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COMPARATIVE STUDY OF DEXMEDETOMIDINE AND FENTANYL USING WITH BUPIVACAINE IN EPIDURAL ANAESTHESIA FOR POST-OP ANALGESIA IN LOWER LIMB ORTHOPAEDIC SURGERY AND LOWER ABDOMINAL SURGERY

Anaesthesiology

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ABSTRACT

Introduction: Post-operative pain is a significant concern following lower limb orthopedic surgery and lower abdominal surgery. Adjuvants to local anesthetic during epidural block are helpful to provide better block characteristics and post-operative analgesia. **Objectives:** To compare the efficacy of epidural dexmedetomidine with bupivacaine versus epidural fentanyl with bupivacaine for post-operative pain. **Methods:** A total of 60 ASA Grade I / II patients aged 19 to 50 years fulfilling the eligibility criteria were enrolled in the study and were randomly allocated either DXM group who received 1 µg/kg injection dexmedetomidine epidurally (n=30; mean age 41.87±7.61 years; 60% females) or to FN group who received 1 µg/kg of injection fentanyl epidurally (n=30; mean age 39.20±8.67 years; 70% females) as adjuvant to received 15 ml of 0.5% bupivacaine respectively. Time to initiation/onset of motor and sensory blocks was noted, duration of sensory and motor blocks, maximum level of block achieved, post-operative VAS scores for pain, duration of analgesia, number of rescue analgesic dosages used upto 24 hour post-operative interval and adverse effects were noted. Data was analyzed using Chi-square and Independent samples 't'-tests. **Results:** Mean onset time of sensory and motor blocks was significantly shorter in DXM as compared to that in FN group. Mean duration of sensory and motor blocks and rescue free analgesia was significantly longer in DXM as compared to that in FN group. No major adverse effect of drugs was seen in either of two groups. Hypotension was the most common adverse effect associated with DXM. **Conclusion:** Dexmedetomidine as compared to fentanyl was offered faster and prolonged blockade, longer analgesic effect and lesser consumption of rescue analgesia, however, it was also associated with an increased risk of hypotension.

KEYWORDS

Lower limb surgery, Lower abdominal surgery, Post-operative pain, Rescue analgesia, Fentanyl, Dexmedetomidine, Bupivacaine.

INTRODUCTION

Epidural administration of amide local anaesthetics in combination with opioids is widely used for pain relief in lower abdominal and pelvic surgeries because of the dose minimizing and side effects reducing benefits[1]. Despite having ability to control the pain perception during the procedure, postoperative pain control is a major problem because regional anaesthesia using only local anaesthetics is associated with relatively short duration of action, and thus early analgesic intervention is needed in the postoperative period. Hence need for additional adjuvant analgesics with local anaesthetic to improve the quality and duration of block. Fentanyl, a low molecular weight, high potency, and lipid soluble synthetic opioid, is a suitable analgesic drug which is in use for prolonging the analgesic effect of epidural anaesthesia since a long time.

Bupivacaine is frequently used as the local anaesthetic for regional blocks because it offers the advantage of providing a long duration of action and a favourable ratio of sensory to motor neural block[2]. However, bupivacaine alone provides analgesia for not more than 4-6 h in peripheral nerve blocks. Hence, in order to enhance the duration of block and also to have a prolonged analgesic effect, adjuvants are often used. A variety of adjuvants have been studied that have a proven role in control of post-operative pain[3-7]. These adjuvants include both opioid and non-opioid agents. Adjuvant use of opioids like fentanyl to hyperbaric bupivacaine improves the quality of intra-operative and early postoperative regional blocks. However, addition of opioids to local anaesthetic solution has their own disadvantages, including complications like pruritis and respiratory depression.

