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Use of Dexmedetomidine as adjunct with Bupivacaine in TAP block for postoperative pain relief in patients undergoing laparoscopic cholecystectomy

Meamoona Shabbir, Ayesha, Atif Nazir, Mahnoor Nasir, Tanzeela Iram, Sidra Shabbir

ABSTRACT:

Objective: To analyze adjunct effect of Dexmedetomidine along with Bupivacain in TAP block for postoperative analgesia in laparoscopic cholecystectomy.

Study Design and Setting: Prospective interventional study was conducted 1st September 2022 to 31st January 2023 at Anesthesia department of PAF Hospital Islamabad, affiliated with Air University.

Methodology: A total of 60 patients undergoing elective laparoscopic cholecystectomy between age 18 to 60 years were included. Patients having hypertension, heart disease, diabetes were excluded. Group A patients were given TAP block using 10ml 0.25 % Bupivacaine on each side.Group B patients were given 10ml of 0.25% Bupivacaine with injection Dexmedetomidine 0.5 µg/kg in divided dose on each side under ultrasound guidance. Patients were followed for postoperative pain in first 24 hours.

Results: Data was analyzed on SPSS 25.Mean ± SD of pain score on VAS was 6.54 ± 1.98 versus 3.54 ± 1.87 at 4 hours (p value =0.0001) , 5.51 ± 1.16 versus 2.89 ± 1.65 at 8 hours (p value=0.0001) , 4.89 ± 1.11 versus 2.13 ± 1.25 at 12 hours (p value=0.0001) ,4.47 ± 1.07 versus 1.63 ± 0.85 at 24 hours (p value=0.0001) in group A and B respectively. Stratification was done with age, gender, ASA status and duration of surgery .Results of study were not affected by these factors.

Conclusion: Dexmedetomidine when added as an adjunct to Bupivacaine is better than Bupivacaine alone in TAP block for postoperative analgesia after laparoscopic cholecystectomy.

Keywords: Dexmedetomidine, laparoscopic cholecystectomy, transverses abdominas plane block

How to cite this Article:
Shabbir M, AA. Nazir A, Nasir M, Iram T, Shabbir S. Use of Dexmedetomidine as adjunct with Bupivacaine in TAP block for postoperative pain relief in patients undergoing laparoscopic cholecystectomy. J Bahria Uni Med Dental Coll. 2025;15(4):306-11 DOI: https://doi.org /10.51985/JBUMDC2025565

Meamoona Shabbir
PG Trainee, Department of Anesthesia
PAF Hospital Islamabad
Email: Meamoonashabbir@gmail.com

Ayesha
Associate Professor, Department of Anesthesia
PAF Hospital Islamabad
Email: Drayesha_kemu@hotmail.com

Atif Nazir
PG Trainee, Department of Anesthesia
PAF Hospital Islamabad
Email: Atifnazir656@gmail.com

Mahnoor Nasir
PG Trainee, Department of Anesthesia
PAF Hospital Islamabad
Email: mahnournasir@gmail.com

Tanzeela Iram
PG Trainee, Department of Anesthesia
PAF Hospital Islamabad
Email: Tanzeela.amc@gmail.com

Sidra Shabbir
PG Trainee, Department of Anesthesia
PAF Hospital Islamabad
Email: Doctor.sidra@gmail.com

Received: 07-04-2025
1st Revision: 12-05-2025
Accepted: 29-08-2025
2nd Revision: 21-08-2025

INTRODUCTION:

Laparoscopic cholecystectomy was introduced four decades back and with the passage of time it has replaced traditional open cholecystectomy.[1] The benefits of laparoscopic cholecystectomy include shorter surgical time and hospital stay, less blood loss and early mobilization. However in 6-8 % of patients complications are still prevalent.[2] The most common complication reported after laparoscopic cholecystectomy is postoperative pain. Moderate to severe pain is reported in first 24 hours. The pathophysiology of postoperative pain involves visceral pain due to gas insufflations.[3] Postoperative pain is the most common cause of readmission in hospital after discharge. If left untreated it may lead to development of chronic postsurgical pain.[4] Review of literature showed multiple modalities for managing postoperative pain after cholecystectomy. Laproscopy using three ports, creating pneumoperitonium with low pressure, extraction of umbilical port, irrigation of abdominal cavity with saline at the end of procedure and ensuring maximum aspiration of pneumoperitonium are key surgical factors that can help to minimize postoperative pain.

