

Comparison of Bupivacaine Alone versus Low Dose Bupivacaine and Dexmedetomidine in Elderly Male Patients undergoing Genitourinary Surgery Under Spinal Anesthesia

Saleem Pervaiz Bajwa, Muhammad Akram, Aftab Hussain, Ahsan Ali, Akhtar Hussain, Abdullah*

Department of Anesthesia, Combined Military Hospital Lahore/National University of Medical Sciences (NUMS) Pakistan, *Department of Anesthesia, Combined Military Hospital, Pano Aqil/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To compare motor and sensory blockade and hemodynamic effects of standard dose Bupivacaine versus low dose Bupivacaine mixed with Dexmedetomidine for spinal anesthesia in elderly male patients undergoing genitourinary surgery.

Study Design: Prospective comparative study.

Place and Duration of Study: Anesthesia Department Combined Military Hospital, Lahore Pakistan, from Sep 2019 to Feb 2020.

Methodology: Hundred elderly male patients of American Society of Anesthesiology status-II undergoing surgery under spinal anesthesia were divided in two Groups. Group B (Bupivacaine Group) was given 11.25mg Bupivacaine and Group BD (Bupivacaine+Dexmedetomidine Group) received 7.5mg Bupivacaine and 5µg Dexmedetomidine intrathecally. Both Groups were given equal volume of 2ml.

Results: Mean time for onset of sensory block for Group B and BD was 2.72±0.81 and 2.28±1.03 minutes respectively (p -value=0.02). Mean time for onset of motor block for Group B and BD was 3.09±0.62 and 2.84±0.64 minutes respectively (p -value=0.045). Mean duration of analgesia in Group B and BD was 171.87±10.19 and 187.60±18.42 minutes (p -value=0.01). Mean heart rate in Group B and BD was 80.04±5.51 and 75.68±6.11 beats/minutes (p -value=0.001). Mean arterial pressure's mean in Group B and BD was 62.78±78.13.49 and 87.96±10.15 (p -value=0.001).

Conclusion: Onset of sensory and motor block was significantly shorter; analgesic effect was longer when Dexmedetomidine was combined with Bupivacaine for spinal anesthesia in comparison to Bupivacaine alone. Hemodynamic complications were also less in combination approach.

Keywords: Bupivacaine, Dexmedetomidine, Elderly, hemodynamic stability, Intrathecal, Spinal anesthesia.

How to Cite This Article: Bajwa SP, Akram M, Hussain A, Ali A, Hussain A, Abdullah. Comparison of Bupivacaine Alone Versus Low Dose Bupivacaine and Dexmedetomidine in Elderly Male Patients Undergoing Genitourinary Surgery Under Spinal Anesthesia. *Pak Armed Forces Med J* 2023; 73(Suppl-1): S23-27. DOI: <https://doi.org/10.51253/pafmj.v73iSUPPL-1.4997>

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Genitourinary surgery in elderly patients is frequently performed under spinal anesthesia with bupivacaine which provides ideal surgical conditions with dense sensory block. Elderly patients are vulnerable to complications when single shot spinal anesthesia with standard doses of local anesthetics (LA) is given.¹ It is attributed to age related changes and comorbidities. Successful anesthetic technique demands early onset of block with prolonged analgesia and minimal hemodynamic changes and few drug related other adverse effects.

Complications of spinal anesthesia due to bupivacaine are primarily because of sympathetic blockade and they include hypotension, bradycardia, nausea vomiting and cardiac arrest in rare cases. Spinal anesthesia offers many advantages.² over general anesthesia in genitourinary surgeries in elderly people

but it can have some serious complications.³ For minimizing the risks many adjuvants combined with LA drugs have been tried to enhance the safety of patients with various degrees of success. These include but not limited to morphine,⁴ Dexmedetomidine,^{4,5} midazolam,⁵ clonidine⁶ and fentanyl.⁶ Dexmedetomidine has been introduced in anesthesia practice recently in Pakistan. It has versatile perioperative utility in addition to being as anesthesia adjunct drug.⁷