The quality of the regional anaesthesia has been reported to be improved by the addition of opioids (as Morphine, Fentanyl and Sufentanyl) and other drugs [Dexmedetomidine (DXM), Clonidine, Magnesium sulphate ($MgSO_4$), neostigmine, ketamine and midazolam], but no drug to inhibit nociception is without associated adverse effects[8]. Dexmedetomidine which is a highly selective $_2$ receptor agonists, having sedative, analgesic, sympatholytic and anxiolytic effects that blunts many of cardiovascular responses in the peri-operative period. It has been reported to be used as adjuvant to initiate and maintain regional blocks with adequate efficacy and efficiency. Its use as an adjuvant during spinal anaesthesia has also been reported to be highly effective.

Keeping in view the emerging evidence reporting Dexmedetomidine to be a safer and effective possible alternative to fentanyl. The present study was planned to compare the efficacy of Dexmedetomidine (1 µg/kg) and Fentanyl (1 µg/kg) as adjuvant to bupivacaine 0.5% (15 ml) for patients undergoing lower limb orthopaedic and lower abdominal surgeries under epidural anaesthesia.

OBJECTIVES OF THE STUDY:

To compare the adjuvant use of dexmedetomidine (1 µg/kg) and fentanyl (1 µg/kg) as adjuvant to bupivacaine 0.5% (15 ml) for patients undergoing lower limb orthopaedic and lower abdominal surgeries under epidural anaesthesia in terms of:

a) Onset time
b) Intensity of post-operative pain, and
b) Duration of analgesia

MATERIAL AND METHODS

A total of 60 ASA Grade I / II patients aged 19 to 50 years fulfilling the eligibility criteria were enrolled in the study and were randomly allocated either DXM group who received 1 µg/kg injection dexmedetomidine epidurally (n=30; mean age 41.87±7.61 years; 60% females) or to FN group who received 1 µg/kg of injection fentanyl epidurally (n=30; mean age 39.20±8.67 years; 70% females) as adjuvant to received 15 ml of 0.5% bupivacaine respectively. Baseline, intra- and post-operative haemodynamic profile was compared. Time to initiation/onset of motor and sensory blocks was noted, duration of sensory and motor blocks, maximum level of block achieved, post-operative VAS scores for pain, duration of analgesia, number of rescue analgesic dosages used upto 24 hour post-operative interval and adverse effects were noted. Data was analyzed using Chi-square and Independent samples 't'-tests

RESULTS

Out of 60 patients scheduled for lower limb orthopaedic or lower abdominal surgery were randomly allocated to two equal groups, 30 (50.0%) patients were administered 15 ml of 0.5% bupivacaine with 1 µg/kg injection dexmedetomidine epidurally were classified as Group I and rest 30 (50.0%) were administered 15 ml of 0.5% bupivacaine with 1 µg/kg of injection fentanyl epidurally were classified as Group II.

Age of patients enrolled in the study ranged from 19 years to 50 years,

mean age was 40.53±8.20 years. Mean age of patients of Group I (41.87±7.61 years) was higher as compared to that of Group II (39.20±8.67 years) but when compared statistically this difference was not found to be significant.

Majority of overall (65%) as well as in both the groups (Group I 60%, Group II 70%) patients were female, rest of the patients were males. M:F ratio of Group I was 0.67 while that of Group II 0.43. Difference in gender ratio in two study groups was not found to be significant statistically.

Out of 60 patients, 49 (81.7%) were ASA Grade I and rest 18.3% were ASA Grade II. In both the study groups majority of patients were ASA Grade I (86.7% & 76.7%). Though proportion of ASA Grade II patients was higher in Group II as compared to Group I (23.3% vs. 13.3%) yet this difference was not found to be significant statistically.

Duration of surgery for overall patients ranged between 45 & 95 minutes, mean duration was 72.53±11.88 minutes. On comparing the mean duration of surgery of patients of Group I (73.73±11.60 min) and of Group II (71.33±12.24 min), difference was not found to be significant statistically.