Pharmacological agents used to treat postoperative pain include NSAIDS, steroids, COX 2 inhibitors, dexamethasone

and local anesthetic infiltration at port side. However, none of them proved to be 100% effective. Intravenous Ketamine, Opioids and preoperative Pregabalin have got a moderate to high quality evidence in comparison to other intravenous analgesics. Most common used drugs for postoperative pain are opioids. However both systemic and neuraxial opioid administration are associated with frequent dose dependent adverse effects including nausea, vomiting, pruritus, sedation, respiratory depression and hyperalgesia. [5] Apart from traditional intravenous analgesics various nerve blocks are also being practiced.TAP block introduced in 2001 involves injection of local anesthetic in triangle of petit between internal oblique and transverses abdominus muscle. Initially it was done by blind landmark technique till 2007, when it was attempted under ultrasound guidance with more success rate reported than blind technique. In ultrasound guided approach, neurovascular fascial plane was identified and drug was injected in this plane to block the dermatomal afferents of T7-11 intercostal nerves, T12 subcostal nerve, ilioinguinal and iliohypogastric nerves and cutaneous branches of L1-3 nerves. These nerves give sensation to the anterior and lateral abdominal wall as well as the parietal peritoneum.[5]

The TAP block can be used for postoperative analgesia management in open and laparoscopic abdominal surgeries as well as inpatient and outpatient surgical procedures. TAP block may be performed unilaterally, left or right sided in specific procedures. Unilateral blocks are preferred in cholecystectomy, appendectomy, nephrectomy, renal transplants, while bilateral TAP blocks are used in midline and transverse abdominal incisions, such as umbilical or ventral hernia repair, cesarean deliveries, hysterectomy, and prostatectomy.TAP blocks are part of multimodal pain management for abdominal surgeries which adds analgesic benefit to the patients by reducing postoperative opioid requirements. Pain relief with TAP block has been found to be superior as compare to infiltration of local anesthetics.[6] Although it can be done at anytime during surgery, the use of preoperative TAP block was associated with decreased intraoperative opiate use during minimally invasive cholecystectomy.[7] The TAP block aims to provide sensory blockage of the anterior abdominal wall and generally does not affect visceral pain.[8] Various approaches used for TAP block includes posterior, sub costal and rectus sheath approach.[9] Since local anesthetics have got short half life, different adjuvants have been practiced to enhance quality and duration of local anesthetics.[10] Dexmedetomidine is one of the most commonly used adjuvant in nerve blocks. It is highly selective alpha 2 agonist with sedative, analgesic and sympatholytic properties. It has got both central and peripheral mediated action. In nerve blocks its mode of action involves vasoconstriction at the site of injection, hence causing delay in absorption of drug and prolongs its action. Moreover it acts directly on peripheral nerves to enhance both duration and quality of block. The rationale of this trial is to evaluate role of dexmedetomidine as adjuvant in TAP block in addition to bupivacaine so as to enhance effect of bupivacaine in terms of pain relief. Since limited data is available at national level, results of this trial will help us to improvise perioperative analgesia management in laparoscopic cholecystectomy in our population using recent modalities of ultrasonography.

