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Comparative Study Between Bupivacaine Versus Bupivacaine With Pethidine In Bilateral Transversus Abdominis Plane Block For Postoperative Pain Relief In Patients Undergoing Cesarean Deliveries

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ABSTRACT

Background: Among the most prevalent surgical procedures in the world is the cesarean section (CS). Postoperative analgesia is too important to prevent unwanted side effects like venous thromboembolism, respiratory complications, and a longer stay in the hospital. Pethidine was used as adjuvants to local anesthesia to improve the quality of TAP block for caesarian section.

Aim of The Work: To evaluate and compare the effects of pethidine in combination with bupivacaine on the quality of the TAP block for caesarian sections.

Patients and Methods: A total of 60 patients with American Society of Anesthesiologists (ASA) physical status I or II who were scheduled for Cesarean deliveries were enrolled in this randomized, prospective, double-blind clinical trial. Al-Azhar University Hospitals were used to conduct the research (Al-Husein and Sayed Galal Hospitals). They have been split into 2 groups of equal size: patients in Group (B) received ultrasound-guided TAP block with 20 ml of bupivacaine 0.25 % bilaterally, while patients in Group (BP) received ultrasound-guided TAP block with 20 ml of bupivacaine 0.25 % and 50 mg of pethidine bilaterally.

Results: The BP group's VAS score was significantly lower at 8 and 12 hours. The time to the first analgesic dose in the BP group was significantly longer than in the B group.

Conclusion: Addition of pethidine was a useful adjuvant to bupivacaine for improving quality of TAP block for caesarian section.

Keywords: Pethidine; Caesarian section; Bupivacaine; Transversus Abdominis Plane block.

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Authorship: All authors have a substantial contribution to the article.

INTRODUCTION

Among the most prevalent surgical procedures in the world is the Caesarean section (CS). Both the mom and the newborn experience post-surgical pain, especially in the first 48 hrs after delivery. The pain might be excruciating, disrupting mother-child bonding.¹ In a dose-dependent way, the analgesic morphine's well-known adverse effects of nausea, vomiting, itchiness, and sedation could interact with the interaction between mom and baby, breastfeeding, and post-partum experience. However, several alternative strategies for reducing morphine consumption after surgery were described.² One of these has been the (TAP) block, which is a regional anesthetic method that offers sensory and motor block of the anterior abdominal wall from T7 to L1, but has no visceral impact. It's utilized in lower abdominal surgeries like CS.³ Since the advent of ultrasound into anesthetic procedures, there has been an increase in the importance of the (TAP) block.⁴ Multiple benefits for mother and baby obtained by TAP block include: long and effective analgesia, earlier oral nutrition, earlier mobilization, and a brief

stay in the hospital.⁵ Recent researches have focused on prolongation of the analgesia provided by the block.⁶ Pethidine is a local anesthetic opioid that binds to peripheral opioid receptors and impacts voltage-gated sodium channels.⁷ Pain in inflamed tissues is linked to peripheral opioid receptors. According to studies, opioid antinociception is triggered by the stimulation of opioid receptors outside the CNS, and the analgesic impact of opioids administered systemically is largely mediated by peripheral opioid receptors.⁸ According to electrophysiological studies, pethidine administration is followed by a sensory and motor block caused by peripheral nerve action. Pethidine is useful in a variety of regional anesthesia methods, including subarachnoid, epidural, intraarticular, as well as regional intravenous.⁹

PATIENTS AND METHODS

A total of 60 patients with American Society of Anesthesiologists (ASA) physical status I or II who were scheduled for Cesarean deliveries were enrolled in this randomized, prospective, double-

blind clinical study. The research took place at Al-Azhar University Hospitals (Al-Husein and Sayed Galal Hospitals) between October 2018 and October 2020.

Patients have been split into 2 equal groups: Group (B) got an ultrasound guided TAP blocks with 20 ml of 0.25 % bupivacaine bilaterally, and Group (BP) received an ultrasound guided TAP blocks with 20 ml of 0.25 % bupivacaine bilaterally and 50 mg of pethidine bilaterally.

