Intrathecal labor analgesia by using bupivacaine alone or combined with fentanyl, midazolam or clonidine

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**Background** The Intrathecal analgesia is a highly effective technique for pain relief in the first stage of labor. Its effectiveness, simplicity, and low incidence of serious complications, less motor blockade and decrease the rate of cesarean section, make it applicable to the physicians.

**Methods**: one hundred twenty patients were equally divided into four groups where epidural catheter was inserted but not activated and intrathecal analgesia was done by using the drugs according to the group as follow: group B (bupivacaine alone), group BF (bupivacaine + fentanyl), group BC (bupivacaine+clonidine) and group BM (bupivacaine+midazolam).

**Results**: there were slight decrease in blood pressure, heart rate, respiratory rate and significant difference in the onset, duration and VAS, also there was slight decrease in fetal heart rate after analgesia with significantly low apgar score at 3 minutes post delivery with clonidine group, insignificant difference in sensory level, bromage and sedation scores. the post operative side effect for the mother and the fetus showed insignificant difference except for nausea and pruritis with fentanyl group.

**Conclusion**: the intrathecal analgesia was very simple, easily applicable, and highly satisfactory for the patient with reliable analgesia, the bupivacaine and fentanyl group had effective analgesia with rapid onset, long duration with minimal side effects on the mother in form of nausea and pruritis.

**Introduction**
Continuous labor support results in a decreased need for medical intervention, improved maternal and newborn outcomes, and increased maternal satisfaction to optimize the birth experience for the mother and family. In the first stage of labor, the Intrathecal analgesia is a highly effective technique for pain relief. Its effectiveness, simplicity, and low incidence of serious complications, less motor blockade and decrease the rate of cesarean section, make it safe drug to the anesthtatist.

The advantages of low dose narcotics used with intrathecal injection are to avoid some side effects seen with larger doses of intravenous narcotics as respiratory depression or neurobehavioral changes, as well as there is no loss of variability on fetal monitoring strips. Intrathecal analgesia for labor is usually performed with fentanyl which provides powerful and fast onset pain relief. The addition of low dose of bupivacaine increases the mean duration of action. Furthermore a benzodiazepine intrathecally provides new methods of improving current analgesic effects, the addition of midazolam in a dose of 1-2 mg intrathecal has a positive effect on perioperative pain therapy. Clonidine, an alpha-2 adrenoreceptor agonist has been used to prolong spinal anesthesia. In small doses, clonidine added to intrathecally local anesthetics and opioids for labor analgesia, increases the duration of spinal analgesia without sever adverse effects.

**Patients and Methods**
After taking a written consent; One hundred twenty patients in spontaneous vaginal delivery were included in the study, ASA physical status I, age 18-35 years, full term gestation (>38 and<41 weeks), singleton pregnancies with cephalic fetal presentation, in spontaneous active labor, with a cervical dilatation of 3-7 cm, an initial pain score greater than 5 mm on a 10-mm visual analog pain scale (VAS). The exclusion criteria was Patient refusal, Cardiac patients, severe respiratory disease, coagulopathy as well as any neuromuscular disease, baseline fetal heart rate (FHR) abnormalities, suspected fetal congenital anomalies, high risk pregnancies.

The intra-study withdrawal criteria included occurrence of wet tape, patients need another dose of analgesia and so activation of epidural component, or delivery within 30 min of the spinal component. Patients were randomly divided into equal four groups: Group B: (30 patients), They received bupivacaine 1.25mg intrathecally. Group BM: (30 patients) They received bupivacaine 1.25mg plus midazolam 2mg intrathecally. Group BF: (30 patients) They received bupivacaine 1.25mg plus fentanyl 25μg intrathecally. Group BC: (30 patients) They received bupivacaine 1.25mg plus clonidine 15 μg intrathecally. Under meticulous aseptic conditions with the Patient in setting position, and between the uterine contractions the L3-4, L4-5 interspace were identified by palpation, the area was then cleansed with an antiseptic solution, and sterile draping was applied. The midline skin is anesthetized with 1% percent lidocaine 5ml before the placement of 18g epidural needle (using air for identification of
the epidural space by loss of resistance technique) though which an epidural catheter was introduced and advanced for 3-5 cm and then the needle was withdrawn. A test dose of 4 ml lidocaine was injected after negative aspiration of CSF or blood, no activation of the epidural was done. The application of recommended intrathecal drug (by 25 gauge spinal needle) was done in the selected interspace (the studied drug was diluted in normal saline to a total volume of 2ml). The needle is now removed and a sterile dressing applied.