METHODOLOGY:

This prospective interventional study was done in Anesthesia department of PAF hospital(affiliated with Air University) over a period of 5 months from 1st September 2022 to 31st January 2023 after taking ethical committee approval dated 10th June 2022 (IRB No CPSP/REU/ANS-2019-137-2237) . Sample size was calculated with following assumptions (power of significance=5%, Power of test = 90% , Test value of population mean = 4.58 , Anticipated Population mean = 1.808 , Population SD = 0.64 [11]) sample size comes out to be 60 (30 patients in each group A and B).Patients with age 18-60 years, ASA [12] status I-II, undergoing elective laparoscopic cholecystectomy were included in this study. Patients with history of hypertension, ischemic heart disease, diabetes and those who were converted to open cholecystectomy were excluded from this trial.[11] Our hypothesis was addition of dexmedetomidine to bupivacain in TAP block improves postoperative analgesic effect as compared to bupivacain alone.All patients included in this study were recruited from operation theatre of PAF Hospital Islamabad. A detailed history and examination was done lab investigations including blood CP, BSR, LFTs, PT, APTT, ECG were checked. An informed written consent was taken from patients. Patients were divided into two groups A and B by random allocation by table of random numbers. Patients were premedicated with injection Midazolam 2 mg intravenously, injection Ondansetron 4mg. Induction of anesthesia was done with injection Propofol 2mg/kg and injection Atracurium 0.5 mg/kg. Patients were ventilated for 3 minutes after induction and intubated with endotracheal tube (ETT) of appropriate size. Vitals were monitored. Anesthesia was maintained with 100% oxygen and 1.2% Isoflurane. Lateral approach for TAP block was selected.Linear probe of ultrasonography was placed in axial plane midway between subcostral margin and iliac crest in midaxillary line. Three layers of abdominal wall muscles named external oblique, internal oblique and transverses abdominus were visualized. Facial plane between internal oblique muscle and transverses abdominus was identified. Using 25 G spinal needle, needle was inserted in midaxillary line and needle tip was advanced into fascial plane between internal oblique and transverses abdominus muscle. After negative aspiration for blood , drug was injected under ultrasound guidance visualizing sausage formation in the targeted fascial plane. Group A was given 10ml of 0.25% Bupivacain in TAP block [13] on each side at end of procedure

before extubation. Group B was given 10ml of 0.25%Bupivacaine along with Dexmedetomidine 0.5µg/kg in divided doses under ultrasound guidance. Both injections were prefilled under aseptic conditions and person who was performing TAP block was blinded to study. At the end of procedure residual neuromuscular blockade was reversed with injection Neostigmine 0.04mg/kg. Patients were extubated and shifted to post anesthesia care unit with stable vitals. Patients were followed in postoperative period for intensity of postoperative pain on visual analog scale [14] where patients were asked to mark their pain on a scale with scoring 0-10, value of 0 being no pain at all and 10 being worst and intolerable pain. Pain scoring was done 4 hourly postoperatively upto 24 hours and recorded on form.

Table 1. Age, sex, ASA status and duration of surgery

		Group A	Group B
Age(years)	18-40	12(40%)	14(46.67 %)
	41-60	18(60%)	16(53.33%)
Sex	Male	6(20%)	7(23.33%)
	Female	24(80%)	23(76.67%)
ASA status	I	11(36.67%)	9(30%)
	II	19(63.33%)	21(70%)
Duration of surgery (minutes)	= 30	10(33.33%)	12(40%)
	= 30	20(66.67%)	18(60%)

Table 2. Mean postoperative pain score on VAS scale

Postoperative pain score on VAS scale	Group A (mean ± SD)	Group B (mean ± SD)	p- value
4 HOURS	6.54 ± 1.98	3.54 ± 1.87	0.0001
8 HOURS	5.51 ± 1.16	2.89 ± 1.65	0.0001
12 HOURS	4.89 ± 1.11	2.13 ± 1.25	0.0001
24 HOURS	4.47 ± 1.07	1.63 ± 0.85	0.0001

RESULTS:

Data was analyzed in SPSS 25. Demographic profile including age, sex, ASA status and duration of surgery is shown in table 1.

