the MBM group had adequate analgesia from the spinal injection before vaginal delivery or decision for caesarean section. Consistent with what was obtained in this study, a previous report on the use of intra-thecal low dose bupivacaine and morphine which is similar to group BM in this study, showed that the mean duration of analgesia was approximately four hours.[7] Intra-thecal 1.0-2.0 mg midazolam has been shown to potentiate the analgesic effect of intra-thecal bupivacaine by two to four hours.[8] This corroborates the findings in this study. A recent meta-analysis that included 672 patients concluded that intra-thecal midazolam delayed the time to request rescue analgesia without any increase in the duration of motor blockade.[8]The analgesic effect of intra-thecal midazolam has been hypothesized to be mediated by the facilitation of inhibitory neurotransmitter γ-aminobutyric acid (GABA) in the substantia gelatinosa in the spinal cord. It may also produce a central antinociceptive effect via the activation of spinal δ-opioid receptors.[8] Therefore the enhanced analgesic effect may be due to synergism with both the local anaesthetic and the opioid.

The establishment of effective analgesia in both groups within five minutes after spinal injection is consistent with the findings of other scholars.[9,10] Although, both groups experienced relatively substantial analgesia, the group that had midazolam in their drug combination (MBM) experienced a significantly longer duration of analgesia. Noteworthy, is that the mean time of onset of analgesia and time to attain maximum sensory block height after spinal injection were significantly longer in MBM group compared to BM group. When bupivacaine is injected intrathecally, the time of onset of action is less than a minute. However, the action peaks at about15 minutes.[11] Intrathecally, morphine, a hydrophobic opioid has slow onset of action of about 30 minutes[12] and requires combination with local anaesthetic to provide immediate analgesia. Therefore, intra-thecal bupivacaine may be the major determinant of the onset of analgesia observed in the two groups in this study. The difference between the two groups in the time of onset of sensory block (analgesia) and time to attain maximum dermatomal height may be associated with the alteration in the characteristics of the injectates as they mix and the modality adopted in the assessment.[13,14]

Irrespective of the group, all participants were able to ambulate without support, at the first assessment, 30 minutes after spinal injection. When low dose mixtures of opioids and/or local anaesthetics are used, the proprioceptive (dorsal column) function can be selectively preserved.[9]

The outcome of this study suggests that this dosage of intra-thecal midazolam, bupivacaine and morphine can provide sufficient analgesia without affecting ambulation. Although a study by Anabah et al reported a mild effect on ambulation in 41 patients, 291 other remaining patients did not experience any impairment in their ability to ambulate. Yeh and co-workers reported no lower extremity weakness in all their participants who also received intra-thecal bupivacaine, however they did not ask their participants to ambulate directly unlike what was done in this study.[15,16] The intra-thecal regimen in the two studies did not include midazolam. Impairment in motor function is always attributed to local anaesthetics. Salimi et al reported a similar outcome as in this study where none of their participants suffered numbness or weakness of the legs in both groups (bupivacaine and sufentanil plus/or minus midazolam**)**.[2] Higher doses of local anaesthetics administered neuraxially may impair motor functions thereby resulting in higher incidence of instrumental delivery and caesarean sections. No obvious motor block was observed in this study. Probably this explains why the maternal expulsive effort was preserved and lower incidence of caesarean section in both groups of this study.

Usually, there is fear of possible untoward effects of maternal intra-partum drug on the foetus and neonate irrespective of route of administration. However, recent studies done utilizing low dose local anaesthetics plus or minus low dose opioids for neuraxial analgesia did not record any significant neonatal complications linked to the procedure.[15,17] In this study, all the APGAR scores of the babies delivered were above 8 in the 1st minute which is similar to what Vitanen et al reported in their study.[10] The neonatal umbilical cord arterial pH was also within normal range in all the babies. The group that had midazolam had longer duration of labour. It could have been expected that this group will have a shorter duration of labour since they had significantly longer effective analgesia compared to the group without midazolam. The provision of effective analgesia decreases the inhibitory effects of endogenous maternal catecholamine on uterine contractility.[18] However, the influence of other factors such as foetal positioning affecting the duration of labour are yet to be fully elucidated.[18] Therefore, it is difficult to conclude if intra-thecal midazolam was responsible for this finding.

Although there is considerable debate as regards the influence of neuraxial analgesia on the progress of labour and mode of delivery, this study did not observe any increased rate of caesarean section among the two groups compared to another study.[6] The commonest maternal adverse event noticed in both groups of this study is pruritus followed by nausea and vomiting, most of them

occurring intra-partum. Although the oral administration of opioid can cause pruritus in about 2-10 percent, intra-thecal and epidural injections increase the incidence of pruritus up to 25-100 percent.[7,19,20] However, the incidence and severity are associated with type of drug and the dose. Intra-thecal drug combination tends to reduce the risk.[20] Asokumar et al reported a rate of 40% in participants that had intra-thecal bupivacaine and fentanyl but 100 % in those that had fentanyl only.[19] This is consistent with the outcome of this study where 44% and 49% in the MBM and BM group experienced pruritus but of mild severity respectively.