Inclusion Criteria: Patients with ASA I to II range in age from 21 to 45 years.

Exclusion Criteria: Refusal by the patient, allergy to local anesthetics, BMI >35 kg/m², chronic opioid use history, emergency CS, coagulopathy, infection at puncture site, and physical status ASA III or more.

Sample size: According to a prior study evaluating bupivacaine versus bupivacaine with pethidine in bilateral TAP blocks for postsurgical pain alleviation in women having undergone caesarean delivery, the alpha error was set at 5% and the power was set at 80% utilizing the STATA program.

Ethical considerations:

The study was performed following the approval of the ethical committee and obtaining the patients' informed consent. The study protocol was explained to the patients after taking their consent to the type of anesthesia and surgical procedure.

All patients were subjected to:

Monitor for vital signs: Noninvasive blood pressure (NIBP), electrocardiograph (ECG), oxygen saturation (SpO₂).

Ultrasound machine (sonosite M turbo).

Spinal anesthesia needle (25G).

Bupivacaine 0.5% - Lidocaine 2%.

Resuscitation equipment and drugs.

The pre-anesthetic assessment was performed with history, clinical examination and investigations. Furthermore, all patients have been given 0.01 mg/kg atropine as a premedication, 1 mg of metoclopramide, and 20 mg of famotidine intravenously before the operation. As a preload, 15 min were spent infusing 20 mL/kg of Ringer's lactate solution. Prior to surgery, mean arterial blood pressure (MAP), oxygen saturation (PO) and heart rate (HR) have been measured and documented. A standard spinal anesthetic containing 10-12 mg of 0.5 % hyperbaric bupivacaine was used on all study participants who obtained spinal anesthesia. After that, the patients were moved to a supine position with a 15° head elevation. Abdominal surgery has been conducted with continuous hemodynamic monitoring of BP and HR following confirmation of an adequate level of anesthesia. If the systolic blood pressure drops by 20% or < 90 mmHg, 6 mg of ephedrine is administered intravenously. Furthermore, 0.6 mg of atropine has been administered IV if the HR has been lowered to 50 bpm or less.

After completion of surgery, fascial plane block was applied to reduce and control pain following the surgery. With the patient supine, a linear US probe (high frequency probe, 10–12 MHz) linked to a portable US unit (SonoSite, USA) has been positioned in the mid-axillary plane midway between the lower costal margin and the highest point of the iliac crest. After disinfecting the skin, a 23-G 50-mm needle with an injection line has been inserted in the probe's plane. After placing the needle tip in the space between the internal oblique abdominal muscle and the transversus abdominis muscle, and after negative aspiration, 5 ml of saline (0.9%) has been injected to distend the TAP, followed by 20 ml of bupivacaine (0.25%), and the procedure has been repeated on the other side.

Group BP: received spinal anesthesia according to the same protocol as in group B and US guided TAP block bilaterally following surgery with 20 ml of 0.25% bupivacaine and 50 mg of pethidine.

The following parameters were assessed and recorded:

Hemodynamic monitoring: The first postoperative hour's MAP and HR have been documented every 15 minutes, followed by 2, 4, 6, 12, and 24 hrs.

Respiratory monitoring: For the first hour after surgery, peripheral oxygen saturation (SPO₂) was recorded every 15 minutes, then at 2, 4, 6, 12, and 24 hrs.

Assessment for post-operative pain using a visual analogue scale score every 15 minutes for the first hour postoperative, then 2, 4, 6, 12, and 24 hrs later.

Analgesic requirements (Rescue analgesic): The time to first rescue analgesic Nalbuphine (0.1 mg/kg) has been recorded in both groups. VAS reached 4 and the total amount of analgesia consumed in the first 24-h following surgery was recorded in both groups.