Activation of epidural was done when the initial relief of pain provided by intrathecal medication was insufficient. If spinal analgesia did not produce satisfactory pain relief within 15 min (analgesic dose: 10-15ml bupivacaine 1.25mg), and also when an emergency cesarean section was needed. Efficacy of the analgesic drugs were assessed using a 100-mm VAS, the subsequent doses through the epidural catheter were determined by the VAS and the parturient request for analgesia. Efficacy was accepted if the visual analog pain score is less than 4.

The following variables were determined for all patients:
- Homodynamic changes, respiratory variables, VAS at baseline and 5, 10, 15, 20, 30, 60 and 120 min after block
- Onset time, duration, highest sensory block, motor block and sedation score for the mother, fetal heart rate was monitored continuously intra-operative need for supplemental analgesia (epidural supplementation), numbers of instrumental deliveries and cesarean sections, duration of the first and the second stage of labor after intrathecal analgesia., the incidence of adverse effects; maternal respiratory depression, hypotension ( and the need of ephedrine supplementation ), nausea and vomiting, shivering, purities, allergic reactions, post-dural puncture headache, backache, neurological damage after 2 days, bladder and bowel dysfunctions and transient bradycardia of the fetus at 5, 15, and 30 min. after block, umbilical arterial blood gases at birth., apgar score, neonatal hypotension, and neurobehavioral changes.

Results: for all comparisons p<0.05 was considered significant. Anova test was used to compare among the four groups in weight, height and age. Mean arterial blood pressure, maternal heart rate, respirator rate, onset, duration, VAS, delivery stage and cervical dilatation, fetal heart rate, fetal Apgar score, fetal bradycardia, and fetal arterial blood gases.

Table 1: Shows demographic criteria of the studied groups:

<table>
<thead>
<tr>
<th></th>
<th>B (n=30)</th>
<th>BM (n=30)</th>
<th>BF (n=30)</th>
<th>BC (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>27.6 ± 6.4</td>
<td>27.8 ± 5.3</td>
<td>28.0 ± 6.7</td>
<td>27.0 ± 5.9</td>
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<tr>
<td>Weight</td>
<td>78.8 ± 7.6</td>
<td>78.4 ± 6.8</td>
<td>78.8 ± 6.6</td>
<td>78.4 ± 7.0</td>
</tr>
<tr>
<td>Height</td>
<td>159.7 ± 6.1</td>
<td>159.3 ± 5.8</td>
<td>161.9 ± 8.6</td>
<td>160.4 ± 5.9</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nullipara</td>
<td>10/20</td>
<td>10/20</td>
<td>8/22</td>
<td>13/17</td>
</tr>
<tr>
<td>Multipara</td>
<td>33.3/66.7</td>
<td>33.3/66.7</td>
<td>73.3</td>
<td>43.3/56.7</td>
</tr>
</tbody>
</table>

\( \chi^2 \) p value>0.05 = insignificant difference
Fig 1: HR of different groups

Fig 2: RR of different groups
Fig 3: Onset of analgesia among different groups

Fig 4: Duration of analgesia among different groups
Fig 5: Mean of VAS among different groups

Fig 6: Mean of Apgar score among different groups
Discussion

Sometimes patients came late to the delivery room, they are full stomach or they want to see her baby without feeling pain; necessitate fast action on the part of the anesthetist - trying to find the best solution quickly. [6]. Neuraxial analgesia is widely accepted as the most effective and the least depressant method of providing pain relief in labor. They provide high quality pain relief with minimal side effects to both the mother and the fetus. [7] Study of the effects of intrathecal analgesia on the mother and the fetus and the best drug or drug combination that offer rapid, good and safe analgesia for the mother and the fetus is the main target of this study.

As regards the Mean arterial blood pressure and the usage of ephedrine among the four groups, statistical significant difference was found. The decrease in mean arterial blood pressure (MAP) was pronounced in group BC (bupivacaine- clonidine) followed by BF (bupivacaine- fentanyl) group, it could be explained as Clonidine inhibits sympathetic preganglionic activity in the spinal medulla, thereby producing a reduction in arterial blood pressure. This result comes in agreement with the study of Chiari et al., who studied the analgesic and hemodynamic effects of clonidine as the sole analgesic agent on the first stage of labor and found that the hypotension occurred in the intrathecal clonidine combined with bupivacaine group. In another study done by Belladji et al., who assess the efficacy of spinal clonidine in 30μg combined with bupivacaine and sufentanil and its effects on maternal and fetal outcome. They observed a small reduction in MAP in intrathecal clonidine combined with bupivacaine group in labor analgesia.

