

# **DISCUSSION**

## DISCUSSION

Lower abdominal and lower limb surgeries may be performed under local, regional (spinal or epidural) or general anaesthesia, but neuraxial blockade is the preferred mode of anaesthesia. Spinal block is still the first choice because of its rapid onset, superior blockade, low risk of infection as from catheter in situ, less failure rates, and cost effectiveness, but has the drawbacks of shorter duration of block and lack of postoperative analgesia. In recent years, use of intrathecal adjuvants has gained popularity with the aim of prolonging the duration of block, better success rate, patient satisfaction, decreased resource utilization compared with general anaesthesia and faster recovery. Adequate pain management is essential to facilitate rehabilitation and accelerate functional recovery, enabling patients to return to their normal activity more quickly. The quality of spinal anaesthesia has been reported to be improved by the addition of opioids (such as morphine, fentanyl and sufentanil) and other drugs (such as dexmedetomidine, clonidine, magnesium sulphate, neostigmine, ketamine and midazolam), but no drug to inhibit nociception is without associated adverse effects.<sup>(124)</sup>

Dexmedetomidine is a highly selective alpha 2 adrenergic agonist which has been used for premedication and as an adjunct to general anaesthesia. It reduces opioids and inhalational anaesthetics requirements. Intrathecal alpha 2 receptor agonists are found to have antinociceptive action for both somatic and visceral pain.<sup>(125)</sup>

The aim of the study was to compare the addition of either dexmedetomidine or fentanyl to intrathecal bupivacaine as regards: the onset and duration of sensory and motor block, hemodynamic effects, postoperative analgesia and adverse effects of either drug.

The study was carried out on 60 patients admitted to the Alexandria Main University Hospitals and scheduled for elective lower abdominal or lower limb surgeries. They were divided into three groups:

- Group B:** Patients received 3ml (15mg) of 0.5% hyperbaric bupivacaine + 0.5ml of normal saline intrathecally.
- Group F:** Patients received 3ml (15mg) of 0.5% hyperbaric bupivacaine + 0.5ml (25 µg) of preservative free fentanyl intrathecally.
- Group D:** Patients received 3ml (15mg) of 0.5% hyperbaric bupivacaine + 0.5ml (5 µg) of diluted, preservative free dexmedetomidine intrathecally.

As regards the age, height, gender, duration of surgery and ASA classification there was no significant difference between the three groups.

In the current study the mean heart rate was significantly lower in group D than in group F at 45min, at 60min and at 90min. Regarding comparison between group F and B, mean heart rate was significantly lower in group B than in group F at 30min and at 45min. Bradycardia occurred in 4 patients of group D (20%), in 4 patients in group F (20%) and in 5 patients in group B (25%) however, this was of no statistical significance, also, regarding the total atropine dose there was no significant change in the three groups. Regarding the mean arterial blood pressure it was significantly lower in group D than in group F at 45min. It was also, significantly lower in group B than D after the intrathecal block and at 15min. Comparing between group F and B, it was significantly lower in group B than in F at after the intrathecal block, and at 15min. Hypotension occurred in 8 patients in group D (40%), 6 patients in group F (30%) and 7 patients in group B (35%) but this was of no statistical significance, also regarding the total ephedrine dose there was no significant difference between the three groups.

The decrease in heart rate in spinal anaesthesia can be explained by three mechanisms: 1-the Bainbridge reflex, in which stimulation of right atrial stretch receptors leads to vagal afferent stimulation of the medulla and subsequent inhibition of parasympathetic activity (increasing the heart rate, or, in the case of decrease atrial pressure, lowering heart rate) 2-a direct effect on the sinoatrial node elicited by atrial stretching and 3-anaesthesia of T1-4 cardioaccelerator fibers.<sup>(131)</sup>

Moreover, it was found that the most significant side effects reported about the use of intrathecal alpha two adrenoceptor agonists are bradycardia and hypotension.<sup>(87)</sup> This may be due to postsynaptic activation of central alpha 2 adrenoceptors which results in sympatholytic effect, leading to hypotension and bradycardia, an effect judiciously used to attenuate the stress response of surgery.<sup>(77)</sup> And this can explain the observations found in the dexmedetomidine group.