Postoperative pain as measured on visual analog scale is shown as mean ± SD in table 2. There was statistically significant difference in postoperative pain score in both groups at different intervals that shows that Dexmedetomidine when added as adjuvant to Bupivacain in TAP block is superior for pain management as compared to Bupivacain alone

Stratification was done with respect to age , gender ,ASA status and duration of surgery as shown in table 3 and 4. Bupivacain along with Dexmedetomidine was found to be statistically superior to Bupivacain alone in terms of pain relief. This shows that adjuvant effect of Dexmedetomidine is not affected by age gender, ASA status or duration of surgery

DISCUSSION:

According to PROSPECT recommendations for pain relief after laproscopic cholecystectomy, perioperative use of NSAIDS and COX 2 inhibitors remains the first line of treatment until and unless there is some well defined contraindication to their use. Second line of treatment includes opiods, however their use was limited due to their side effects. Gapapentinoids are other modalities for pain relief especially in patients who are allergic to NSAIDS, however their use is limited by dizziness, sedation and vomiting as their potential side effects. Keeping in view these limitations, port side infiltration of local anesthetics or regional blocks started gaining priority as compare to traditional intravenous analgesics.[5]

TAP block was first introduced by Rafi [15] as an effective alternative to intravenous analgesics as local pain control

Table 3: stratification with respect to age and gender

		Group A	Group B	p value
		Postoperative pain score on VAS scale (mean ±SD)	Postoperative pain score on VAS scale (mean ±SD)	
Age	18-40	4.58 ± 1.08	1.86 ± 0.86	0.0001
	41-60	4.39 ± 1.09	1.44 ± 0.81	0.0001
Gender	Male	4.67 ± 0.82	1.86 ± 0.38	0.0001
	Female	3.42 ± 1.14	1.57 ± 0.95	0.0001

Table 4: stratification with respect to ASA status and duration of surgery

		Group A	Group B	p value
		Postoperative pain score on VAS scale (mean ±SD)	Postoperative pain score on VAS scale (mean ±SD)	
Age	I	4.45 ± 1.13	1.44 ± 0.88	0.0001
	II	4.47 ± 1.07	1.71 ± 0.85	0.0001
Gender	= 30 minutes	4.60 ± 1.08	1.75 ± 0.75	0.0001
	= 30 minutes	4.40 ± 1.10	1.56 ± 0.92	0.0001

for patients undergoing surgical procedures. At that time TAP block was performed with landmark technique. Owen et al demonstrated that the same procedure can be done by open surgical approach. TAP block by laparoscopic technique was first introduced in 2011. Both techniques allow surgeons to apply TAP block under direct vision prior to the surgery.[16] A study by Dr. Usha Shukla has shown that VAS for pain score were statistically significantly to be low at different time interval in patients who were given 0.25% Bupivacaine and 1 µg/kg Dexmedetomidine then those who were given Bupivacaine 0.25% alone. Mean ± standard deviation of pain score on VAS at 2 hours was 2.06 ± 0.90 versus 5.02 ± 1.00, at 6 hours was 2.02 ± 0.20 versus 4.12 ± 0.90, at 12 hours was 1.61 ± 0.50 versus 5.00 ± 0.80, at 24 hours was 1.06 ± 0.81 versus 3.00 ± 0.86 in study group and control group respectively. Overall VAS in 24 hours was also significantly lower in study group (1.80 ± 0.36) then control group (4.5 ± 0.92).[11] Moreover time for rescue analgesia was high and average analgesic consumption was significantly less in Dexmedetomidine group as compared to placebo and Tramadol group. Results of this study were similar to our trial as far as pain score is considered however in our trial we hadn't measured time for rescue analgesia and postoperative analgesic consumption.

The effect of Bupivacaine and Dexmedetomidine added to Bupivacaine used in TAP block by ultrasound guidance on postoperative pain was evaluated by Aksu et al. He selected patients with age 18-65 years, ASA status 1-2, undergoing lower abdominal surgeries (open appendicectomy and inguinal hernia repair). He divided patients in three groups having 21 patients in each group.After induction of anesthesia, he performed TAP block under ultrasound guidance. Group B was given injection Bupivacain in normal saline, group C was given normal saline only and group BD was given injection Bupivacain with Dexmedetomidine. Patients were followed in postoperative period for pain score on VAS scale, postopewrative analgesic requirement in terms of morphine consumption, postoperative nausea and vomiting and patient satisfaction score. Results demonstrated that the addition of Dexmedetomidine with Bupivacain was superior to placebo group and Bupivacain alone in terms of postoperative pain (p value < 0.05), analgesic requirement (p value < 0.001), as well as patient satisfaction (p value < 0.001) . However No difference was found on nausea and vomiting score (p value 0.129) , neither in the requirement of antiemetics.[17] The result of this study were similar to our trial.

