Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2023i1.184
*Biol. Clin. Sci. Res. J., Volume, **2023**: 184*
Original Research Article

COMPARISON OF PROLONGATION OF ANALGESIA AND CONSUMPTION OF OPIOIDS IN PATIENTS GIVEN SAB WITH LOCAL ANESTHESIA ALONE VERSUS WITH TRAMADOL AS ADJUVANT THERAPY UNDERGOING LOWER LIMB SURGERY

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(Received, 10th September 2022, Revised 18th January 2023, Published 19th January 2023)

Abstract: *The purpose of this study was to determine whether or not adding intrathecal tramadol to bupivacaine for lower limb procedures increased the duration of analgesia and decreased the mean post-operative opioid intake. This research was carried out between June 1 and November 30, 2022, in the Department of Anaesthesiology at Aziz Bhatti Shaheed Teaching Hospital in Gujrat, Pakistan. Non-probabilistic sequential sampling was used to pick the patients. One hundred patients from the ASA I, II, and III categories who met the inclusion criteria and were scheduled for lower limb surgery were randomly assigned to one of two groups. The tramadol-bupivacaine group (T) was given 15 milligrams of tramadol and 10 milligrams of bupivacaine (0.5 percent). In comparison, the bupivacaine-alone group (B) was given 1 milliliter of saline and 10 milligrams of bupivacaine (0.5 percent). The duration of analgesia was recorded by tracking the time until the patient first asked for pain medication. The average amount of opioid analgesia taken by both groups in the first 24 hours after surgery was also compared. SPSS version 22 was used for the data analysis. Anesthesia lasted much longer, 174.26 ± 15.21 minutes in the tramadol group, compared to 132.5 ± 14.48 minutes in the bupivacaine group. (p = 0.006). As expected, there was a significant (p 0.001) reduction in 24-hour opioid intake (308.2 ± 23.8) in group T compared to group B (470.5 ± 36.2mg). This research confirmed that intrathecal tramadol (15mg) could be safely used with bupivacaine in subarachnoid blocking to increase the duration of analgesia and reduce the need for opioids in the post-operative period following lower limb procedures.*

Keywords: subarachnoid block, prolongation, analgesia, tramadol, opioids

Introduction

Adverse physiological effects of pain can significantly increase morbidity and mortality (Alenezi et al., 2021). It is crucial to provide adequate post-operative analgesia since it is linked to reduced physiological disturbance, speedier recovery, and easier ambulation. For lower limb procedures, subarachnoid block (SAB) is a popular type of anesthesia. It offers better analgesia than general anesthesia and decreases perioperative complications (Malhotra et al., 2020). To give intraoperative and persistent post-operative analgesia, a variety of intrathecal adjuvants are used with local anesthetics (LA). Opioids, clonidine, dexmedetomidine, neostigmine, midazolam, dexamethasone, and others have all been used as adjuvants to LA with variable degrees of success and a variety of side effects (Swain et al., 2017). It has always been extremely sensitive to employ local anesthetics for intrathecal usage. Intrathecal injections of numerous substances have been used to treat post-operative and surgical pain (Edinoff et al., 2021). The most used medication, buprenorphine, has an 80-minute maximum effective half-life. However, some patients may not want the lengthy sensory and motor block and the substantial sympathetic block that can result from using a standard dose of bupivacaine (Venkata et al., 2015). While diluted low-dose bupivacaine limits the extent of the spinal block and facilitates a speedy recovery, it may not be enough to achieve a complete sensory block or to last long enough for surgical anesthesia (Nanda and Van de Velde, 2022). Although significant side effects from local anesthetics are uncommon, they do occur and can include hypotension, bradycardia, urinary retention, neurological impairment, etc. The volume, dosage,

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and height of spinal anesthetic are determined to be the main determinants of these complications (Lawrie et al., 2017).