Post operative nausea and vomiting: In both groups, the prevalence of postsurgical nausea and vomiting has been assessed in the first 24 hours, and average consumption of rescue antiemetic doses of Granisetron (1mg) was recorded in both groups.

The time to hospital discharge was recorded.

Statistical analysis:

Using the SPSS statistical computer package, the gathered data was organized, tabulated, and statistically analyzed (IBM Corp., Armonk, NY, USA). Age and body weight were numerical variables with a normal distribution, and the mean ± SD have been utilized to summarize them. The mean values of the two groups have been compared utilizing an independent t-test. Other non-normally distributed variables are expressed as the median and interquartile range (IQR). As a significance test, the Mann–Whitney U-test has been utilized. The Chi-square test has been utilized to determine the significance of qualitative data, which was expressed as a number and a percentage. A statistically significant P-value of <0.05 has been considered.

RESULTS

The study enrolled 60 patients, 30 of whom had been randomized to receive TAP block with 20 ml of 0.25 % bupivacaine bilaterally + 2 ml of normal saline and the remaining 30 patients received TAP block with 20 ml of 0.25 % bupivacaine bilaterally + 50 mg of Pethidine (meperidine) bilaterally.

The demographics between groups B (bupivacaine) and BP (bupivacaine-Pethidine) exhibited no statistically significant differences as shown in (Table 1).

Demographic data	Group B TAP block (n=30)	Group BP TAP block (n=30)	p-value
Age (years)	28.67±6.45	27.10±6.35	0.608
Mean±SD			
BW (kg)	63.70±6.83	65.33±5.97	0.704
Mean±SD			
Duration of surgery (min)	46.37±9.25	48.13±8.70	0.449
Mean±SD			

Table 1: Demographic data comparison between groups B (TAP block) and BP (TAP block).

According to mean arterial blood pressure, the two study groups' baseline MAPs were comparable, with no statistically significant differences. When contrasted to group B, the MAP in group BP was significantly lower after 15 minutes, 30 minutes, and 45 minutes in PACU. Following that, no statistically significant differences among both groups were found in subsequent recordings, as displayed in (Table 2) and (Figure 1).

Time of assessment	Group BP TAP block (n=30)	Group B TAP block (n=30)	p-value
Baseline (At PACU)	79.91±12.25	77.90±11.76	0.505
After 15 min.	68.88±9.51	74.81±10.98	0.0291*
After 30 min.	65.87±8.52	72.37±9.52	0.008*
After 45 min.	62.94±7.52	69.53±8.44	0.002*
After 2 hrs	63.86±7.67	66.55±8.52	0.203
After 4 hrs	64.88±8.77	67.65±9.14	0.236
After 8 hrs	68.32±7.92	70.87±10.43	0.291
After 12 hrs	67.98±11.75	69.88±9.43	0.492
After 24 hrs	62.87±9.33	65.87±7.93	0.184

Table 2: Comparison of mean arterial blood pressure (mmHg) between group B (TAP block) and group BP (TAP block)

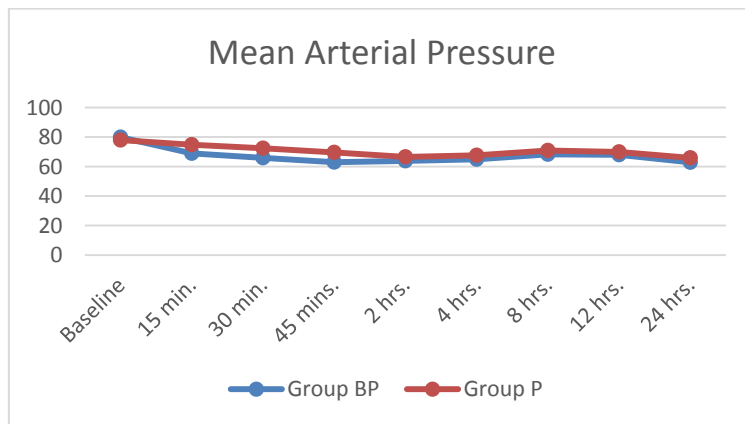


Fig. 1: Comparison between Group B and Group BP according to Mean arterial blood pressure.