In addition to human studies, animal studies also support adjuvant effect of Dexmedetomidine in terms of analgesia. Brummett et al. [18] have presented that high dose Dexmedetomidine added to Bupivacain improved local anesthetic blockade in rats without exhibiting any neurotoxicity. He performed bilateral sciatic nerve block in rats using Bupivacain alone, Bupivacain mixed with Dexmedetomidine and normal saline. After block, sensory and motor functions were assessed at thirty minutes interval. After 24 hours and 14 days of applying block sciatic nerve was analyzed for nerve damage aswell as perineural inflammation. He found that when Dexmedetomidine 0.005% is added as adjunct to Bupivacain, it enhances the duration of both sensory and motor block. However when used alone it doesn't cause any sensory or motor deficit. No neurological damage to axon or myelin sheath was identified after 24 hours and upto 14 days after procedure. Signs of perineural inflammation were less marked in Dexmedetomidine group as compared to Bupivacain group. This trial depicting safe use of high dose of Dexmedetomidine in rats regarding enchancement of antinociception effect of bupivacain, proved to be a milestone for encouraging studies in human beings. On the other hand, Ozalp et al.[19] compared Dexmedetomidine-Ropivacaine combination to Ropivacaine alone in patient controlled interscalene analgesia. He selected 40 patients undergoing upper limb surgeries. Before administering general anesthesia ,through posterior approach of interscalene block of brachial plexus, a catheter was introduced. Catheter placement was confirmed by positive contraction of bicep, tricep and deltoid muscle at less than 0.5milliampere of intensity. Group A was given 0.2 % Ropivacain alone while group 2 was given 0.2% Ropivacain with 1 ug/ml Dexmedetomidine. After procedure pain was managed by PCA infusion that deliver 5 ml of drug bolus at 30 minutes interval. Pain score was measured at rest and at movement and compared in both groups. They stated similar pain scores in both groups without any beneficial effect of Dexemedetomidine. This is in contrary to our trial where addition of Dexmedetomidine as adjunct prolongs analgesic effect of local anesthetic. However in our study local anesthetic agent used was Bupivacain and our trial was done in TAP block, so adjuvant effect of Dexmedetomidine in terms of analgesia may not be as significant in interscalene block as compare to TAP block.

A systematic review for randomized controlled trials by Fusco P et al, that assessed the efficacy of ultrasound guided TAP block following cesarean delivery and concluded that there was a lot of controversy regarding utility of ultrasound guided TAP block in cesarean section. This controversy may be operator dependant and due to expertise of person performing block. However evidence suggests that when correctly executed as part of a multimodal analgesic regimen, TAP block may reduce postoperative opioid consumption and opioid-related side effects, improving postoperative pain control and patient satisfaction.[20]

Similarly, Abdulatif M et al. performed a randomized double blinded study in patients undergoing arthroscopy of knee under femoral block. He observed effects of different doses of Dexmedetomidine when administered perinuerally in femoral nerve block. Procedure was done under general anesthesia. Using ultrasound guidance femoral nerve block

was done. Control group was given 25 ml of Bupivacain plain with normal saline. There were three treatment groups receiving 25,50 and 75 ug of Dexmedetomidine. He reported that addition of 25 mcg of Dexmedetomidine did not make any difference in the pharmacodynamics of Femoral Nerve Block noted with Bupivacaine alone ($p>0.05$). Addition of 50 and 75 mcg of Dexmedetomidine were associated with a decrease in time to onset of sensory as well as motor block, postoperative analgesia consumption and increase in duration of sensory and motor block and time to first rescue analgesia ($p< 0.05$). 75 mcg of Dexmedetomidine was associated with increased incidence of preoperative and intraoperative hypotension episodes ($p=0.002$). [21] These results may support dose dependent analgesic effect of Dexmedetomidine when used as an adjuvant. However this dose dependant response was not addressed in our trial.