Onset of sensory block in Group I was earlier (7.97±0.76 min) as compared to Group II (12.00±1.64 min). This difference was found to be significant statistically. Similarly, motor block onset time of Group I cases was earlier as compared to Group II (10.53±0.94 min vs. 14.57±1.59 min), this difference too was found to be significant

Range of duration of sensory block of Group I and Group II were 290-337 min and 270-326 min. Mean duration of sensory block of Group I was significantly higher than that of Group II (315.10±14.69 vs. 299.97±18.12 min). Range of duration of motor block of Group I and Group II were 299-344 min and 277-340 min respectively. Mean duration of motor block of Group I was significantly higher than that of Group II (321.70±14.07 vs. 311.03±18.66 min). statistically as depicted in Table.1.

Table 1: "Comparison Of Two Study Groups For Sensory/motor Block Duration (in min)"

SN	Block	Group I (n=30)		Group II (n=30)		Student 't' test	
		Mean	SD	Mean	SD	't'	'p'
1-	Sensory block	315.10	14.69	299.97	18.12	3.553	0.001
	(Range)	(290-337)		(270-326)			
2-	Motor block	321.70	14.07	311.03	18.66	2.499	0.015
	(Range)	(299-344)		(277-340)			

Comparison of Median Pain (VAS score) of patients of two study groups at different time intervals, at 1h and 2h all the patients (irrespective of study group) had Pain score 0. At 3h none of the patient of Group I reported any pain, median pain score of Group II patients was significantly higher [Median (IQR): 1 (0-2)].At 6h too significant difference in pain score of Group I [1(0.75-2.25)] and Group II [2(1-3)] patients was observed. Though median pain score of Group II patients was higher than that of Group I at 9h [3(3-4) vs. 4(3-4)], 12h [3(3-4) vs. 4(3-4)] and 24h [3(1-3) vs. 2(2-3)] yet these differences were not significant as depicted in Table 2.

Table 2: Comparison Of Level Of Pain (VAS score) Of Patients Of Two Study Groups At Different Time Intervals [Median (IQR)]

SN	Time	Group I	Group II	Mann-Whitney U test
1-	1h	0 (0-0)	0 (0-0)	Z=0.000; p=1.000
2-	2h	0 (0-0)	0 (0-0)	Z=0.000; p=1.000
3-	3h	0 (0-0)	1 (0-2)	Z=5.515; p<0.001
4-	6h	1 (0.75-2.25)	2 (1-3)	Z=2.073; p=0.038
5-	9h	3 (3-4)	4 (3-4)	Z=1.625; p=0.104
6-	12h	3 (3-4)	4 (3-4)	Z=1.203; p=0.229
7-	24h	3 (1-3)	2 (2-3)	Z=0.656; p=0.512

Mean duration of analgesia was significantly longer in Group I (331.5±13.80 min) as compared to that in Group II (319.03±19.31 min) (p=0.006) as depicted in Fig 1.

Patients in Group II also required significantly higher number of rescue analgesic dosages (2.50±0.68) as compared to that in Group I (2±0.87) as depicted in Fig 2.

None of the patient had hypertension, tachycardia, headache, respiratory depression. Hypotension was observed in significantly higher proportion of Group I cases as compared to Group II (26.7% vs. 0.0%). Rest of the adverse effects were higher among Group I but differences were not found to be significant statistically (Nausea: 16.7% vs. 6.7%; Vomiting: 6.7% vs. 3.3%; Shivering 3.3% vs. 0.0%; Bradycardia: 3.3% vs. 0.0%).