Dexmedetomidine binds to alpha-2 receptors located in brainstem and spinal cord. Activation of these receptors inhibits neuronal firing and potentiates the effects of regional anesthesia. Due to these properties Dexmedetomidine can be an attractive choice as adjuncts to local anesthetics. It has high affinity for alpha-2 receptors. Its vagomimetic action results in bradycardia and hypotension when an intravenous bolus dose. Fortunately such complications are unlikely when it is given intrathecally. Co-administration of intravenous and inhalational anesthetics, sedatives and opioids with intravenous Dexmedetomidine leads to potentiation of their effects.

Correspondence: Dr Muhammad Akram, Department of Anesthesia, Combined Military Hospital, Lahore Pakistan
Received: 13 Aug 2020; revision received: 01 Oct 2020; accepted: 06 Oct 2020

Comparison of Bupivacaine Alone Versus

Trans-urethral resection of prostate is the surgical gold standard treatment for benign prostatic hyperplasia. Since this procedure is mostly performed on elderly patients with multiple coexisting diseases, it is associated with high morbidity and mortality.

Spinal anesthesia is usually anesthesia of choice for these patients although there is no evidence of any difference in outcome between general and spinal anesthesia.⁸ Spinal anesthesia however offers several advantages. It is safer in patients with respiratory disease.⁹ It gives good post-operative analgesia and reduces stress response to surgery. Spinal anesthesia allows the anesthetist to monitor the conscious level of the patient for detection of early signs of TURP syndrome and delirium. However severe hypotension and bradycardia can occur with standard dose of intrathecal Bupivacaine resulting in adverse outcome. There have always been efforts to find an adjunct to LA which can reduce complications because of sympathetic blockade and yet providing ideal anesthetic conditions for such surgeries. Dexmedetomidine has promised such advantages in many international studies.

Purpose of this study was to rationalize the intrathecal use of Dexmedetomidine with low dose Bupivacaine if trial suggests that it is equally effective but carries lesser complications in comparison to Bupivacaine alone.

METHODOLOGY

The prospective comparative study was carried out after permission was taken from Ethical Review Committee of CMH Lahore (ERB Ref No. 1325/2019/Trg/Adm) from September 2019 to February 2020.

Inclusion Criteria: Patients of American Society of Anesthesiology (ASA) status II patients undergoing genitourinary surgery were included.

Exclusion Criteria: Patients having contraindication to spinal anesthesia and those unwilling to participate in study were excluded from the study. Patients having history of cardiac disease, hypertension or diabetes mellitus were also excluded from the study.

Hundred elderly patients were recruited for this study using non-probability consecutive sampling technique. The sample size calculation was done a priori ($\alpha=0.05$ and $\beta=0.90$) using statistical software G Power 3.1. Patients were divided in equal Groups of B and BD. Draw method was followed to randomly assign the Group to patients. Group B patients

received Bupivacaine only while Group BD patients received Bupivacaine and Dexmedetomidine combination. Dexmedetomidine 100 μg was diluted in 20 ml normal saline to get a dilution of 5 μg /1 ml. After intravenous cannulation and application of standardized monitoring, 300ml of ringers lactate was infused to all patients. Spinal anesthesia was initiated in sitting position at L3-L4 or L4-L5 level with 25 gauge quinke needle in both Groups after successful subarachnoid puncture. Both Groups were given equal volume of 2ml intrathecally. Group B patients were administered 11.25mg Bupivacaine (1.5 ml 0.75% Bupivacaine + 0.5ml normal saline) intrathecally and Group BD received 7.5mg Bupivacaine mixed with 5 μg of Dexmedetomidine (1ml of 0.75% Bupivacaine + 1ml of normal saline containing 5 μg of Dexmedetomidine). Anesthesiologists, nursing staff and record keepers were blinded to avoid the bias. Base line values of heart rate (HR), mean arterial pressure (MAP) were recorded. Level, onset, peak and duration of sensory block & analgesia were assessed with blunt tip needle. Onset and extent of motor blockade was recorded using Modified Bromage scale as described in Table-I.