These local anesthetics can occasionally cause patients discomfort due to their prolonged total effective surgical anesthetic times. Different adjuvants have been used in clinical practice to significantly extend local anesthetics' adequate surgical anesthetic time to overcome the time limitation issue (Lirk et al., 2018). Additionally, with the fewest adverse effects possible, they decrease the overall dose of local anesthetics while increasing the density of spinal blockade. But like all medications, these adjuvants have negative effects, which have historically been the subject of discussion over their usage in such a sensitive framework (Prabhakar et al., 2019). With a dual mechanism of action, tramadol is a synthetic 4-phenyl-piperidine counterpart of codeine. It activates the -receptor and the - and -opioid receptors to a lesser extent. Reducing the absorption of norepinephrine and serotonin stimulates spinal inhibition of pain, much like tricyclic antidepressants do. As a result, a non-opioid basis of analgesia is produced (Ganjali et al., 2016). Only a few trials utilizing tramadol in the subarachnoid space have been conducted in Pakistan. Despite having significant benefits and few side effects, it is frequently used as an IV analgesic drug. The study's objective was to determine which group produced analgesia for a more extended period, as determined by the initial request for analgesia and the mean amount of opioids used post-operatively.

Methodology

One hundred and eight participants were examined in this randomized controlled research. After receiving approval from the Ethics Committee of the Institute and the College of Physicians and Surgeons of Pakistan, this study was carried out in the Department of Anaesthesiology, Aziz Bhatti Shaheed Teaching Hospital Gujrat, Pakistan, from June 1 through November 30, 2022. (CPSP). For lower limb surgery under spinal anesthesia, we selected 108 ASA I, II, and III patients by non-probability consecutive sampling, aged 30 to 70, of both genders. Every patient provided their informed permission. The study eliminated cases with the cerebrovascular illness that were contraindicated for spinal anesthesia or converted to general anesthetic for any reason.

All eligible patients were divided into two groups at random. By opening an unmarked envelope and revealing the type of coded spinal solution package to be used, Group B (Bupivacaine alone) and Group T (Tramadol-Bupivacaine), each group, including 54 patients, were randomized. The spinal solutions were made and labelled by a second anesthetist who was not a part of the study. The spinal solution was delivered without the anesthesiologist's knowledge.

Baseline measurements of each patient's heart rate, non-invasive blood pressure, and oxygen saturation were taken in the operating room prior to the induction of the spinal anaesthesia and again throughout the surgery. An 18-gauge intravenous cannula was used to establish venous access before causing spinal anaesthesia, and the patient received Ringer Lactate (10 ml/kg) beforehand. Spinal anaesthesia was delivered aseptically with the patient seated using a 25G Quincke spinal needle at the L3-4 vertebral level. After establishing that cerebrospinal fluid was flowing freely, each patient was given one of the coded spinal solutions. While patients in Group B (n=54) received intrathecal 0.5 percent hyperbaric bupivacaine 10mg in 2ml and 1ml normal saline, patients in Group T (n=54) received intrathecal tramadol 15 mg plus 10mg of 0.5 percent hyperbaric bupivacaine (total 3ml).

The first request for an analgesic dose during the recovery period was regarded as the time limit for that group, and rescue analgesia was given in accordance.

After the patient was transported to the step-down unit following surgery, an anesthesia resident who was unaware of the patient's group assignment measured the pain using the visual analogue scale (VAS). They were given 0.5 mg/kg of tramadol intravenously whenever their VAS score was more than 3. This was done every 10 minutes until their VAS score was under 3. Tramadol consumption over 24 hours. Data were acquired and examined using SPSS version 22 for Windows before results could be deciphered. Quantitative factors were expressed as mean SD, whilst qualitative data were expressed as percentages. For parametric data, the student's unpaired t-test was used, and chi-square tests were used for non-parametric data. The cut-off for significance was 0.05.

Results

Our analysis included a total of 128 patients, from which 20 were disqualified because they did not meet the study's inclusion requirements. The 108 subjects were then randomly split into two groups. Four patients out of 54 were removed from the tramadol group because they received general anesthesia, three out of a total of 54 were removed from the bupivacaine group for the same reasons, and one did not have complete documentation. (Figure 1).