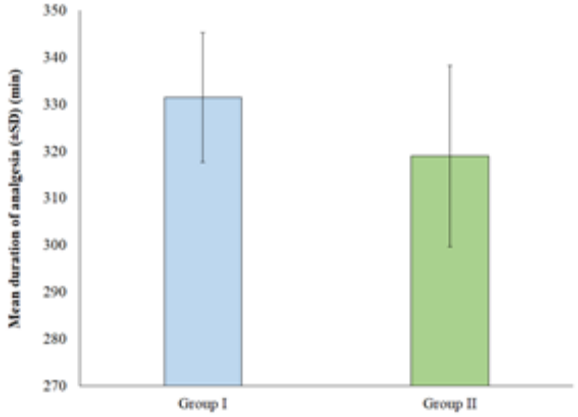

Fig.1: Comparison of Mean duration of post-operative analgesia between two groups

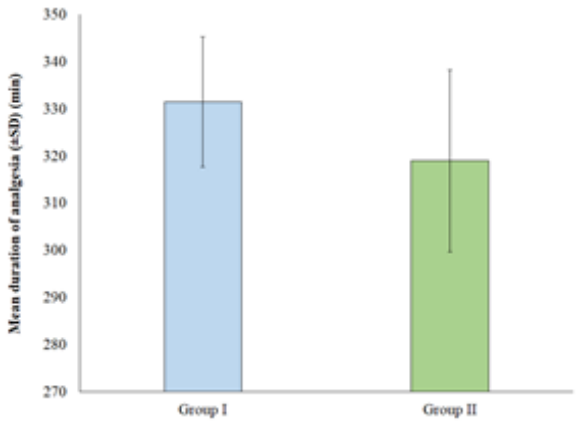

Fig 2- Comparison Of Mean Number Of Rescue Analgesic Dosages Consumed Between Two Groups

DISCUSSION

Post-operative pain is a significant concern following lower limb orthopedic surgery and lower abdominal surgery, impacting patient recovery and overall outcomes. The pain typically arises from tissue trauma, inflammation, and nerve irritation. Effective management strategies include multimodal analgesia, combining opioids, non-steroidal anti-inflammatory drugs (NSAIDs), and regional anesthesia techniques like nerve blocks. Lower abdominal surgery also results in significant post-operative pain, primarily due to the incision and manipulation of internal organs. The pain can be visceral, somatic, or both, and may be exacerbated by factors like surgical technique and individual patient factors. Multimodal analgesia is the cornerstone of effective pain management, often involving a combination of opioids, NSAIDs, and regional techniques such as epidural analgesia or transversus abdominis plane (TAP) blocks. In order to meet up the post-operative analgesic requirements, adjuvant use of some low dose anesthetic drugs is becoming common. These low-dose adjuvant drugs are used in epidural anaesthesia to prolong the postoperative analgesic effect by enhancing the efficacy and duration of local anaesthetics. Common adjuvants include opioids (e.g., fentanyl), α2-adrenergic agonists (e.g., clonidine and dexmedetomidine), and steroids (e.g., dexamethasone)[81]. These agents synergistically work with local anaesthetics to provide more extended and effective pain relief.

The present study was carried out to compare the efficacy of epidural dexmedetomidine with bupivacaine versus epidural fentanyl with bupivacaine for post operative pain relief in lower limb orthopedic surgery and lower abdominal surgery. For this purpose, a total of 60

ASA Grade I / II patients aged 19 to 50 years fulfilling the eligibility criteria were enrolled in the study and were randomly allocated either DXM group who received 15 ml of 0.5% bupivacaine with 1 µg/kg injection dexmedetomidine epidurally (n=30; mean age 41.87±7.61 years; 60% females) or to FN group who received 15 ml of 0.5% bupivacaine with 1 µg/kg of injection fentanyl epidurally (n=30; mean age 39.20±8.67 years; 70% females) respectively.