Table-I: Modified Bromage Scale

Score	Criteria
0	Able to move hip, knee and ankle
1	Unable to move hip but able to move knee and ankle
2	Unable to move hip and knee but able to ankle
3	Unable to move hip, knee and ankle

Sensory block was checked every 02 minutes until the peak sensory level was achieved. Surgery was allowed when up to T10 level was achieved. Regression from the peak sensory level was noted after every 10 minutes for effectiveness and duration of analgesia.

Hemodynamics parameters of patients of both Groups were assessed with HR and MAP. HR and MAP were recorded for each patient preoperatively. Same were recorded every 5 minutes for 15 minutes and then every 15 minutes intra-operatively. Hemodynamic alterations and other complications were also noted in both Groups. Bradycardia was labeled when HR was less than 45/minute. Bradycardia was treated with 0.5 mg Atropine. Hypotension was labeled when MAP decreased by 20% of baseline. Hypotension was treated with 5mg Ephedrine. The Student t-test was used to analyze age, BMI and duration of surgery. Visual analogue scale was used to assess analgesia. Statistical analysis was done with SPSS version 24. *p*-value <0.05 was considered significant.

RESULTS

In this study the age range of the patients was from 65 to 83 years with mean age of 72.26±5.36. Mean age of patients in Group B was 72.80± 5.36 years while in Group BD it was 71.72± 5.37 years with *p*-value of 0.317. Mean BMI was 22.45±1.65 Kg in Group B and 23.01±1.35 Kg in Group BD with *p*-value of 0.067.

Mean of duration of surgery in Group B was 49.16±12.65 while in Group BD it was 50.82±10.96 with *p*-value of 0.485. Onset and peak for sensory block was significantly rapid in Group BD with *p*-values of 0.02 and 0.019 respectively. Duration of analgesia was also significantly longer in Group B as compared to the Group BD with a *p*-value of 0.001. Detailed comparison is shown in Table-II.

Table-II. Comparison Between two Groups for time of Onset of Sensory block, Peak Sensory Level & Duration of Analgesia (n=100)

	Group	Mean±SD	<i>p</i> -value
Time of onset of sensory block(Minutes)	B	2.72±0.81	0.02
	BD	2.28±1.03	
Peak level achieved(Minutes)	B	6.32±1.33	0.019
	BD	5.78±0.88	
Duration of analgesia(Minutes)	B	171.87±10.19	0.001
	BD	187.60±18.42	

Group B=Bupivacaine Group, Group BD=Bupivacaine + Dexmedetomidine Group, Onset and peak of motor block was significantly rapid in Group BD with *p*-values of 0.045 and 0.015 respectively. Detailed comparison is shown in Table-III.

Table-III: Comparison of motor block in both Groups (n=100)

	Group	Mean±SD	<i>p</i> -value
Freely move legs and feet (Minutes)	B	3.09±0.62	0.045
	BD	2.84±0.64	
Just able to flex knees & freely move feet (Minutes)	B	4.90±1.35	0.004
	BD	4.22±0.93	
Unable to flex knees but can move feet (Minutes)	B	6.06±1.23	0.02
	BD	5.32±1.02	
Unable to flex knees & feet (Minutes)	B	8.07±1.14	0.015
	BD	7.30±1.86	

Group B=Bupivacaine Group, Group BD=Bupivacaine+Dexmedetomidine Group, HR and MAP remained significantly stable in BD Group as compared to Group B.Comparison of hemodynamic parameters of both Groups are shown in Table-IV.

Group B=Bupivacaine Group, Group BD=Bupivacaine+Dexmedetomidine Group, Comparison of number of cases of hypotension, bradycardia and cardiac arrest is shown in Table-V.

