How to Cite:
Patil, K., Tripathi, D. C., & Patel, J. (2022). Clinical evaluation of dexmedetomidine versus clonidine as an adjuvant to bupivacaine in subarachnoid block for gynecological procedure: A prospective, randomized, double blind, controlled study. *International Journal of Health Sciences*, *6*(S3), 1182–1195. https://doi.org/10.53730/ijhs.v6nS2.5116

Clinical evaluation of dexmedetomidine versus clonidine as an adjuvant to bupivacaine in subarachnoid block for gynecological procedure: A prospective, randomized, double blind, controlled study

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***Abstract*---**Clonidine is a partial α2 adrenergic agonist used intrathecally with well-established efficacy and safety profile with effective prolongation of both motor and sensory spinal blockade. Dexmedetomidine, another member of α2 agonist's family, is recently being introduced in Indian market and is approved as an intravenous sedative and co-analgesic drug. This study examines and compares the usefulness and safety of dexmedetomidine versus clonidine as an adjuvant to bupivacaine in subarachnoid block for gynecological vaginal surgeries. Hundred patients, aged 30-60 years of ASA Physical status I and II, scheduled for elective gynecological vaginal surgery were enrolled in this study. Patients were randomly allocated to one of the two groups of 50 patients each by distributing sealed envelopes. Group C (n=50) received 0.5% hyperbaric Bupivacaine 2.5ml + 0.5ml distilled water containing 30μgm clonidine intrathecally. Group D (n=50) received 0.5% hyperbaric Bupivacaine 2.5ml +0.5ml distilled water containing 5μg Dexmedetomidine intrathecally. The sensory block was assessed by skin sensation to pin prick. The motor block was assessed according to the Modified Bromage Scale. Hemodynamic variables were recorded at 1, 3, 5, 10, 15, 20, 30

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
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Manuscript submitted: 27 Nov 2021, Manuscript revised: 09 Feb 2022, Accepted for publication: 18 March 2022

minutes and then at 15 minutes interval throughout the surgical period.

***Keywords*---**clonidine, dexmedetomidine, hyperbaric bupivacaine, motor block.

Introduction

Alleviation of postsurgical pain is one of the most fundamental goals in anaesthesiology. Postoperative pain relief is not only desirable but also important for reduction of postoperative morbidity. Postoperative pain, apart from patient's suffering, has many other adverse consequences like respiratory depression, circulatory disturbances and metabolic stress responses. Postoperative pain relief helps in early patient mobilization, reduction of respiratory complications, good patient's outcome, reduced morbidity and improved patient's satisfaction. And hence, its alleviation should be a prime objective in anaesthesia practice.[1]Spinal anaesthesia is a popular technique for gynecological surgery. Vaginal surgery including vaginal hysterectomy, tension free vaginal tape and vaginal repair are often done under regional anaesthesia. Surgery on the uterus and other genital organ performed under epidural or spinal block is often accompanied with visceral pain which requires treatment for postoperative pain relief.[2,3]

Spinal anaesthesia has the advantage of simplicity of technique, rapid onset of action and reliability in producing uniform sensory and motor blockade. Its main disadvantage relates to its limited duration of action and hence, lack of long lasting postoperative analgesia. To overcome this problem, administration of local anaesthetics in combination with different adjuvants is an excellent technique which not only relieves postoperative pain but also refines the quality of sensory and motor blockade of subarachnoid block and hence, acts as synergistic to local anaesthetics with lower local anaesthetic requirement, decreased side effect and excellent postoperative analgesia. Newer opioids are the popular adjuvants for this purpose.[4,5] Midazolam has also shown promising results in various studies.[6,7,8] Ketamine is also used intrathecally in various studies.[9,10] However the search for a better adjuvant which provides all the benefits desirable during regional anaesthesia is always existed.

Over the last two decades, there has been considerable accumulation of experimental and clinical data relating to the pharmacology of α2 adrenoceptor agonist and their clinical use in anaesthesia has steadily increased. Most of the clinical studies about α2 receptor agonists are related to the clonidine. Clonidine, an α2 adrenergic agonist, potentiates the effect of local anaesthetics and allows decrease in the required doses. Clonidine is a partial α2 adrenergic agonist used intrathecally with well-established efficacy and safety profile with effective prolongation of both motor and sensory spinal blockade.[11-15] Dexmedetomidine, another member of α2 agonist's family, is recently being introduced in Indian market and is approved as an intravenous sedative and co-analgesic drug.