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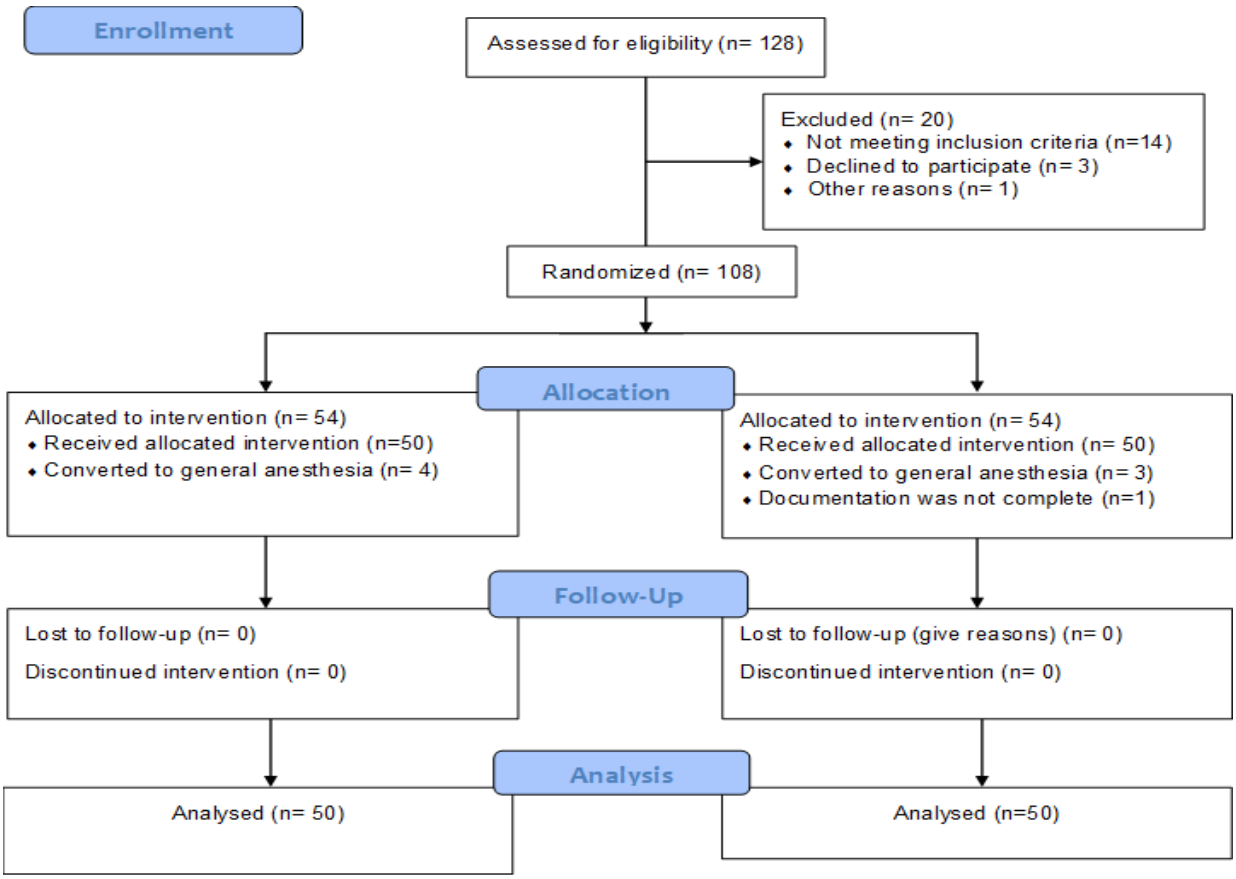

Figure 1: Enrolment flow chart

Age, sex, height, weight, and surgical time were not significantly different between the two groups. (Table I).