Table-IV: Comparison of Hemodynamic Parameters of Both Groups (n=100)

	Group	Mean±SD	<i>p</i> -value
Average heart rate during procedure/min	B	80.04±5.51	0.001
	BD	75.68±6.11	
Average mean arterial pressure during procedure	B	62.78±13.49	0.001
	BD	87.96±10.15	

Table-V: Comparison of Complications in Both Groups (n=100)

	Group B		Group BD		<i>p</i> -value
	n=50	%	n=50	%	
Hypotension	9	18%	2	4%	0.025
Bradycardia	3	3%	4	8%	0.69
Cardiac arrest	0	-	0	-	-

Group B=Bupivacaine Group, Group BD=Bupivacaine+Dexmedetomidine Group.

DISCUSSION

Neuraxial anesthesia is a popular and most commonly used anesthesia technique for elderly patients undergoing genitourinary surgery. Despite being widely used, its perioperative complications can have serious unwanted outcomes. Several researches in recent past have shifted the focus from conventional approach of spinal anesthesia to the concept of low dose Bupivacaine with various adjuncts. Opioids have been most commonly used as adjuncts to spinal anesthetics with consistent results of better hemodynamic stability.¹⁰ Various other drugs have been tried other than opioids. Dexmedetomidine is one of the most recent drug in this regard with promising results and even fewer complications. Unfortunately there is limited number of studies on the subject.

Dexmedetomidine being a very highly lipophilic drug rapidly diffuses in cerebrospinal fluid and attaches to alpha-2 receptors. This provides effective and superior analgesia and may prolong duration of analgesia.¹¹ Intrathecal opioids can have delayed respiratory depression and pruritus which is unlikely with Dexmedetomidine as LA adjunct.¹²

In our study, onset of sensory and motor blockade was significantly shorter when Dexmedetomidine was combined with Bupivacaine for spinal anesthesia. Duration of analgesia and motor blockade was also extended in BD Group so there was lesser requirement of post-operative analgesics. Mean arterial pressure MAP and HR were toward the lower side in B Group whereas BD Group has shown better hemodynamic stability. Seven patients had symptomatic bradycardia, 3 belonged to Group B was whereas 4 were from the

Group BD. Eleven patients had hypotension,⁹ belonging to Bupivacaine Group whereas two were from the BD Group, expressing clear advantage in mixed Group. None of the patients in either Group had delayed respiratory depression or any other major complication.

In a systemic review and meta-analytic study, researchers independently searched PUBMED, EMBASE and other search engines for randomized controlled trials comparing the effects of Dexmedetomidine and fentanyl as adjuvants to LA for intrathecal use (total of 639 patients from 9 studies). It was observed that Dexmedetomidine as LA adjuvant in spinal anesthesia was more effective than fentanyl. Dexmedetomidine prolonged the duration of spinal anesthesia, improved perioperative analgesia, reduced the incidence of pruritus and did not increase the incidence of bradycardia and hypotension.¹³

Kanazi *et al.* in a prospective randomized double blind study on 60 patients undergoing TURP surgery used clonidine or Dexmedetomidine as an intrathecal adjunct to Bupivacaine. In their study, time of onset to reach peak sensory and motor blockade and sensory and motor regression times were recorded. Shorter onset of motor and sensory block with favorable hemodynamic stability was observed when dexmedetomidine and clonidine were used as an adjunct to LA as compared to LA only.¹⁴

EL-Hennaway *et al.* carried a randomized clinical trial on 60 children in a comparative prospective study. In this study, Dexmedetomidine was used as an adjunct to Bupivacaine for caudal block. They concluded that addition of Dexmedetomidine to LA significantly enhanced analgesia in children undergoing lower abdominal surgery without any increase in incidence of complications.¹⁵

Xia *et al.* conducted a prospective double blind randomized study on 70 patients undergoing caesarian deliveries. They observed that the effect of intrathecal Dexmedetomidine reduces the dose requirement of hyperbaric Bupivacaine and effective anesthetic conditions can be achieved with lesser dose.¹⁶

Liu *et al.* did a systematic review and meta-analysis on effects of 5µg of Dexmedetomidine in combination with intrathecal Bupivacaine versus placebo. In their analysis, they observed that intrathecal Dexmedetomidine significantly hastened the onset and prolonged both sensory and motor blockade.¹⁷

Sushruth *et al.* conducted a study which concluded that onset of sensory and motor block was early and duration of sensory and motor blockade prolonged when Dexmedetomidine added to Bupivacaine for spinal anesthesia.¹⁸ Same was observed in our study.