It has eight times higher affinity for α2 receptors than clonidine.[16] In previous clinical studies, intravenous dexmedetomidine resulted in significant opioid

sparing effect and decrease in inhalational anaesthetic requirement.[17,18] Analgesic properties were found when intrathecal or epidural dexmedetomidine was used in animal models.[19,20] However, there are very limited studies in human to establish dexmedetomidine as an effective and safe adjuvant to local anaesthetics in spinal anaesthesia.[21-24] There is need for further studies to establish dexmedetomidine as an effective and safe adjuvant to local anaesthetics in sub-arachnoid block. This study examines and compares the usefulness and safety of dexmedetomidine versus clonidine as an adjuvant to bupivacaine in subarachnoid block for gynecological vaginal surgeries.

Material and Methods

After approval from the Institutional Review Board [(IRB No. 242/2012) and (CTRI registration no. REF/2013/08/005573)] and informed written consent from patients, this prospective, randomized, double blind study was carried out in the Department of Anaesthesiology, Govt. Medical College and Sir. T. Hospital, Bhavnagar, Gujarat. Hundred patients, aged 30-60 years of ASA Physical status I and II, scheduled for elective gynecological vaginal surgery were enrolled in this study. All the patients were subjected to detailed pre-anaesthetic evaluation with clinical history and systemic examination. Routine investigations like Haemogram, Random Blood Sugar, Renal Profile, and ECG for patients above 40 years of age were done as per patient clinical evaluation.

Inclusion criteria

- Informed written consent for participation in study.
- Age: 30 to 60 years.
- Gender: Female
- Patients posted for vaginal surgery, i.e. vaginal hysterectomy, vaginal tape, tension repair.
- ASA physical status I and II
- Body mass index (BMI) ≤ 30 kg/m^2.

Exclusion criteria

- Contraindication to Subarachnoid block.
- Allergy to local anaesthetic or study drug.
- Uncontrolled or labile hypertension.
- Body mass index >30 kg/ m^2.
- Patients taking any analgesics, sedative or antihypertensive drugs.
- Neurological disorders.
- Psychiatric disorders.
- Unco- operative patients.

In the pre anaesthetic preparation room, monitoring consisting of heart rate, non -invasive blood pressure, and peripheral oxygen saturation was established and baseline vital parameters were recorded. Every patient was informed in detail regarding nature and purpose of the study and was explained 0-10 point visual analogue scale (VAS) on a sheet of paper where (0) labelled as(no pain) and (10) as

(worst possible pain). Patients were randomly allocated to one of the two groups of 50 patients each by distributing sealed envelopes. 50 envelopes of each group were made with group mentioned inside and were mixed up. Patient was asked to pick one envelope in pre anaesthetic preparation room. One member of the team opened the envelope and filled up the drug as per the group assigned.

Group C (n=50) received 0.5% hyperbaric Bupivacaine 2.5ml + 0.5ml distilled water containing 30µgm clonidine intrathecally. (Clonidine group)
Group D (n=50) received 0.5% hyperbaric Bupivacaine 2.5ml +0.5ml distilled water containing 5µg Dexmedetomidine intrathecally. (Dexmedetomidine group)
Peripheral venous access was secured on hand with 18G cannula and preloading with Inj. Ringer Lactate 10-15ml/kg was initiated. None of the patients received any pre-medication. Then patients were shifted to operation theatre.

Under strict antiseptic precaution, subarachnoid block was performed in left lateral position, using midline approach with 25G spinal needle in L_3-L_4 intervertebral space. After the appearance of free flow of CSF, the mixture of drugs according to assigned group was injected. Principle investigator who performed the sub arachnoid block and injected the solution in the sub arachnoid space was unaware of the content of the solution injected in the subarachnoid space. Immediately after the block, patient was turned supine and assessment of sensory and motor characteristics of subarachnoid block was done as per the criteria shown in table A at 30 seconds interval till the peak of the blockade achieved. The sensory block was assessed by skin sensation to pin prick. The motor block was assessed according to the Modified Bromage Scale. At this point patient was given lithotomy position and surgery started. Hemodynamic variables were recorded at 1, 3, 5, 10, 15, 20, 30 minutes and then at 15 minutes interval throughout the surgical period. Sedation was rated at the same time interval as for haemodynamic variables as per the scale shown in table C.