Table 1 Demographic variables of both groups

Variables	Group B 50	Group T 50	*p*-value
Age (years)	58.86 ± 7.32	57.48 ± 8.28	0.754
Sex Distribution			
Male	27 (54%)	28 (56%)	0.986
Female	23 (46%)	22 (44%)	
ASA Status			
I	9 (18%)	12 (24%)	0.714
II	22 (44%)	20 (40%)	
III	19 (38%)	18 (36%)	
Operative Time (Minutes)	117.65 ± 23.84	121.32 ± 33.12	0.397

Tramadol patients experienced longer-lasting analgesia compared to bupivacaine patients. The mean duration of analgesia in the tramadol group was 174.26 ± 15.21 mins, whereas, in the bupivacaine group, it was 132.5 ± 14.48 mins, as shown in table-II (p= 006). (Figure 2)

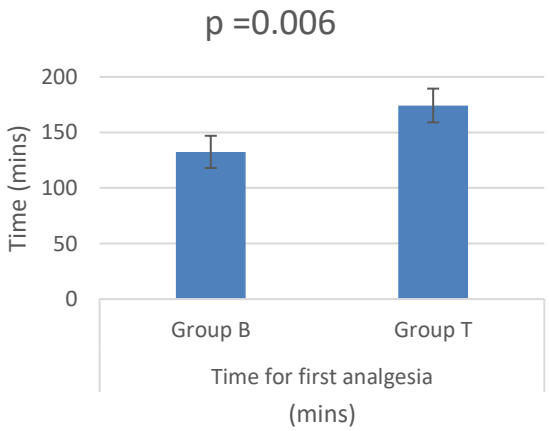

Figure 2 Comparison of time for the first use of analgesia between the groups

Mean total tramadol intake in the first 24 hours after surgery was significantly different between the two groups, with group B taking 470.5 ± 36.2 mg and

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group T taking 308.2 ± 23.8 mg (P < 0.001) (table 3, figure 3). Patients who had SAB block with tramadol reported significantly decreased overall pain (49.72 ± 5.89) compared to the control group B (66.26 ± 4.78) after the first 24 hours (P < 0.001). (Table 2).

Table 2 Comparison of Mean opioid consumption and pain score between the groups.

Parameters	Group B (n=50)	Group T (n=50)	p-value
Mean tramadol use	470.5 ± 36.2	308.2 ± 23.8	< 0.001
Mean Pain Score	66.26 ± 4.78	49.72 ± 5.89	< 0.001

Table 3 Comparison of hourly use of mean opioid use between the groups

Hours	Group B 50	Group T 50
0	57.8	31.5
2	59.3	22.5
4	52.3	18.1
6	48.7	18.0
8	48.4	19.4
10	40.2	24.9
12	38.3	22.7
14	33.2	18.2
16	27.1	19.7
18	20.0	26.7
20	19.2	31.5
22	15.1	28.8
24	10.7	26.7

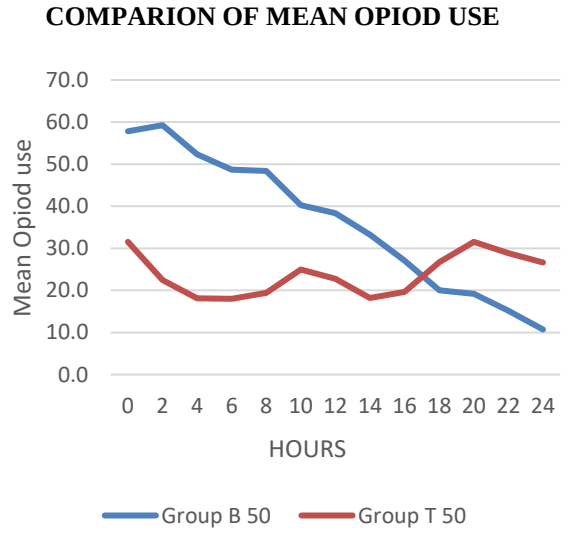

Figure 3 shows the graphical representation of every two hourly use of mean opioid use between the groups.

Discussion

Since their discovery, opioids have been at the center of the analgesic and pain management fields. Patients who have had surgery have had pain medication administered to them by intravenous, intrathecal, or epidural methods. To get optimal results, opioids are frequently used with local anesthetics in treatment protocols. According to many research findings, morphine, fentanyl, and sufentanil are the most commonly employed drugs that produce satisfactory results (Bajwa et al., 2017; Honca et al., 2015; Subramani et al., 2020).