In a study conducted by Kurhekar *et al.* showed Intrathecal Dexmedetomidine prolonged the motor and sensory blockade without any undesirable side effects but intraoperative hypotension was more frequent.¹⁹

Dexmedetomidine has synergistic effects for anesthesia, sedative and analgesic. Its perioperative and intensive care use has created lot of interest in local practice. Judicious use of this drug can improve the safety standards of anesthesia. This study has its limitation as only ASA-II patients were included in this study. Hence the results of this study cannot be generalized for ASA-III and ASA-IV patients. Further research and experience for the safe use of Dexmedetomidine is required to establish its role in anesthesia.

CONCLUSION

Onset of sensory and motor blockade is significantly shorter in patients who were given Dexmedetomidine combined with low dose Bupivacaine as spinal anesthesia compared to standard intrathecal dose of Bupivacaine. Duration of analgesia was longer combination Group compared to isolated use of Bupivacaine. There were no hemodynamic or other major complications in patients receiving Dexmedetomidine as an adjunct drug hence rationalizing this combination for future practice.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SPB: & MA: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

AH: & AA: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

AH: & A: Critical review, concept data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Kwak K, Park SS. Regional anesthetic management of elderly patients. J Korean Medical Association 2017; 60(5): 377-400. <http://doi.org/10.5124/jkma.2017.60.5.377>