Compared to the present study, Sarkar *et al.*[71] in their study reported the mean age of patients in two groups to be 32.77 and 36.10 years and a dominance of males (80% and 76.7% respectively). However, Kumar *et al.*[73] not only reported the mean age of patients in two groups as 38.22 and 37.28 years which is close to that in the present study but also had a dominance of females (78% and 66% respectively) as in the present study. A much higher mean age (47.13 and 42.6 years) and a high dominance of males over females (M:F 20.6 and 16.02 respectively) was reported by Kumari and Agarwal[76]. In fact, from age and sex point of view these drugs have been evaluated for their comparative efficacy in a vast spectrum of age and sex combinations with age of patients ranging from 36 to 43.9 years and sex-ratio ranging from 1.5 to 3.37[77,79,84]. In general, in most of the studies the mean age of patients had remained in 35 to 45 years range though sex-ratio generally shows a dominance of males.

In the present study, mean onset time of sensory and motor blocks was significantly shorter in DXM as compared to that in FN group. Median block level was significantly higher in DXM group (T6) as compared to that in FN Group (T9). In the present study, mean time to attain sensory block was 7.97±0.76 min in DXM as compared to 12.00±1.64 min in FN group while mean time taken to achieve motor block was 10.53±0.94 min in DXM as compared to 14.57±1.59 min in FN group, thus showing that sensory motor block was almost 1.5 times and motor block was almost 1.4 times faster in dexmedetomidine as compared to that in fentanyl group. In their study, Sarkar *et al.*[71] found the mean time to achieve sensory and motor blocks in DXM group to be 8.10 and 15.10 min respectively in the DXM and 15.03 and 22.77 min respectively in the FN group thus showing them to be 1.85 and 1.5 times faster in dexmedetomidine as compared to that in fentanyl group. In another study, Kiran *et al.*[72] found the achievement of sensory block to be 1.2 times faster in dexmedetomidine as compared to that in fentanyl group when used as adjuvant with ropivacaine. In the present study, we used bupivacaine as the local anaesthetic and found it to be even faster. Bupivacaine is a stronger local anaesthetic as compared to ropivacaine and hence can facilitate a faster block achievement. In fact, in other studies too that used DXM and FN with ropivacaine, though the relative differences in onset times of sensory and motor blocks were lesser as compared to that in the studies using them with bupivacaine yet in these studies too, the onset times were shorter in DXM as compared to that in the FN group. For example, the study by Kumar *et al.*[73] who used the trial drugs with ropivacaine reported the mean Onset time of sensory and motor blocks as 9.22±0.86 and 10.12±1.01 min respectively in DXM group as compared to 11.30±0.99 and 13.36±1.11 min respectively in the FN group, thus showing them to be 1.2 and 1.3 times shorter in the DXM as compared to that in the FN group. Nevertheless, irrespective of whether they were used with ropivacaine or bupivacaine, almost all the studies similar to the present study found the onset times of block to be significantly shorter in DXM as compared to that in FN group[76-84].

In this study, we observed mean duration of sensory and motor blocks was significantly longer in DXM (315.10±14.69 and 321.70±14.07 min respectively) as compared to that in FN group (299.97±18.12 and 311.03±18.66 min respectively). In the present study, mean duration of sensory and motor blocks was prolonged by 15.19 and 10.67 minutes respectively. Compared to this, Kumar *et al.*[73] reported that DXM increased duration of motor block by 42.18 min as compared to that in FN group. In another study, Kumari and Agarwal[76] found this difference to be even higher for sensory block (67 min). In the present study, however, though we found DXM to have significantly longer sensory and motor block durations yet did not found the differences between the two groups to be that longer as in these studies. However, despite magnitude of difference between DXM and FN group for block durations in the present study showing some variability in the present study, it was in trend with most of the existing literature showing it to be longer in DXM as compared to that in FN group[73,77,78,80,84].

With respect to post-operative pain, in the present study we found mean post-operative VAS scores for pain were generally lower in DXM group as compared to that in FN group and difference was significant statistically too at 3 and 6 hour post-operative intervals. A better effect of DXM on intensity of pain has also been reported in other studies too[79,80,82,84]. As far as absence of significant differences beyond six hours, it may be affected by consumption of rescue analgesia as most of the cases had used rescue analgesia by that time.