A partial opioid analgesic with a central action, tramadol has a terminal half-life of 5.5 hours and retains its analgesic effects for 10 hours following epidural analgesia. Tramadol is a useful substitute for opioid agonists because of how extremely different its analgesic effect is from that of those medicines. Tramadol works as a weak agonist for the receptor as well as, albeit to a lesser extent, as an agonist for the opioid receptors. By preventing the reuptake of serotonin and norepinephrine, respectively, analgesic effects are also increased. According to certain studies, tramadol may also have a local anaesthetic effect on the peripheral system's nerves.(Sousa and Ashmawi, 2015). According to the results of our study, there are various advantages of delivering intrathecal tramadol in addition to bupivacaine. These advantages include extending the patient's pain-free period and obtaining higher block levels. Tramadol was added, however it had no negative impact on the hemodynamic profile or other side effects that are frequently related to pure opioid agonists, such as vomiting, nausea, pruritus, or respiratory depression.

Numerous studies have demonstrated that combining tramadol with bupivacaine during spinal anaesthesia can extend the period that patients can be pain-free and unconscious. In a research on orthopaedic patients, Hussain A found that intrathecal tramadol considerably increased the duration of analgesia while having few negative effects.(Hussain et al., 2016). Intrathecal tramadol 25 mg was shown to be a safe alternative to intrathecal fentanyl 25 mcg in a different study by Afolayan J. The patients in this study had undergone an open appendectomy. They reported that post-operative vomiting was the most common complication associated with tramadol; however, they did not mention any adverse outcomes (Afolayan et al., 2014).

When the length of time under anesthesia was compared between the two groups and the VAS scores, Chakarbarty S revealed that using tramadol in conjunction with bupivacaine in major gynecological procedures produced beneficial results (Chakraborty

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et al., 2008). The duration of analgesia was effectively prolonged in his study by adding 20 mg of tramadol to 15 mg of bupivacaine. This combination increased the duration of analgesia from 210 ± 10.12 minutes in the bupivacaine saline group to 380 ± 11.82 minutes in the bupivacaine-tramadol group10. Although the sedation score was higher in the tramadol group, a study that compared the effects of 50 mg tramadol and 2 mg nalbuphine used in the subarachnoid block was carried out by Mostafa MG (Mostafa et al., 2011). This investigation showed that both medications had an equal impact on extending analgesia duration and reducing VAS ratings. In addition, these medications' negative effects were rather mild.

With intrathecal tramadol coupled with lignocaine in spinal anaesthesia, Parthasarathy S showed a noticeably longer duration of analgesia and lower VAS scores in the treatment of post-appendectomy patients. Along with the patients having spinal anaesthesia, this was done. 10 milligrams of tramadol significantly increased the post-operative period's interim analgesia when administered to 1.8 millilitres of lignocaine at a concentration of 5%. (Parthasarathy and Ravishankar, 2002). Additional research on the use of tramadol in regional anesthetic, including that conducted by Kumari P, Brijesh J, and Ozcengiz D, has shown that the drug is effective when used as an adjuvant in spinal, epidural, or caudal anesthesia rather than pure opioid agonists (Brijesh and Sarasawat, 2001; Chatrath et al., 2015; Ozcengiz et al., 2001).

However, several investigations, including the one by Abdulhasan, found that introducing tramadol to the subarachnoid area had no beneficial effects (Abdulhasan and Hassoon, 2019). When intrathecally administered tramadol was employed, his research did not improve post-operative analgesia for TURP patients. Both Grace D and Wilder-smith CH have neglected to indicate any potential advantages of administering bupivacaine in combination with intrathecal tramadol (Grace and Fee, 1995; Wilder-Smith et al., 1998). There were a lot of different hypotheses that could have been made about why this experiment failed, but the specific process was still a mystery to them. It was recommended that more research be done to figure out the exact mechanism at play here. Our study has a few limitations as well. The sample size was due to single-centric research, and we used only a single dose of tramadol to assess its analgesic effect. To ascertain the most effective dose of tramadol for intrathecal administration and its safety profile, more research comprising multiple quantities and a protracted follow-up period should be carried out.