Comparison of Bupivacaine Alone Versus

- Lessing NL, Edwards CC, Brown CH, Ledford EC, Dean CL, Lin C, et al. Spinal anesthesia in elderly patients undergoing lumbar spine surgery. *Orthopedics* 2016; 40(2): e317-e322. <https://doi.org/10.3928/01477447-20161219-01>
- Lim HH, Ho KM, Choi WY, Teoh GS, Chiu KY. The use of intravenous atropine after a saline infusion in the prevention of spinal anesthesia-induced hypotension in elderly patients. *Anesth Analg* 2000; 91(5): 1203-1206. <https://doi.org/10.1213/00000539-200011000-00029>
- Qi X, Chen D, Li G, Huang X, Li Y, Wang X, et al. Comparison of intrathecal Dexmedetomidine with morphine as adjuvants in cesarean sections. *Biol Pharm Bull* 2016; 39(9): 1455-1460. <https://doi.org/10.1248/bpb.b16-00145>
- Shukla U, Prabhakar T, Malhotra K, Srivastava D. Dex-medetomidine versus midazolam as adjuvants to intrathecal bupivacaine: A clinical comparison. *J Anaesthesiol Clin Pharmacol* 2016; 32(2): 214-219. <https://doi.org/10.4103/0970-9185.182105>
- Routray S, Raut K, Pradhan A, Dash A, Soren M. Comparison of intrathecal clonidine and fentanyl as adjuvant to hyperbaric Bupivacaine in subarachnoid block for lower limb orthopedic surgery. *Anesthesia: Essays Res* 2017; 11(3): 589-592. https://doi.org/10.4103/aer.aer_91_17
- Weerink MA, Struys MM, Hannivoort LN, Barends CR, Absalom AR, Colin P. Clinical pharmacokinetics and pharmacodynamics of Dexmedetomidine. *Clin Pharmacokinet* 2017; 56(8): 893-913. <https://doi.org/10.1007/s40262-017-0507-7>
- Feng F, Chen Z, Cromer J, Doerr A, Glow A, Horstman-Reser A, et al. Anesthetic concerns for patients undergoing a Transurethral resection of the prostate (TURP). *Urologic Nur* 2016; 36(2): 75-78. <https://doi.org/10.7257/1053-816x.2016.36.2.75>
- Bayrak M, Altintas Y. Comparing laparoscopic cholecystectomy in patients with chronic obstructive pulmonary disease under spinal anesthesia and general anesthesia. *BMC Sur* 2018; 18(1): 1-6. <https://doi.org/10.1186/s12893-018-0396-1>
- Farzi F, Mirmansouri A, Naderi NB, Atrkar RZ, Ghazanfar TS, Nematollahi SM, et al. Comparing the effect of adding fentanyl, sufentanil and placebo with intrathecal Bupivacaine on duration of analgesia and complications of spinal anesthesia in patients undergoing cesarean section. *Anesthesiology and Pain Medicine*. 2017; 7(5): e12738. [doi:10.5812/aapm.12738](https://doi.org/10.5812/aapm.12738)
- Mostafa MF, Herdan R, Fathy GM, Hassan ZE, Galal H, Talaat A, et al. Intrathecal Dexmedetomidine versus magnesium sulphate for postoperative analgesia and stress response after caesarean delivery; randomized controlled double-blind study. *European Journal of Pain*. 2019; 24(1): 182-191. [doi:10.1002/ejp.1476](https://doi.org/10.1002/ejp.1476)
- Hess SR, Lahaye LA, Waligora AC, Sima AP, Golladay GJ. Safety and side-effect profile of intrathecal morphine in a diverse patient population undergoing total knee and hip arthroplasty. *European Journal of Orthopaedic Surgery & Traumatol* 2019; 29(1): 125-129. <https://doi.org/10.1007/s00590-018-2293-9>
- Sun S, Wang J, Bao N, Chen Y. Comparison of Dexmedetomidine and fentanyl as local anesthetic adjuvants in spinal anesthesia: A systematic review and meta-analysis of randomized controlled trials. *Drug Design, Development Therapy* 2017; 11(1): 3413-3424. <https://doi.org/10.2147/dddt.s146092>
- Kanazi GE, Aouad MT, Jabbour-Khoury SI. Effect of low-dose Dexmedetomidine or clonidine on the characteristics of Bupivacaine spinal block. *Acta Anaesthesiol Scand* 2006; 50(2): 222-227. <https://doi.org/10.1111/j.1399-6576.2006.00919.x>
- El-Hennawy A, Abd-Elwahab A, Abd-Elmaksoud A, El-Ozairy H&Boulis S. Addition of clonidine or Dexmedetomidine to Bupivacaine prolongs caudal analgesia in children. *Br J Anaesth* 2009; 103(2): 268-274. <https://doi.org/10.1093/bja/aep159>
- Xia F, Chang X, Zhang Y, Wang L, Xiao F. The effect of intrathecal Dexmedetomidine on the dose requirement of hyperbaric Bupivacaine in spinal anaesthesia for caesarean section: A prospective, double-blinded, randomized study. *BMC Anesthesiol* 2018; 18(1): 74-78. <https://doi.org/10.1186/s12871-018-0528-2>
- Liu S, Zhao P, Cui Y, Lu C. Effect of 5-µg dose of Dexmedetomidine in combination with intrathecal Bupivacaine on spinal anesthesia: A systematic review and meta-analysis. *Clin Ther* 2020; 42(4): 676-690.e5. <https://doi.org/10.1016/j.clinthera.2020.02.009>
- Sushruth MR. Effect of adding intrathecal-Dexmedetomidine as an adjuvant to hyperbaric Bupivacaine for elective cesarean section. *Anesthesia, Pain & Intensive Care* 2018; 22(3): 348-354. Retrieved from <http://apicareonline.com/index.php/view/71>
- Kurhekar P, Kumar S. Comparative evaluation of intrathecal morphine and intrathecal Dexmedetomidine in patients undergoing gynaecological surgeries under spinal anaesthesia: A prospective randomised double blind study. *Ind J Anaesth* 2016; 60(6): 382-387. <https://doi.org/10.4103/0019-5049.183387>