Regarding heart rate, baseline heart rate was comparable between the two study groups with no statistically significant differences. In subsequent recordings, no statistically significant differences among both groups were found, as displayed in (Table 3).

Time of assessment	Group BP TAP block (n=30)	Group B TAP block (n=30)	p-value
Baseline (At PACU)	81.39±5.44	80.50±6.33	0.561
After 15 min.	75.33±4.55	76.36±5.24	0.419
After 30 min.	72.62±6.56	73.34±4.54	0.623
After 45 min.	75.83±4.55	75.09±3.28	0.4728
After 2 hrs.	76.74±7.25	77.09±6.28	0.842
After 4 hrs.	76.83±6.55	78.43±5.73	0.318
After 8 hrs.	75.85±7.44	78.70±6.49	0.119
After 12 hrs.	76.70±8.38	77.74±6.36	0.590
After 24 hrs.	77.70±3.57	76.70±2.40	0.2080

Table 3: A comparison of postoperative heart rate (beats/min) between groups B (TAP block) and BP (TAP block).

According to pain VAS S score, postoperative pain was evaluated at rest through assessment of the mean VAS score, at PACU, 2, 4, 8, 12, and 24 hrs after surgery. The average VAS S scores in the BP group showed a significant decrease during recovery time at 2 and 8 hrs postoperatively. At other time points, however, no significant differences in mean pain intensity among both groups have been noticed ($P > 0.05$) (Table 4) and (Figure 2).

Time of assessment	Group BP TAP block (n=30)	Group B TAP block (n=30)	p-value
Baseline (At PACU)	3.14±0.48	2.81±0.34	0.250
After 2 hrs.	2.51±1.21	3.59±1.54	0.004*
After 4 hrs.	4.53±1.8	6.21±1.21	0.811
After 8 hrs.	3.42±1.63	4.15±1.81	0.013*
After 12 hrs.	3.06±2.8	5.37±1.1	0.997
After 24 hrs.	2.71±3.2	3.07±1.6	0.312

Table 4: Comparison of VAS S scores between group B (TAP block) and group BP (TAP block).

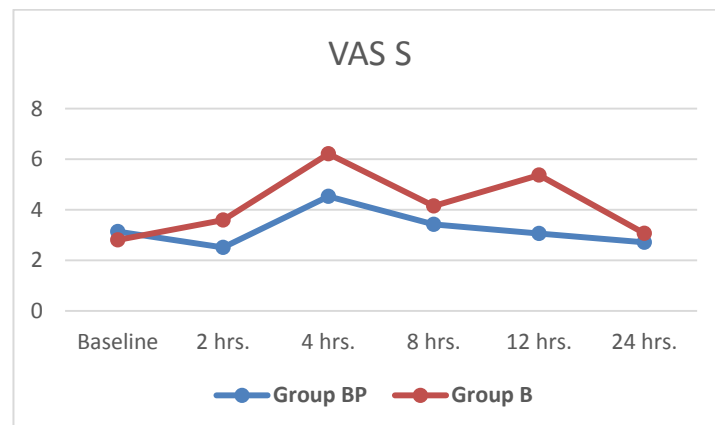


Fig. 2 : Comparison between Group B and Group BP according VAS S score

According to pain VAS D score, postoperative dynamic pain score was evaluated through assessment of the mean VAS score, at PACU, 2, 4, 8, 12, and 24 hours postoperatively. During the first two hours, the dynamic pain score can not be assessed, due to the inadequate motor activity. The mean dynamic VAS scores in the BP group showed a significant decrease throughout recovery time at 4 and 8 hours postoperatively. At other time points, however, no significant differences in mean pain intensity among both groups have been noticed ($P > 0.05$) (Table 5) and (Figure 3).