Conclusion

This study demonstrated that intrathecal tramadol (15 mg) and bupivacaine could be used in subarachnoid blocking safely to extend the duration of analgesia and lessen the need for opioids after surgery for lower limb procedures.

Conflict of interest

The authors declared absence of conflict of interest.

References

Abdulhasan, A. I., and Hassoon, S. M. (2019). A COMPARATIVE STUDY BETWEEN TRAMADOL AND FENTANYL IN SPINAL ANESTHESIA IN CESAREAN SECTION.

Afolayan, J. M., Olajumoke, T., Amadasun, F., and Edomwonyi, N. (2014). Intrathecal tramadol versus intrathecal fentanyl for visceral pain control during bupivacaine subarachnoid block for open appendicectomy. *Nigerian journal of clinical practice* **17**, 324-330.

Alenezi, A., Yahyouche, A., and Paudyal, V. (2021). Current status of opioid epidemic in the United Kingdom and strategies for treatment optimisation in chronic pain. *International journal of clinical pharmacy* **43**, 318-322.

Bajwa, B. S., Singh, A. P., and Rekhi, A. K. (2017). Comparison of intrathecal clonidine and fentanyl in hyperbaric bupivacaine for spinal anesthesia and post-operative analgesia in patients undergoing lower abdominal surgeries. *Saudi journal of anaesthesia* **11**, 37.

Brijesh, J., and Sarasawat, V. (2001). Efficacy of intrathecal tramadol for post-operative pain relief in cases of LSCS and major gynecological surgeries-A clinical evaluation. *Indian J Anaesth* **45**, 282.

Chakraborty, S., Chakrabarti, J., and Bhattacharya, D. (2008). Intrathecal tramadol added to bupivacaine as spinal anesthetic increases analgesic effect of the spinal blockade after major gynecological surgeries. *Indian journal of pharmacology* **40**, 180.

Chatrath, V., Khetarpal, R., Sharma, S., Kumari, P., and Bali, K. (2015). Fentanyl versus tramadol with levobupivacaine for combined spinal-epidural analgesia in labor. *Saudi journal of anaesthesia* **9**, 263.

Edinoff, A. N., Houk, G. M., Patil, S., Siddaiah, H. B., Kaye, A. J., Iyengar, P. S., Cornett, E. M., Imani, F., Mahmoudi, K., and Kaye, A. M.

[Citation: Sheikh, N.G., Javed, H.M., Sheikh, M.G., Avais, B., Butt, Z., Jamshaid, B. (2023). Comparison of prolongation of analgesia and consumption of opioids in patients given sab with local anesthesia alone versus with tramadol as adjuvant therapy undergoing lower limb surgery. *Biol. Clin. Sci. Res. J.,* **2023***: 184*. doi: https://doi.org/10.54112/bcsrj.v2023i1.184]

(2021). Adjuvant drugs for peripheral nerve blocks: The role of alpha-2 agonists, dexamethasone, midazolam, and non-steroidal anti-inflammatory drugs. *Anesthesiology and Pain Medicine* **11**.

Ganjali, M. R., Larijani, B., and Pourbasheer, E. (2016). Fabrication of an all solid state (ASS) polymeric membrane sensor (PME) for tramadol and its application. *Int. J. Electrochem. Sci* **11**, 2119-2129.

Grace, D., and Fee, J. (1995). Ineffective analgesia after extradural tramadol hydrochloride in patients undergoing total knee replacement. *Anaesthesia* **50**, 555-558.

Honca, M., Dereli, N., Kose, E. A., Honca, T., Kutuk, S., Unal, S. S., and Horasanli, E. (2015). Low-dose levobupivacaine plus fentanyl combination for spinal anesthesia in anorectal surgery. *Revista Brasileira de Anestesiologia* **65**, 461-465.

Hussain, A., Siddiqui, S., Sharma, M., and Madhesiya, G. (2016). Intrathecal Tramadol added to bupivacaine as spinal anesthetic increases analgesic effect of the spinal blockade after lower limb orthopedic Surgeries. *Indian J Appl Res* **6**, 4-6.