Nag DS conducted a prospective randomized controlled trial in patients undergoing cesarean sections. He selected 100 patients and divide them in two groups. All patients underwent cesarean section under spinal anesthesia. At the end of surgery patients in group R were given injection Ropivacian diluted in normal saline and patients in group RD were given injection Ropivacain with Dexmedetomidine in TAP block. Vital monitoring was compared intraoperatively and no statistically significant difference was observed. VAS was compared at rest and on coughing among two groups. There was no statistically significant difference at shifting and at 4 and 8 hours postoperatively, however at 12 and 24 hours postoperatively, there was a significant difference in pain score among both groups showing that analgesic effect of Dexmedetomidine group is superior to Ropivacain alone. Demand for rescue analgesic was also low in Dexmedetomidine group. These results are partially contrary to our results as in our trial Dexmedetomidine proved to be superior in early postoperative hours also. However requirement for rescue analgesic was not measured in our trial.[22]

Korkutata et al conducted a prospective randomized controlled trial in patients undergoing laproscopic cholecystectomy to compare adjuvant effect of Tramadol versus Dexmedetomidine in TAP block. He enrolled 67 patients aged 20-60 years with ASA 1-2 status. After standard anesthesia induction and intubation, group T was given 0.25% Bupivacain with Tramadol 1.5mg/kg while group D was given Bupivacain 0.25% with Dexmedetomidine 0.5ug/kg in TAP block. At end of procedure patients were extubated postoperative pain was measured on VAS scale at varying intervals. Postoperative analgesia consumption was also compared among two groups. This trial showed that Dexmedetomidine and Tramadol were equally effective in terms of postoperative pain and postoperative analgesia consumption as well as side effects, however when hemodynamic stability was compared among both groups, Dexmedetomidine was found to be superior to Tramadol. [23]

Sinha J compared Dexmedetomidine with Dexamethasone as adjuvant to Levobupivacain in TAP block in patients undergoing total abdominal hysterectomies. Procedure was done in spinal anesthesia and after completion of surgical procedure, group 1 was given injection Levobupivacain 0.25% with 4 mg Dexamethasone in TAP block and group 2 was given Levobupivacain 0.25% with Dexmedetomidine 1 ug/kg in TAP block. Postoperatively patients were followed for pain intensity on VAS, rescue analgesia and patient satisfaction. Results of this study showed that VAS was same in both groups in first hour postoperatively, however at 6,9 and 12 hours VAS was significantly low in Dexmedetomidine group as compared to Dexamethasone group. Moreover rescue analgesia consumption was less in Dexmedetomidine group than Dexamethasone group. Results of this study are similar to our trial except that in our study Dexmedetomidine has significantly high analgesic effect in first hour as well. However this difference may be due to fact that we have compared Dexmedetomidine with placebo while in this study Dexmedetomidine was compared with another adjuvant Dexamethasone. [24]

CONCLUSION:

Dexmedetomidine in dose of 0.5 ug/kg when added as adjunct to Bupivacain in TAP block is superior to Bupivacain alone for postoperative pain score.

LIMITATIONS:

Main limitation in our study was sample size. Since results of previous studies are controversial, we need to have data on large population. Moreover dose of drug used may be different in other setups. Clinical expertise of person doing the procedure is another factor that can affect results.

Authors Contribution:
Meamoona Shabbir: Concept & Design of Study, Drafting, Revisiting Critically, Data Analysis, Final Approval of version
Ayesha: Concept & Design of Study, Drafting, Revisiting Critically, Data Analysis, Final Approval of version
Atif Nazir: Concept & Design of Study, Revisiting Critically, Final Approval of version
Mahnoor Nasir: Concept & Design of Study, Drafting, Final Approval of version
Tanzeela Iram: Concept & Design of Study, Drafting, Final Approval of version
Sidra Shabbir: Concept & Design of Study, Drafting, Final Approval of version

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