Time of assessment	Group BP TAP block(n=30)	Group B TAP block(n=30)	p-value
Baseline (At PACU)	ND	ND	--
After 2 hrs.	ND	ND	--
After 4 hrs.	1.53±5.16	6.51±1.21	0.011*
After 8 hrs.	3.42±1.63	4.91±1.81	0.013*
After 12 hrs.	3.06±4.61	5.37±1.1	0.997
After 24 hrs.	2.71±2.71	3.17±1.6	0.312

Table 5: Comparison of VAS D scores between group B (TAP block) and group BP (TAP block)

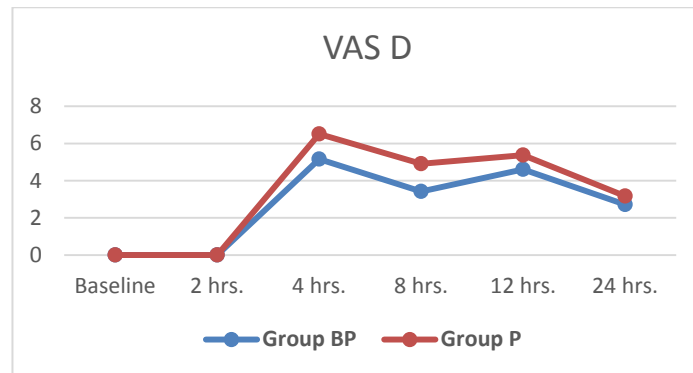


Fig. 3: Comparison between Group B and Group BP according VAS D score

According to the time of first postoperative analgesia, the time to postsurgical analgesia has been measured and contrasted between the two groups. The time to first postoperative analgesia in the BP group has been reported to be significantly longer than in the B group (256.9 vs. 160.5 minutes, P=0.0005) (Table 6) .

Time to first postoperative analgesia (minutes)	Group BP TAP block(n=30)	Group B TAP block(n=30)	p-value
Mean±SD	256.9±112.2	160.5±65	0.0005**
Range	135-314	139-285	

Table 6: Comparison of study groups based on time to first postoperative analgesia with nalbuphine (minutes)

According to the total analgesic requirements, the amount of diclofenac and nalbuphine consumed in 24 h by both the groups were compared. We found that the consumption of diclofenac and nalbuphine was significantly lower among the BP group (Table 7).

Variable	Group BP TAP block(n=30)	Group B TAP block(n=30)	P value
Diclofenac	96.3±11.25	117.6±9.8	0.023*
Nalbuphine	7.4±1.3	9.6±1.7	0.017*

Table 7 : Comparison of analgesic requirements between groups B (TAP block) and BP (TAP block).

According to adverse effects, there was no difference in the occurrence of nausea (P=0.25), vomiting (P=0.14), hypotension (P=0.66), or bradycardia (P=0.17) between the groups. When compared to the B group, the occurrence of pruritus was significantly higher in the BP group (P=0.01) (Table 8).

Variable	Group BP TAP block (n=30)	Group B TAP block (n=30)	p-value
Hypotension	20 (66.7)	19 (63.3)	0.66
Bradycardia	2 (6.6)	0 (0)	0.17
Nausea	16 (53.3)	11 (36.7)	0.25
Vomiting	9 (30)	8 (26.7)	0.14
Pruritus	2 (6.6)	0 (0)	*0.01

Table 8: A comparison of the adverse effects of groups B (TAP block) and BP (TAP block)