Also, considering the effect of subarachnoid blockade on the cardiovascular system, hypotension and bradycardia were most commonly expected, because the usual consequence of sympathectomy is a decrease in venous return and hypotension.<sup>(18)</sup>

In agreement with the results of the present study, Subhi M, Al-Ghanem et al<sup>(126)</sup> demonstrated significant decrease in the heart rate and mean arterial blood pressure when comparing the addition of 5µg dexmedetomidine to intrathecal bupivacaine versus 25µg fentanyl in gynecological procedure. This was also, supported by Abdelhamid SA, El-lakany MH<sup>(132)</sup> who had significant decrease in the heart rate in the dexmedetomidine group when comparing the use of 5µg dexmedetomidine to hyperbaric bupivacaine only.

Sunil BV, Sahana KS.<sup>(133)</sup> compared adding dexmedetomidine and magnesium sulphate to hyperbaric bupivacaine in spinal anaesthesia and found no clinically significant bradycardia or hypotension. In the referred study bradycardia was defined as heart rate less than 50 beat/min and hypotension as systolic blood pressure less than 90mmHg. (Similar to the current study) Emphasis should be done that in both the current study and Sunil's there were bradycardia and hypotension but, they were clinically insignificant between the studied groups and when compared to the whole number of the studied patients. Again, in agreement to the current study, Sunil B.V. et al.<sup>(134)</sup> who compared the addition of dexmedetomidine, fentanyl and magnesium sulphate to hyperbaric bupivacaine and Sunil BV, Sahana KS, Jajee PR<sup>(135)</sup> who studied dexmedetomidine as an adjuvant to hyperbaric bupivacaine for spinal anaesthesia reached the same conclusion. Sunil BV, Sahana KS.<sup>(133)</sup>, Sunil B.V. et al.<sup>(134)</sup>, Sunil BV, Sahana KS, Jajee PR<sup>(135)</sup> and the current study showed no significant difference in the doses of atropine and ephedrine.

However, this was opposed by Kanazi et al.<sup>(136)</sup> who found no significant decrease in heart rate or mean arterial blood pressure when studying the effect of 3µg dexmedetomidine and 30µg clonidine added to intrathecal bupivacaine, but this may be attributed to the use of lower dose of dexmedetomidine and lower total volume injected in the intrathecal space, as he used 1.9ml versus 3.5ml in the current study.

As regards the arterial oxygen saturation, there was no significant difference between the three groups all through the measuring intervals which may be due to; firstly: the dose of local anaesthetic used while designing the study was kept to minimal possible levels, with non-involvement of the intercostal muscles and/or diaphragm during motor blockade.<sup>(30)</sup> Secondly, supplemental oxygen administration through a face-mask throughout the procedure. This was in agreement with what Sunil BV, Sahana KS.<sup>(133)</sup> and Shukla D et al.<sup>(124)</sup> deduced.

About the sensory onset it was significantly faster in group D than groups F and B.

In agreement with the present study, Deepika Shukla et al.<sup>(124)</sup> found that the sensory onset of intrathecal dexmedetomidine was faster when comparing it with magnesium sulphate as adjuvants to hyperbaric bupivacaine in spinal anaesthesia. In Deepika Shukla study the mean onset time in the dexmedetomidine group was 2.27min  $\pm$  1.09min, while, in the current study it was 4.32min  $\pm$  0.28min. In both studies those onsets were significantly faster than the other groups and for the difference between the two onsets this may be because of the use of different definitions for the sensory onset, in Deepika Shukla study it was till T10 only while, in the current study it was till the highest sensory level reached.