Intraoperatively, any supplementation required for inadequate block, nausea, vomiting, pruritus and haemodynamic disturbances were also recorded. Bradycardia was defined as a pulse rate of < 60 beat/ min and was treated with boluses of 0.3- 0.5 mg atropine. Hypotension was defined as a decrease in systolic or Diastolic blood pressure > 30% of the baseline value, and was treated with crystalloid fluids and intravenous bolus of 6 mg ephedrine, if required. After the completion of surgery, patients were shifted to Post Anaesthesia Care Unit (PACU) where sensory and motor blockade was assessed at 30 minutes interval till regression of sensory and motor blockade. Thereafter, patients were monitored at 4 hourly intervals for next 24 hours for complications and adverse events if any.
Postoperatively, patients were asked to rate their pain intensity as per Visual Analogue Scale and first rescue analgesic was injected when VAS approached ≥ 5. Recue analgesic used was Inj. Diclofenac Sodium 75mg intravenously and time for first rescue analgesic given was also noted down. Time from onset of sensory blockade to use of first rescue analgesic was taken as duration of effective analgesia.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Results

Table 1
Patients characteristics in two groups

Variables	Group C	Group D	P value
Age (years)	47.18±09.72	47.28 ± 10.14	0.9600
Weight(Kg)	50.24 ± 08.49	51.46 ± 09.63	0.5033
Height (m)	01.63 ± 00.05	01.61 ± 00.06	0.4806
BMI(kg/m^2)	19.70 ± 03.08	19.84 ± 02.85	0.8215
ASA Physical Status I/II	16/34	13/37	

Values are mean±SD.
BMI=body mass index.

Patients characteristics in terms of age, weight, height and BMI were comparable in both the groups (P >0.05).

Table 2
Sensory charachteristics of subarachnoid block

Variables		Group C	Group D	P Value
Highest sensory level achieved (range)		T_6 - T_8	T_6 - T_8	0.1713
Onset of sensory block (min)	At L_1 Dermatome	01.4 ± 00.45	01.50 ± 00.40	0.2466
	At T_{10} Dermatome	03.32 ± 01.17	03.59 ± 00.68	0.1703
	At highest sensory level	10.45 ± 01.91	10.99 ± 01.69	0.1364
Time to reach peak of sensory block (min)	L_1 Dermatome	02.71 ± 00.84	02.9 ± 00.47	0.3591
	T_{10} Dermatome	04.64 ± 01.36	04.81 ± 00.93	0.4555
		14.69 ± 01.36	16.26 ± 0.72	0.1218

	Highest sensory level			
Time for regression of sensory block (min)	2 segment regression	120.9 ± 24.61	147.04 ± 32.09	< 0.0001
	Complete regression	264.8 ± 38.87	325.76 ± 38.49	< 0.0001

There is no statistically significant difference in mean time for onset, peak of sensory block in two groups. But there is statistically significant difference in two segment and complete regression of sensory block. Regression of sensory block was prolonged in group D as compared to group C. (P<0.0001)

Table 3
Duration of effective analgesia in two groups

Variable	Group C (Mean ± SD)	Group D (Mean ± SD)	P value
Duration of effective analgesia (Minutes)	401 ± 34.71	526.4 ± 27.38	< 0.0001

There is statistically significant difference in duration of analgesia in two groups. Postoperative analgesia was significantly prolonged in group D as compared to group C.

Table 4
Motor characteristics of subarachnoi block

Variables	Group C Mean ± SD	Group D Mean ± SD	P Value
Time to achieve grade I motor block (min)	03.72 ± 00.78	03.75 ± 00.88	0.8582
Time to achieve grade II motor block (min)	05.95 ± 01.13	05.92 ± 01.15	0.8964
Time to achieve grade III motor block (min)	10.91 ± 01.85	10.88 ± 01.72	0.9335
Regression of motor block to previous grade	147.18 ± 24.94	161.38 ± 24.05	< 0.0001
Time to complete regression of motor block	194.72 ± 22.57	213.44 ± 22.27	< 0.0001

There is no statistically significant difference in onset of motor block in two groups. But there was statistically significant difference in regression of motor

block. There was delayed regression of motor block in group D as compared to group C. (P<0.0001)