DISCUSSION

For more than 30 years, adding opioids to local anaesthetics has improved analgesia and minimised the dosage of local anaesthetics as well as their side effects. Nevertheless, selecting the ideal opioid with the highest effectiveness and the fewest side effects is still a source of debate.¹⁰ The VAS score at rest and motion, the duration of first postsurgical analgesia, and the cumulative dose of nalbuphine required have been utilized to assess the postsurgical analgesic effectiveness of TAP blocks with meperidine combined with bupivacaine versus bupivacaine alone in this study. According to this study, the administration of meperidine was significantly associated with decreased pain levels at rest or in motion during the first 8 hrs postoperatively. At the other time points, the VAS recordings in the BP group were also lower, but the result was not significant. In addition, the BP group's analgesia lasted significantly longer than the B group's (256.9 versus 160.5 minutes, $P=0.0005$). The amount of diclofenac and nalbuphine consumed in 24 h by both the groups were also compared. We found that the consumption of diclofenac and nalbuphine was significantly lower among the BP group. Indeed, the precise mechanism underlying such a long-lasting analgesic effect is unknown. However, the analgesic efficacy of meperidine can be attributed to multiple etiologies.¹¹ Although it has been believed that these impacts were caused by an impact on opiate receptors in the peripheral nerves, systemic uptake of the opioids undoubtedly happened, and this might have caused the analgesic effects. It may also affect the nociceptive synaptic connections in the spinal cord's dorsal horn. This is the only study that we are aware of that evaluates the efficiency of meperidine as an adjuvant to local anaesthesia in TAP block for caesarean delivery.

Intrathecal meperidine combined with local anaesthetics was used as a spinal adjuvant, as a solitary agent for epidural or subarachnoid for labour pain, and also for anesthesia-analgesia during caesarean section in many clinical settings. Cheun and Kim¹² evaluated 182 parturients having caesarean birth, using meperidine 50 mg in combination with 10% dextrose 0.5 mL administered in the lumbar spinal region to achieve sensory and motor blocking in all patients, as well as extended analgesia [453 ±158.1 minutes] and motor recovery [75.9±17.2 minutes]. Nausea, hypotension, and pruritus were the only side effects that were noticeable. At the conclusion of surgery, 18 patients reported slight pain. In 60 women having caesarean delivery with spinal anaesthetic, Shrestha and colleagues¹³ contrasted meperidine 1mg/kg to 0.5 % hyperbaric bupivacaine 2.2 mL administered intrathecally. The meperidine group had 8.30 hrs of analgesia, while the bupivacaine group had 2.36 hrs. Yu et al.¹⁴ examined the analgesia duration and adverse impacts of combining meperidine with intrathecal bupivacaine for spinal anaesthesia in elective caesarean delivery. The analgesia duration was longer in the Pethidine group, which is consistent with our results.

The average duration of analgesia in the meperidine group was 15.3 h in research by Chaudhari et al.¹⁵ on

patients undergoing perianal operations under spine anaesthesia with meperidine or lidocaine. Hypotension was more common in the lidocaine group than it was in the meperidine group. In that study, the meperidine group had a higher rate of adverse impacts like nausea, vomiting, and pruritus. We discovered no statistically significant differences in the incidence of vomiting and nausea, as well as hypotension, among the lidocaine and meperidine groups in that study, that could be owing to the reduced dosages of meperidine. When the duration of postsurgical analgesia and negative impacts of meperidine and fentanyl have been contrasted to placebo, the meperidine group had the longest duration of analgesia compared to the other two groups, while the placebo group had the shortest. Apart from sedation, there was no significant difference between the three groups in the occurring of adverse impacts. The fentanyl group had a significantly higher rate of sedation.

We demonstrated that using 50 mg of meperidine as an adjuvant for TAP block efficiently prevented shivering and reduced the requirement for rescue analgesics, but it did raise the risk of vomiting and nausea. Lin et al.¹⁶ conducted a meta-analysis on the impact of intrathecal pethidine (5/25 mg) on numerous surgical procedures and found that a small dose of pethidine lowered shivering and increased the requirement for sedatives; nevertheless, the patient's risk of nausea and vomiting rose. Popping et al.¹⁷, Shami et al.¹⁸, Rastegarian et al.¹⁹, and Nasser et al.²⁰ all reported that opiates had an intrathecal anti-shivering impact, which is consistent with the current study's findings.