As regards the maternal heart rate changes and respiratory rate assessment among the four groups, significant statistical decrease in the heart rate and respiratory rate were noticed after injection in the BM group. The study done by Saxena et al.[8] who studied the effect of low dose intrathecal clonidine with bupivacaine in the patients underwent umbilical surgeries and concluded that it improves onset and duration of spinal block with hemodynamic stability. This results also comes in agreement of Boussofara et al.[11] who studied the effect of addition of intrathecal bupivacaine alone or a combination with midazolam or fentanyl on nausea and vomiting on cesarean section and found that respiratory rate was decreased in midazolam group but not to a significant degree.

In view of the time for onset of sensory blockade, the duration of sensory blockade; and the visual analogue score (VAS) in the present study, there was a statistical significant difference among the studied groups. The more rapid onset and the longest duration of sensory and lower VAS blockade was noticed in the BF group which can be explained by the highly lipid solubility of fentanyl. This result is confirmed by the study done by Celestki et al.[12] who studied the effect of minidose of intrathecal fentanyl combined with bupivacaine and concluded that in fentanyl groups there was significant difference in the onset and duration of the sensory block as there was rapid onset in fentanyl group. This results was confirmed by the study done by Chu et al[11] who compared the use of intrathecal bupivacaine alone or the combination of the intrathecal bupivacaine and fentanyl and found that the analgesia in the bupivacaine and fentanyl group was highly significant in comparison to the bupivacaine alone.

As regards the delivery stages and the cervical dilatation, there was no statistical difference among the four groups; however there was a decrease in the duration of the first stage of labor and the time of delivery was noticed in all groups. This could be explained by the co-ordination of the action of uterine contractions on the cervix with subsequent decrease in circulating catecholamines. This results are confirmed by the study done by Adam et al.[14] who studied the effects of intrathecal midazolam or intrathecal fentanyl or the combination of them on the labor analgesia and concluded that the cervical dilatation is comparable in all groups and there was shortening in the first stage of labor in all groups.

About the Fetal heart rate changes and the fetal apgar score assessment. There was a significant statistical difference among the four groups but not reach beyond the normal ranges. In contrast to the present study Missant et al.[15] who studied the effect of intrathecal clonidine on the labor analgesia and the fetal outcomes and found that the fetal outcome is affected significantly. This difference can be explained by the high dose of clonidine (30μg) and its combination with sufentanil. Also In contrast to our study the study of Sia et al. [16]; it showed worse apgar score in combined spinal epidural analgesia which may be explained by the maternal hypotension and its drawbacks on uterine blood flow and the fetus.

As regards the fetal artery blood gases, it showed no statistical difference among the four groups; the PH ranges (7.18-7.35) PaCO2 (38-44mmHg) and PaO2 (16-22mmHg) in all groups which are in the normal range, but with slight acidosisis (in BC, and BM) that could be due to the slight maternal hypotension that happened in some patients with clonidine group, and due to the slight decrease in respiratory rate in midazolam group.

This comes in agreement with the study done by Topcu T et al.[17] who studied the addition of the fentanyl and clonidine to ropivacaine in patient controlled analgesia in epidural labor analgesia and found that there was no effect on the umbilical cord blood gases.

As regards the high sensory level, the bromage scale, and the sedation scale assessment, it showed no statistical difference among the four groups. This results are confirmed by the study done by Narayaran SM et al.[18] who studied the effect of addition of intrathecal midazolam to bupivacaine on the duration of analgesia on the knee surgery and concluded that there was insignificant difference as regards the sensory level or the bromage scale does not produce a significant sedation.

In contrast to present result, the result done by Yegen et al.,[19] who study The analgesic and sedative effects of intrathecal midazolam combined with bupivacaine in comparison with intrathecal bupivacaine alone in
perianal surgery and concluded that there was significant difference as regards sedation score. This may be explained with the high doses that were used in this study relative to the present study.

In study of Neonatal complications, it showed insignificant difference among the four groups in hypotension and neurobehavioral changes. This could be explained by the relative stability of the maternal hemodynamics and respiration throughout the time of the first and the second stage of delivery.

This result is confirmed by the study done by Celeski et al[12] who studied the effect of minidose of intrathecal fentanyl combined with bupivacaine and concluded that there was no differences among the studied groups regarding neonatal complications. On the study done by Prakash et al[29], who study the combination of two doses of midazolam with bupivacaine in cesarean section and found that there was no differences among the studied groups regarding neonatal complications.

In the study of the maternal complications, and The incidence of instrumental delivery there was insignificant difference among the four groups in hypotension, Vomiting, Post-dural puncture headache, backache, and respiratory changes and the incidence of instrumental delivery. There was significant difference in pruritus and nausea. This results comes in contrast with the study done by Harsoor et al[6] on spinal anesthesia with low dose bupivacaine with intrathecal fentanyl in a dose of 12.5µg for caesarean section and found no difference in the maternal adverse effects. This result can be explained by the high dose that used in the present study (25µg).

Reference


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