In the present study mean time to first rescue analgesia was significantly longer and mean number of rescue analgesics were significantly fewer in DXM (331.5±13.80 min and 2±0.87 respectively) as compared to that in FN group (319.03±19.31 min and 2.50±0.68 respectively).

In the present study, none of the patients in DXM group received more than 3 dosages of rescue analgesia, however, in FN group, some patients required 4 dosages too. These findings are in agreement with the observations of Sarkar *et al.*[71] who found 3 or more rescue analgesic dosages need in 80% of FN as compared to 6.67% of DXM group patients. They also reported median time to rescue analgesia to be 330 min in DXM as compared to only 210 min in FN group. In another study, Kiran *et al.*[72] reported mean time to rescue analgesia to be 312.4 and 243 min respectively in DXM and FN groups. Kumari *et al.*[76] reported it as 335 and 268 min respectively. In other studies too, DXM was found to be instrumental in increasing the duration of analgesia and decreasing the rescue analgesic need as observed in the present study[79-84].

In the present study, we did not observe any major adverse effect of drugs in either of two groups. Among various adverse effects, hypotension was the most common adverse effect associated with DXM use and it was significantly higher in DXM as compared to that in FN group. Most of the studies do not report major adverse effects of the drugs[71,80]. Among studies reporting adverse effects of the drugs, the nature and pattern shows some variability. However, hypotension has been reported to be the most common adverse effect requiring intervention in DXM group[71,76]. Sarkar *et al.*[71] in their study reported vasopressor need in 69.6% of DXM group as compared to 30.4% of fentanyl group patients. However, there are few studies that report a lower incidence of hypotension and bradycardia in DXM group[80]. Some studies report nausea and vomiting to be higher in fentanyl group while urinary retention, shivering and dry mouth to be higher in dexmedetomidine group[74], however, did not find a significant difference between the two groups for any of these adverse effects. Some studies also report sedation as a side effect associated with dexmedetomidine[76]. Some other perceive sedation as a beneficial rather than adverse attribute associated with DXM[81]. One study reported incidence of dry mouth to be higher in DXM as compared to that in the FN group[82]. Thus, except for hypotension, for other adverse effects, inconsistent results are reported in literature. Hypotension, definitely is an adverse effect associated with DXM and must be given a due consideration while planning its use.

CONCLUSION

The findings of the study showed that addition of both fentanyl as well as dexmedetomidine was effective in offering post-operative analgesia in lower limb and lower abdominal surgeries under epidural anaesthesia. Of the two, dexmedetomidine as compared to fentanyl was offered faster and prolonged blockade, longer analgesic effect and lesser consumption of rescue analgesia, however, it was also associated with an increased risk of hypotension, hence selection of appropriate adjuvant drug use be done by proper trade-off between safety and efficacy. Further studies on a larger sample size are recommended to validate the findings of the present study.

REFERENCES

1. Leone S, Di Cianni S, Casati A, et al. Pharmacology, toxicology, and clinical use of new long acting local anesthetics, ropivacaine and levobupivacaine. Acta Biomed 2008; 79:92–105.
2. Polley LS, Columb MO, Naughton NN, et al. Effect of intravenous versus epidural fentanyl on the minimum local analgesic concentration of epidural bupivacaine in labor. *Anaesthesiology*2000; 93:122–128. Link
3. Chattopadhyay A, Maitra S, Sen S, Bhattacharjee S, Layek A, Pal S, Ghosh K. A Study to Compare the Analgesic Efficacy of Intrathecal Bupivacaine Alone with Intrathecal Bupivacaine Midazolam Combination in Patients Undergoing Elective Infraumbilical Surgery. Anesthesiology Research and Practice 2013; 2013: Article ID 567134, 1-5.
4. Rayburn W, Rathke A, Leuschen MP, et al. Fentanyl citrate analgesia during labor. *Am J Obstet Gynecol* 1989; 161:202–206. Link
5. De Jong R. Local anesthetic pharmacology. In Brown DL,ed Regional anaesthesia and analgesia. Philadelphia, Pa: Saunders; 1996:124-142.
6. Cox CR, Faccenda KA, Gilhooly C, Bannister J, Scott NB, Morrison LMM. Extradural S(-) Bupivacaine: comparision with racemic RS bupivacaine. Br J Anaesth. 1998;80:289-293. Link
7. Yadav RK, Sah BP, Kumar P, Singh SN. Effectiveness of addition of neostigmine or