Shivering is a multi-factor mechanism that occurs during spinal anaesthesia. Due to spinal anaesthesia, sympathetic block induces compensatory vasoconstriction and automatic adaptation underneath the blockage level, slowing temperature regulation and eventually leading to vasodilation and hypothermia. Shivering is the result of all of these factors.²¹

Pethidine is a commonly utilized drug for managing and stopping shivering as well as pain, as its equi-analgesic dosages are far more effective than other opioids like fentanyl, alfentanil, sufentanil or morphine.

Even though the mechanism of pethidine's influence on shivering and pain control is unknown, it is thought to be owing to either its direct impact on the thermoregulation center or its agonistic impacts on the receptors sedative of μ and κ .²² There were no statistically significant differences in nausea as well as vomiting among the two pethidine and control groups in the studies of Shami et al.¹⁸, Farzi et al.²³ and Rastegarian et al.¹⁹. On the other hand, in their meta-analysis, Lin et al.¹⁶ revealed a raised risk of vomiting and nausea that is in line with the findings of this research. The occurrence of vomiting and nausea during surgery was examined in a study performed by Yu et al.¹⁴, and it was discovered to be greater in the meperidine group than in the control group. Although postsurgical vomiting and nausea were more common in our study, the two groups had no statistically significant differences.

CONCLUSION

In conclusion, adding meperidine as an adjuvant to local anaesthetic in TAP block remarkably increased the postoperative analgesia duration and reduced the need for rescue analgesia after cesarean delivery. Finally, due to the longer duration of analgesia and fewer adverse impacts, meperidine has been recommended as an additive.