In another study, Sunil BV, Sahana KS, Jajee PR<sup>(135)</sup> deduced that the onset of 10 $\mu$ g dexmedetomidine was faster than 5 $\mu$ g and faster than bupivacaine groups with mean times of (3.1  $\pm$  0.5min, 3.5  $\pm$  0.8min, 4.7  $\pm$  1.1min respectively).

In contrast to the current study, Subhi M, Al-Ghanem et al.<sup>(126)</sup> found no significant difference between the onset times of the different groups in their study when comparing dexmedetomidine and fentanyl as adjuvants to bupivacaine in gynecological surgeries. This may be due to the following: he used isobaric bupivacaine versus hyperbaric bupivacaine in the current study, he had different definition for the onset time (having it till reaching T10, which can be reached similarly and rapidly by the studied drugs versus till reaching the highest sensory level in the current study) lastly, the patients were put in lithotomy position in his study while in the current study they were lying supine.

Regarding the motor onset, in the current study there was statistically significant difference between the three groups with conclusion of faster onset in group D than F and B.

Similarly, this was concluded by Deepika Shukla et al.<sup>(124)</sup> and Sunil BV, Sahana KS, Jajee PR.<sup>(135)</sup> Also, Ogan SF et al.<sup>(137)</sup> had found faster motor onset in the dexmedetomidine group when compared with fentanyl as adjuvants to intrathecal bupivacaine on labour outcome.

In contrast to the current study, this was opposed by Subhi M, Al-Ghanem et al.<sup>(126)</sup> and this can be defended by the same reasons for the differences in the sensory onset. Also, the motor onset was not significantly faster in the dexmedetomidine group than the other groups as observed by Mahendru V et al.<sup>(138)</sup> when comparing intrathecal dexmedetomidine, clonidine and fentanyl as adjuvants to hyperbaric bupivacaine. This may be due to lower total volume injected intrathecally by the author total of 3ml versus 3.5ml in the current study.

Intrathecal dexmedetomidine when combined with spinal bupivacaine prolongs the sensory block by depressing the release of C-fiber transmitters and by hyperpolarization of post-synaptic dorsal horn neurons.<sup>(139)</sup> Motor block prolongation by alpha 2 adrenoceptor agonists may result from binding these agonists to motor neurons in the dorsal horn of the spinal cord.<sup>(140)</sup> Intrathecal alpha 2 receptor agonists have antinociceptive action for both somatic and visceral pain.<sup>(141)</sup>

Li et al.<sup>(89)</sup> observed that glutamate is involved in excitatory neurotransmission nociception and plays an essential role in relaying noxious stimuli in the spinal cord. Intrathecal injection of alpha 2 adrenergic agonists produces potent antinociceptive effects by altering spinal neurotransmitter release and effectively treats acute pain.

Group D significantly had longer sensory and motor durations than group F and B also, group F had significantly longer duration than group B. This was in agreement with Mahendru V, Tewari A et al<sup>(138)</sup> who found significantly prolonged durations of the sensory and motor blocks. Again this was concluded by Subhi M, Al-Ghanem et al,<sup>(126)</sup> Kanazi GE et al,<sup>(136)</sup> and Al-Mustafa MM et al.<sup>(142)</sup> who studied the effect of dexmedetomidine on spinal bupivacaine for urological procedures and observed dose dependent prolongation of motor and sensory blockade when increasing the dose of dexmedetomidine from 5 to 10µg.