Table 5
Changes in heart rate

Heart rate per minute at different time points.	Group C (Mean ±SD)	Group D (Mean ±SD)	P Value
Baseline	84.66 ± 07.03	83.80 ± 07.04	0.54
Just after block	84.66 ± 06.85	85.12 ± 06.88	0.73
1 min after block	83.82 ± 06.65	84.22 ± 07.44	0.77
3 min	80.92 ± 06.43	82.82 ± 07.24	0.16
5 min	80.02 ± 05.72	81.78 ± 06.84	0.16
10 min	78.94 ± 05.50	79.90 ± 06.95	0.44
15 min	76.46 ± 04.71	78.74 ± 06.79	0.05
20 min	75.42 ± 05.73	77.26 ± 05.49	0.10
30min	74.06 ± 04.70	75.72 ± 05.28	0.10
45min	73.12 ± 05.56	74.98 ± 04.76	0.07
60min	74.18 ± 04.89	74.40 ± 05.29	0.82
1.25hr	72.28 ± 04.55	73.2 ± 05.20	0.34
1.50hr	71.08 ± 05.09	72.86 ± 04.47	0.06
1.75hr	71.18 ± 04.19	72.90 ± 04.86	0.06
2.0hr	71.30 ± 04.06	73.00 ± 04.70	0.05
2.25hr	71.68 ± 03.58	72.90 ± 04.83	0.15
2.50hr	71.12 ± 03.52	72.30 ± 09.74	0.42
2.75hr	72.36 ± 02.95	73.76 ± 04.20	0.05
3hr	72.52 ± 03.14	73.90 ± 04.28	0.06
3.5hr	74.00 ± 03.48	74.92 ± 04.78	0.27
4hrs	74.00 ± 03.76	75.18 ± 04.34	0.14
4.5hr	74.48 ± 03.84	75.36 ± 04.55	0.29
5hr	74.96 ± 03.92	75.88 ± 04.27	0.26
5.5hr	75.38 ± 04.83	75.76 ± 04.81	0.69
6hr	77.64 ± 05.56	76.32 ± 04.63	0.20
8hr	78.04 ± 04.37	79.36 ± 05.13	0.16
10hr	79.50 ± 04.19	77.88 ± 04.86	0.07
12hr	80.26 ± 05.07	78.68 ± 05.43	0.13
14hr	81.34 ± 05.10	79.44 ± 05.07	0.06
16hr	81.32 ± 04.34	79.82 ± 05.93	0.15
20hr	81.50 ± 05.00	80.42 ± 05.83	0.32
24hr	81.90 ± 04.97	81.28 ± 05.20	0.54

The changes observed in heart rate were comparable in both the groups throughout the study period. Heart rate remained stable and comparable at different time points in two groups. Except three patients in group C and one patient in group D, no other patient in either group developed bradycardia.

Table 7
Changes in blood pressure (mm of Hg)

Blood Pressure at different time points	Systolic Blood Pressure			Diastolic Blood Pressure			Mean Arterial Pressure		
	Group C	Group D	P	Group C	Group D	P	Group C	Group D	P
Baseline	125.0 ± 05.94	122.3 ± 07.83	0.05	77.82 ±04.60	77.20± 04.60	0.51	93.50 ± 03.65	92.10 ± 04.40	0.08
Just after block	125.2 ± 07.84	122.7 ± 07.19	0.09	77.62± 04.28	76.32± 06.24	0.22	93.34 ± 04.57	94.98 ± 25.11	0.65
1 min after block	121.4 ± 06.65	120.2 ± 07.26	0.41	75.30± 04.83	74.94± 05.80	0.74	90.72 ± 04.33	90.00 ± 05.06	0.44
3 min	119.6 ± 05.87	118.4 ± 06.95	0.33	74.42 ± 05.76	74.42± 06.89	0.99	89.04 ± 05.36	89.04 ± 05.95	0.99
5 min	117.3 ± 06.64	115.9 ± 07.79	0.35	74.16 ± 04.40	72.80± 07.34	0.26	88.44 ± 04.27	86.98 ± 07.46	0.23
10 min	113.2 ± 06.26	113.9 ± 07.82	0.62	72.16 ± 05.08	72.70± 06.80	0.65	86.04 ± 05.08	86.40 ± 06.52	0.76
15 min	111.6 ± 06.11	111.9 ± 08.29	0.82	72.12 ±04.85	71.94± 06.27	0.87	85.14 ± 04.40	85.32 ± 05.88	0.86
20 min	110.7 ± 06.11	111.1 ± 07.99	0.76	71.66± 05.17	71.32± 06.01	0.76	84.72 ± 04.52	84.64 ± 05.73	0.93
30min	108.2 ± 04.98	109.3 ± 08.40	0.41	70.44± 04.17	69.68± 05.38	0.43	83.06 ± 03.84	82.82 ± 05.26	0.79
45min	105.6 ± 05.94	108.1 ± 08.16	0.08	70.86± 07.03	68.60± 05.80	0.08	82.42 ± 05.85	81.72 ± 05.25	0.53
60min	106.7 ± 04.86	108.7 ± 09.97	0.21	70.02± 04.60	69.20± 05.80	0.43	82.26 ± 03.80	82.36 ± 05.93	0.92
1.25hr	108.9 ± 05.59	110.3 ± 08.32	0.32	71.62± 03.90	69.82± 05.63	0.06	83.92 ± 03.39	83.26 ± 05.17	0.45
1.50hr	110.3 ± 05.61	111.5 ± 08.08	0.38	71.46± 05.25	70.18± 09.44	0.40	84.26 ± 04.31	83.98 ± 06.60	0.80
1.75hr	112.9 ± 5.62	112.7 ± 07.89	0.88	71.74± 03.33	71.46± 04.04	0.64	85.38 ± 02.50	85.26 ± 04.29	0.86
2hr	114.6 ± 05.64	114.6 ± 08.87	0.99	72.36± 03.89	71.96± 04.13	0.61	86.40 ± 03.30	86.18 ± 04.57	0.78
2.25hr	114.5 ± 05.69	116.4 ± 08.71	0.19	71.98± 03.72	72.14± 04.33	0.84	86.12 ± 03.44	86.88 ± 04.87	0.37
2.50hr	115.3 ± 06.16	116.5 ± 08.85	0.41	71.44± 03.87	72.80± 03.85	0.08	86.06 ± 03.65	87.52 ± 04.45	0.07
2.75hr	117.7 ± 05.74	116.6 ± 09.07	0.49	73.08± 03.96	72.76± 03.07	0.65	87.98 ± 03.66	87.42 ± 04.04	0.46
3hr	118.6 ± 06.65	116.6 ± 09.01	0.21	72.50± 03.78	72.3± 03.84	0.78	87.82 ± 03.41	87.08 ± 04.64	0.37
3.5hr	119.1 ±	116.5 ±	0.0	72.92±	72.90±	0.9	88.36 ±	87.42 ±	0.19