Lawrie, C. M., Ong, A. C., Hernandez, V. H., Rosas, S., Post, Z. D., and Orozco, F. R. (2017). Incidence and risk factors for post-operative urinary retention in total hip arthroplasty performed under spinal anesthesia. *The Journal of arthroplasty* **32**, 3748-3751.

Lirk, P., Hollmann, M. W., and Strichartz, G. (2018). The science of local anesthesia: basic research, clinical application, and future directions. *Anesthesia & Analgesia* **126**, 1381-1392.

Malhotra, A., Singh, U., Singh, M. R., Sood, D., Grewal, A., and Mahajan, A. (2020). Efficacy of premixed versus succedent administration of fentanyl and bupivacaine in subarachnoid block for lower limb surgeries: A randomised control trial. *Indian Journal of Anaesthesia* **64**, S175.

Mostafa, M. G., Mohamad, M. F., and Farrag, W. (2011). Which has greater analgesic effect: intrathecal nalbuphine or intrathecal tramadol. *J Am Sci* **7**, 480-84.

Nanda, A., and Van de Velde, M. (2022). Regional anaesthesia: what surgical procedures, what blocks and availability of a "block room"? *Current Opinion in Anaesthesiology* **35**, 698-709.

Ozcengiz, D., Gunduz, M., Ozbek, H., and Isik, G. (2001). Comparison of caudal morphine and tramadol for post-operative pain control in children undergoing inguinal herniorrhaphy. *Pediatric Anesthesia* **11**, 459-464.

Parthasarathy, S., and Ravishankar, M. (2002). Single dose intrathecal tramadol in the management of post appendicectomy pain. *J Anaesthesiol Clin Pharmacol* **18**, 419-22.

Prabhakar, A., Lambert, T., Kaye, R. J., Gaignard, S. M., Ragusa, J., Wheat, S., Moll, V., Cornett, E. M., Urman, R. D., and Kaye, A. D. (2019). Adjuvants in clinical regional anesthesia practice: A comprehensive review. *Best Practice & Research Clinical Anaesthesiology* **33**, 415-423.

Sousa, A. M., and Ashmawi, H. A. (2015). Local analgesic effect of tramadol is not mediated by opioid receptors in early post-operative pain in rats. *Revista Brasileira de Anestesiologia* **65**, 186-190.

Subramani, Y., Nagappa, M., Kumar, K., Fochesato, L.-A., Chohan, M. B. Y., Zhu, Y. F., Armstrong, K., and Singh, S. I. (2020). Effect of intrathecal lipophilic opioids on the incidence of shivering in women undergoing cesarean delivery after spinal anesthesia: a systematic review and bayesian network meta-analysis of randomized controlled trials. *BMC anesthesiology* **20**, 1-13.

Swain, A., Nag, D. S., Sahu, S., and Samaddar, D. P. (2017). Adjuvants to local anesthetics: Current understanding and future trends. *World journal of clinical cases* **5**, 307.

Venkata, H. G., Pasupuleti, S., Pabba, U. G., Porika, S., and Talari, G. (2015). A randomized controlled prospective study comparing a low dose bupivacaine and fentanyl mixture to a conventional dose of hyperbaric bupivacaine for cesarean section. *Saudi journal of anaesthesia* **9**, 122.

Wilder-Smith, C., Wilder-Smith, O., Farschtschian, M., and Naji, P. (1998). Preoperative adjuvant epidural tramadol: the effect of different doses on post-operative analgesia and pain processing. *Acta anaesthesiologica scandinavica* **42**, 299-305.

[Citation: Sheikh, N.G., Javed, H.M., Sheikh, M.G., Avais, B., Butt, Z., Jamshaid, B. (2023). Comparison of prolongation of analgesia and consumption of opioids in patients given sab with local anesthesia alone versus with tramadol as adjuvant therapy undergoing lower limb surgery. *Biol. Clin. Sci. Res. J.,* **2023***: 184*. doi: https://doi.org/10.54112/bcsrj.v2023i1.184]

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