REFERENCES

- Ahmed A. R. Metwally, Khalid M. Abo-El-Enin, Sabry I. Abd Allah, Nevin M. Soliman and Walid A. Abo-Omar. Ultrasound-guided transversus abdominis plane block for lower abdominal surgeries: bupivacaine alone or combined with fentanyl or *epinephrine*. 2016; Volume 30 | Number 2 | April-June 2017.
- Baaj JM, Alsatli RA, Majaj HA, Babay ZA and Thallaj AK. Efficacy of ultrasound-guided transversus abdominis plane (TAP) block for post caesarean section delivery analgesia--a double-blind, placebo-controlled, randomized study. *Middle East J Anaesthesiol*. 2010; 20: 821-6.
- Cunha TM, Souza GR, Domingues AC, Carreira EU, Lotufo CM, Funez MI, et al. Stimulation of peripheral Kappa opioid receptors inhibits inflammatory hyperalgesia via activation of the PI3K/AKT/nNOS/NO signaling pathway. *Mol Pain*. 2012; 8:10 doi: 10.1186/1744-8069-8-10
- Hong JY, Lee IH. Comparison of the effects of intrathecal morphine and pethidine on shivering after Caesarean delivery under combined-spinal epidural anaesthesia. *Anaesthesia*. 2005; 72(12):60 . doi: 10.1111/j.1365-2044.2005.04158.x
- Jabalameh M, Safavi M, Honarmand A, Saryazdi H, Moradi D, Kashefi P. The comparison of intrathecal injection tramadol, pethidine and bupivacaine on postcesarean section pain relief under spinal anesthesia. *Adv Biomed Res*. 2012. doi: 10.4103/2277-9175.10016553 :1 .
- Liu SS, Richman JM, Thirlby RC and Wu CL. Efficacy of continuous wound catheters delivering local anesthetic for postoperative analgesia: a quantitative and qualitative systematic review of randomized controlled trials. *J Am Coll Surg* . 2006; 203:914-32
- McDonnell NJ and Paech MJ. The transversus abdominis plane block and post-cesarean analgesia: are we any closer to defining its role? *Int J Obstet Anesth*. 2012; 21: 109-11.
- Tan TT, Teoh WH, Woo DC, Ocampo CE, Shah MK and Sia AT. A randomised trial of the analgesic efficacy of ultrasound-guided transversus abdominis plane block after caesarean delivery under general anaesthesia. *Eur J Anaesthesiol*. 2012; 29: 88-94.
- Verstraete S, Van De Velde M. Post-cesarean section analgesia *Acta Anaesthesiol Belg*. 2012; 63: 147-67.
- PÖPPING, Daniel M., et al. Opioids added to local anesthetics for single-shot intrathecal anesthesia in patients undergoing minor surgery: a meta-analysis of randomized trials. *PAIN®*, 2012, 153.4: 784-93.
- WONG, Stanley Sau Ching; CHEUNG, Chi Wai. Analgesic Efficacy and Adverse Effects of Meperidine in Managing Postoperative or Labor Pain: A Narrative Review of Randomized Controlled Trials. *Pain physician*, 2020, 23: 175-201.
- Cheun JK, Kim AR. Intrathecal meperidine as the sole agent for cesarean section. *Journal of Korean medical science*. 1989 Sep 1; 4(3):135-8.
- Shrestha BR, Maharjan SK, Thapa C. Comparative study between bupivacaine heavy vs pethidine intrathecally to study early haemodynamic changes and postoperative analgesia in patients undergoing caesarean section. *Kathmandu Univ Med J (KUMJ)*. 2007; 5(2) : 166 -72
- Yu SC, Ngan Kee WD, Kwan AS. Addition of meperidine to bupivacaine for spinal anaesthesia for Caesarean section. *Br J Anaesth*. 2002; 88(3) :379-83
- Chaudhari LS, Kane DG, Shivkumar B, Kamath SK. Comparative study of intrathecal pethidine versus lignocaine as an anaesthetic and a postoperative analgesic for perianal surgery. *J Postgrad Med*. 1996; 42(2) : 43 -5
- Lin YC, Chen CY, Liao YM, Liao AH, Lin PC, Chang CC. Preventing shivering with adjuvant low dose intrathecal meperidine: A meta-analysis of randomized controlled trials with trial sequential analysis. *Sci Rep*. 2017; 7(1):15323.
- Pöpping DM, Elia N, Marret E, Wenk M, Tramèr MR. Opioids added to local anesthetics for single-shot intrathecal anesthesia in patients undergoing minor surgery: a meta-analysis of randomized trials. *PAIN®*. 2012 Apr 1; 153(4):784-93.
- Shami S, Nasser K, Shirmohammadi M, Sarshivi F, Ghadami N, Ghaderi E, et al. Effect of low dose of intrathecal pethidine on the incidence and intensity of shivering during cesarean section under spinal anesthesia: A randomized, placebo-controlled, double-blind clinical trial. *Drug Des Devel Ther*. 2016; 10:3005-12. doi: 10.2147/DDDT.S115201.
- Rastegarian A, Ghobadifar MA, Kargar H, Mosallanezhad Z. Intrathecal meperidine plus lidocaine for prevention of shivering during cesarean section. *Korean J Pain*. 2013; 26(4):379-86. doi: 10.3344/kjp.2013.26.4.379.
- Nasser K, Ghaderi E, Khezripour E. Comparison of the effects of intrathecal meperidine and morphine on incidence and intensity of shivering after caesarean sections under spinal anesthesia: A randomized controlled trial. *Iran Red Crescent Med J*. 2017; 19(7). e55567. doi: 10.5812/ircmj.55567.
- Lopez MB. Postanaesthetic shivering—from pathophysiology to prevention. *Romanian journal of anaesthesia and intensive care*. 2018 Apr; 25(1):73.
- Khezri MB, Mosallaei MA, Ebtehaj M, Mohammadi N. Comparison of preemptive effect of intravenous ketorolac versus meperidine on postoperative shivering and pain in patients undergoing cesarean section under spinal anesthesia: A prospective, randomized, double-blind study. *Caspian J Intern Med*. 2018; 9(2):151-7. doi: 10.22088/cjim.9.2.151.