Intra-thecal morphine whether high or low dose has been reported to cause a higher incidence of nausea and vomiting compared to morphine free regimen.[16,21] The significantly lower incidence of nausea and vomiting in "midazolam" group (MBM) compared to" without midazolam" group (MB) in this study is consistent with the findings from a review article that intrathecal midazolam significantly reduces the risk of nausea and vomiting up to 50%, when used as adjunct to other spinal medications, although the mechanism is not clear.[8] Dural puncture exposes patients to PDPH. However, the incidence increases with increasing size of needle, use of resistance to air technique for locating the epidural space and repeated dural puncture with spinal needle.[21,22] There was no incidence recorded in this study. Loss of resistance to saline instead of air was used in locating the epidural space in this study and none of the patients had repeated intra-thecal injection. Other side effects such as urinary incontinence or retention or difficulty emptying bowel were not detected in this study. This is consistent with other studies that utilized low dose of local anaesthetics (bupivacaine), or local anaesthetic free drugs.[7,10]

CONCLUSION

The addition of midazolam to the bupivacine-morphine co-mixture significantly prolonged the analgesia derived from the local anaesthetic-opioid mixture without increase in any adverse effect on the participants or their babies. It also did not affect the ability of the participants to move freely. Intra-thecal midazolam, bupivacaine and morphine combination could effectively be used not only at advanced stage of labour but also once diagnosis of active labour is made in poor resource centres where combined spinal epidural services may not be available.

Limitations

Limitations of the study include that: It was a single centre study which could hamper its generalization. Also, the sample population was of pregnant women irrespective of parity or augmentation of labour. This could affect their overall perception of pain and satisfaction. Hence a study designed to consider only multipara or primipara may be able to eliminate bias associated with previous experience or anticipation. The minimal cervical dilatation of 4-6cm before initiation of block deprived the parturients from having some benefit of analgesia prior to the spinal injection.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Ogboli-Nwasor E, Adaji SE, Bature SB, Shitu OS. Pain relief in labour: a survey of awareness, attitude and practice of health care providers in Zaria, Nigeria. J Pain Res. 2011;4:227-32.
2. Salimi A, Nejad RA, Sefari F, Mohajaerani SA, Naghade RJ, Mottaghi K. Reduction in labour pain by intrathecal midazolam as adjunct to sufentanil. Korean J Anesthesiol 2014;66(3):204-9.
3. Raveendran R, Gitanjali B. In: Raveendran R, Gitanjali B, editors. A practical approach ` to PG Dissertation. 1st ed. New Delhi: Lordson Publishers (p) Ltd; 1997: 37-45.
4. Doig GS, Simpson F. Randomization and allocation concealment: A practical guide for researchers. J Crit Care. 2005;20:187-93.
5. Fyneface-Ogan S, Job OG, Enyinda CE. Comparative effects of single shot intrathecal bupivacaine with dexmedetomidine and bupivacaine with fentanyl on labour outcome. Anesthesiol. 2012;10:984.
6. Hein A, Rosblad P, Norman M, Ryniak S, Tingakar B, Jakobson J, et al. Addition of low-dose morphine to intrathecal bupivacaine/ sulfentanil labor analgesia: A randomized controlled study. Int J Obstet Anaesth. 2010;19(4):384-9.
7. Wiles MD, Nathanson MH. Local anaesthetics and adjuncts- Future development. Anaesthesia. 2010; 65(1):22-37.
8. Ho KM, Ismail H. Use of intrathecal midazolam to improve perioperative analgesia: a meta- analysis. Anaesth Intensive Care. 2008;36:365-75.
9. Olufolabi A, Vernon R, Medge O. A spinal labour analgesia protocol for Ghana. Afr Anaesthesia Cong. 2009;10:67-8.
10. Viitanen H, Viitanen M, Heikkda M. Single shot spinal blosck for labour in multiparous parturient. Acta Anaesthesiol Scand. 2005;49:1023-9.
11. Baraka A, Noueihid R, Haji S. Intrathecal injection of morphine for obstetric analgesia. Anesthesiol. 1981;51:136- 40.
12. Hocking G, Wildsmith JAW. Intrathecal drug spread-Review. Br J Anaesth. 2004;93:568-78.
13. Rocco AG, Raymond SA, Murray E, Dhingra U, Freiberger D. Differential spread of blockade of touch, cold and pinprick during spinal anaesthesia. Anesth Analg. 1985;64:917-23.
14. Shinder SM, Abdoud TK, Artal R, Henriksen EH. Maternal catecholamine decreases during labour after lumbar epidural anaesthesia. Am J Obstet Gynecol. 1999;147:13-5.

15. Anabah T, Olufolabi A, Boyd J, George R. Low-dose spinal anaesthesia provides effective labour analgesia and does not limit ambulation. South Afr J Anaesth Analg. 2015;21(1):19-22.
16. Yeh HM, Chen L, Shya M, Lin C, Sun W, Wang M, Mok MS, Tsai S. The addition of morphine prolongs fentanyl-bupivacaine spinal analgesia for the relief of labour pain. Anesth Analg. 2001;92:665-8.
17. Tshibuya PN, Olang PO, Ogutu O, Chokwe TM. A comparative study on the efficacy of two regimens of single-shot spinal block for pain relief in women presenting in established labour. East Afri Med J. 2013;90(1):12-8.
18. Chaney MA. Side effects of intrathecal and epidural opioids. Can J Anaesth. 1995;42:891-903.
19. Asokumar B, Newman LM, McCarthy RJ, Ivankovich A, Tuman KJ. Intrathecal bupivacaine reduces pruritus and prolongs duration of fentanyl analgesia during labour: A prospective Randomized controlled trial. Anesth Analg. 1998;87(6):1309-15.
20. Borgeat A, Ekatodramus G, Schenker CA. Postoperative nausea and vomiting in regional anesthesia. Anesthesiol. 2003;98:530-47.
21. Ai da S, Taga K, Yamakura T, Endoh H, Shimoji K. Headache after attempted epidural block. The role of intrathecal air. Anesthesiol. 1998;88:76-81.
22. Bajwa BS, Cheema HK, Kaur K. Comparison of size of two spinal needles in postdural puncture headache: a retrospective study. J Evol Med Dent Sci. 2015; 4(100):16499-501.

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