dexamethasone to local anaesthetic in providing perioperative analgesia for brachial plexus block: A prospective, randomized, double blinded, controlled study. Kathmandu Univ Med J (KUMJ) 2008; 6: 302–9. Link
8. Madhusudhana R, Kumar K, Kumar R, Potli S, Karthik D, Kapil M. Supraclavicular brachial plexus block with 0.75 % ropivaciane and with additives tramadol, fentanyl-a comparative pilot study. Int J Biol Med Res. 2011; 2(4): 1061 – 1063. Link
9. Mukherjee K, Das A, Basunia SR, Dutta S, Mandal P, Mukherjee A. Evaluation of Magnesium as an adjuvant in Ropivacaine-induced supraclavicular brachial plexus block: A prospective, double-blinded randomized controlled study. J Res Pharm Pract. 2014 Oct-Dec; 3(4): 123–129. Link
10. Fritsch G, Danninger T, Allerberger K, Tsodikov A, Felder TK, Kapeller M, Gerner P, Brummett CM. Dexmedetomidine added to ropivacaine extends the duration of interscalene brachial plexus blocks for elective shoulder surgery when compared with ropivacaine alone: a single-center, prospective, triple-blind, randomized controlled trial. Reg Anesth Pain Med. 2014 Jan-Feb;39(1):37-47. Link
11. Faria-Silva R, de Rezende DC, Ribeiro JM, Gomes TH, Oliveira BAMFM, et al. Association of clonidine and ropivacaine in brachial plexus block for shoulder arthroscopy. Rev Bras Anestesiol. 2014; 6 pages, doi:10.1016/j.bjane.2013.06.022. Link
12. Hunt CO, Naulty JS, Bader AM, Hauch MA, Vartikar JV, Datta S, et al. Perioperative analgesia with subarachnoid fentanyl-bupivacaine for Cesarean delivery. Anesthesiology. 1989; 71: 535–40.
13. Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kushwaha JK. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. J Anaesthesiol Clin Pharmacol. 2011 Jul-Sep; 27(3): 339–343.
14. Boussofara M, Carlès M, Raucoules-Aimé M, Sellam MR, Horn JL. Effects of intrathecal midazolam on postoperative analgesia when added to a bupivacaine-clonidine mixture. Reg Anesth Pain Med. 2006; 31: 501–5.
15. Shukla D, Verma A, Agarwal A, Pandey HD, Tyagi C. Comparative study of intrathecal dexmedetomidine with intrathecal magnesium sulfate used as adjuvants to bupivacaine. J Anaesthesiol Clin Pharmacol. 2011 Oct-Dec; 27(4): 495–499.
16. Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. Anesth Analg. 2003;97(2):534-540. Link
17. Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, et al. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain. 2016 Feb;17(2):131-57. doi: 10.1016/j.jpain.2015.12.008. Erratum in: J Pain. 2016;17(4):508-10. Link
18. Wu CL, Raja SN. Treatment of acute postoperative pain. Lancet. 2011;377(9784):2215-25. Link
19. Breazu CM, Ciobanu L, Hadade A, Bartos A, Mitre C, Mircea PA, Ionescu D. The efficacy of oblique subcostal transversus abdominis plane block in laparoscopic cholecystectomy - a prospective, placebo controlled study. Rom J Anaesth Intensive Care. 2016;23(1):12-18. Link