The time to first analgesia request was significantly longer in group D in comparison to group F and B. It was significantly longer in group F in comparison to group B. Also, there was no need for rescue analgesia in 75% of patients in group D, 50% in group F and in 10% in group B. There was significantly reduced 24 hour requirements of total analgesics (pethidine and diclofenac sodium) in group D than F and B. this was similarly noted by Mahendru V, Tewari A et al<sup>(138)</sup> when comparing 5µg dexmedetomidine to 30µg clonidine and 25µg fentanyl, which supports the analgesic efficacy of dexmedetomidine as an intrathecal adjuvant. Similarly significantly improved analgesic efficacy was reported by Gupta et al.<sup>(125)</sup> when studying the comparison of dexmedetomidine and fentanyl as intrathecal adjuvant. Also, Al-Mustafa MM et al.<sup>(142)</sup> noticed reduced analgesic requirement in a dose dependent pattern when comparing 5µg versus 10µg of dexmedetomidine.

Regarding the Visual Analogue Scale, similar to our current study Gupta R<sup>(125)</sup> noticed lower VAS values in the dexmedetomidine than in the bupivacaine group. Similarly, Mahendru V, Tewari A et al<sup>(138)</sup> showed less VAS values in the dexmedetomidine than in the other compared groups.

Regarding side effects such as nausea, vomiting, shivering, pruritus, respiratory depression and sedation, their occurrence was of no significant value in all the groups in this study. This was similarly deduced by Sunil B.V. et al.<sup>(134)</sup> In the current study all the patients were “awake” by Ramsay Sedation Score but in contrast to this Hala EA Eid et al.<sup>(143)</sup> who studied different intrathecal doses of dexmedetomidine (5,10 and 15µg) added to bupivacaine, showed significantly higher sedation scores when using 15µg, which can be beneficial for patients undergoing lengthy complex surgeries as an alternative to epidural or prolonged general anaesthetics and can preclude the use of iv sedatives. However, such high sedation scores may be harmful in elderly and high risk surgical patients owing to the risk associated with excessive sedation and respiratory depression.

In contrary to the results of the current study, Abdelhamid SA, El-lakany MH<sup>(132)</sup> had found significant shivering in the bupivacaine group (12patients) than in the dexmedetomidine group (2 patients) and this may prove that alpha 2 adrenergic agonists have antishivering property as observed by Talke et al.<sup>(144)</sup>

# **SUMMARY**

## SUMMARY

The simplicity of the technique of spinal anaesthesia and its reliability has made it one of the preferred techniques in lower abdominal and lower limb surgeries. Unexpected early regression of spinal block or prolonged operation can cause intraoperative pain. Increasing the dose of local anaesthetics, addition of opioids to local anaesthetics for spinal anaesthesia would be helpful for prolonging the spinal blockade but may cause haemodynamic instability, nausea, urinary retention, respiratory depression and delayed recovery from motor block. Therefore emerged the need for new adjuvants to the intrathecal local anaesthetics.

The aim of the study was to compare the addition of either dexmedetomidine or fentanyl to intrathecal bupivacaine as regards: the onset and duration of sensory and motor block, hemodynamic effects, postoperative analgesia and adverse effects of either drug.

The study was carried out on 60 patients admitted to the Alexandria Main University Hospitals and scheduled for elective lower abdominal or lower limb surgeries. They were divided into three groups:

- Group B: Patients received 3ml (15mg) of 0.5% hyperbaric bupivacaine + 0.5ml of normal saline intrathecally.
- Group F: Patients received 3ml (15mg) of 0.5% hyperbaric bupivacaine + 0.5ml (25 microgram) of preservative free fentanyl intrathecally.
- Group D: Patients received 3ml (15mg) of 0.5% hyperbaric bupivacaine + 0.5ml (5 microgram) of diluted, preservative free dexmedetomidine intrathecally.

Preoperative evaluation was done by complete history taking, physical examination and necessary laboratory investigations.

Patients were premedicated by H2 antagonist. Before commencing regional anaesthesia, standard monitoring was established: ECG for heart rate and rhythm, non-invasive measurement of arterial blood pressure and oxygen saturation.

They were given intravenous lactated Ringer's solution 10 ml/kg as volume preload. Spinal anaesthesia was performed in the sitting position at the L3-4 interspace with midline or paramedian approach by using a 25 gauge Quinke's spinal needle with all aseptic precautions. Injection was given according to the groups

After injection was given, patients lied supine and low flow oxygen (4L/minute) was administered via oxygen mask.

The following parameters were measured:

- Patient data: 1. Patient's age (in years). 2. Patient's height (in cm).
- Duration of the operation: (in minutes).
- Hemodynamic measurements: (measured pre-spinal anaesthesia, intra and post operatively) Heart rate, mean arterial blood pressure and oxygen saturation.
- Sensory assessment: Onset of sensory block, sensory level of analgesia, duration of sensory block and pain assessment postoperatively by evaluation of VAS, time to first request of analgesia and total doses of analgesics within the first 24 hours.
- Motor assessment: Onset of motor block and duration of motor block.
- Side effects: also, were documented intra and post operatively.

As regards the age, height, gender, duration of surgery and ASA classification there was no significant difference between the three groups.

At 45min mean heart rate in group D was significantly lower than in group F ( $P=0.045$ ), also, at 60min ( $P=0.027$ ) and at 90min ( $P=0.047$ ). there was no other significant difference in the change of mean heart rate between group D and F in the rest of the studied times. Regarding comparison between group F and B, mean heart rate was significantly lower in group B than in group F at 30min ( $P=0.040$ ) and at 45min ( $P=0.048$ ), there was no other significant difference between group F and B in the rest of the studied times.

The mean arterial blood pressure was significantly lower in group D than in group F at 45min ( $P= 0.031$ ), while there was no other significant difference between the two groups in the studied times. There was significant decrease in MABP in group B than D at after the intrathecal block ( $P=0.006$ ) and at 15min ( $P=0.044$ ). Comparing between group F and B, MABP was significantly lower in group B than in F at after the intrathecal block ( $P=0.003$ ) and at 15min ( $P=0.050$ ).

There was no statistical difference between the three groups regarding the oxygen saturation.

About the sensory onset it was significantly faster in group D than groups F and B ( $P=0.000$ ).

The motor onset in group D was significantly faster than in groups F and B ( $P= 0.00$ ) also, it was significantly faster in group F than in group B ( $P=0.016$ ).

Group D significantly had longer sensory and motor durations than group F and B ( $P=0.000$ ) also, group F had significantly longer duration than group B ( $P=0.000$ ).

The mean VAS was lower in group D than in group F and B and in group F lower than in group B.

The time to first analgesia request was significantly longer in group D in comparison to group F ( $P=0.013$ ) and B ( $P=0.002$ ). It was significantly longer in group F in comparison to group B ( $P=0.015$ ). There was no need for rescue analgesia in 75% of patients in group D, 50% in group F and in 10% in group B.

The total dose of Diclofenac sodium was significantly less in group D in comparison to group F and B ( $P=0.030$ ,  $0.000$  respectively). Also, it was significantly less in group F than in group B ( $P=0.000$ ).

Group D did not need any doses of Pethidine. While the total dose of Pethidine required in group F was significantly less than in group B ( $P=0.026$ ).

There was no significant change between the three groups regarding bradycardia, hypotension, total atropine dose and total ephedrine doses, nausea, vomiting, shivering, pruritus, respiratory depression and sedation.

# CONCLUSIONS

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From this study we concluded that:

1. The intrathecal use of 5 $\mu$ g dexmedetomidine in addition to hyperbaric bupivacaine induced faster onset and longer duration of the sensory and motor blocks than the use of 25 $\mu$ g fentanyl.
2. The intrathecal use of dexmedetomidine in addition to hyperbaric bupivacaine caused prolonged analgesia and marked reduction in the analgesic consumption postoperatively.
3. No sedative effect was observed when using either dexmedetomidine or fentanyl intrathecally in addition to hyperbaric bupivacaine.
4. Side effects were few and accepted when using intrathecal dexmedetomidine.