	06.41	08.48	8	03.74	03.52	7	03.42	03.81	
4hr	119.1 ± 06.16	117 ± 08.06	0.14	73.20± 03.71	73.80± 03.45	0.39	88.42 ± 03.32	88.20 ± 03.98	0.76
4.5h	118.9 ± 07.42	116.6 ± 07.72	0.13	73.34± 03.80	74.04± 03.48	0.36	88.54 ± 04.19	88.26 ± 03.89	0.73
5hr	120.0 ± 05.59	118.9 ± 07.57	0.43	73.88± 03.79	75.12± 04.08	0.11	89.18 ± 03.39	89.74 ± 04.27	0.47
5.5hr	119.3 ± 06.16	118.1 ± 07.56	0.37	73.64± 03.82	74.48± 03.67	0.26	88.90 ± 03.86	89.08 ± 04.25	0.82
6hr	120.68 ± 06.00	119 ± 07.84	0.23	72.98± 03.98	73.88± 03.39	0.22	88.88 ± 03.82	88.91 ± 03.92	0.91
8hr	119.4 ± 06.39	119 ± 07.45	0.80	73.34± 04.71	73.84± 04.27	0.58	88.68 ± 04.47	88.91 ± 04.72	0.74
10hr	119.6 ± 07.16	119.6 ± 07.61	0.68	73.28± 04.69	74.32± 03.73	0.22	88.74 ± 04.76	89.24 ± 04.19	0.57
12hr	120.2 ± 06.69	118.7 ± 07.01	0.25	73.22± 05.31	74.10± 04.11	0.35	88.92 ± 05.27	88.94 ± 04.36	0.98
14hr	120.6 ±06.17	120.6 ± 06.79	0.09	73.52± 05.02	74.58± 04.17	0.25	89.22 ± 04.71	89.18 ± 04.35	0.96
16hr	121.4± 04.34	119.6 ± 05.93	0.08	73.50± 4.59	75.00 ± 04.18	0.09	89.46 ± 04.42	89.72 ± 04.56	0.77
20hr	120.7 ± 04.58	119.3 ± 07.08	0.25	74.04± 05.16	74.92 ± 04.08	0.34	84.7 ± 04.63	89.69 ± 04.52	0.93
24hr	122 ± 5.38	120.2 ± 06.50	0.12	74.36± 05.32	74.40 ± 04.48	0.96	90.24 ± 04.78	89.66 ± 04.31	0.48

Changes observed in systolic, diastolic and mean blood pressure were comparable in both the groups at different time points (P>0.05). Three patients in group C and in group D developed hypotension which responded to intravenous fluid therapy.

Table 8
Changes in SpO_2 (%)

Time	Group C (Mean ± SD)	Group D (Mean ± SD)	P value
Baseline	98.74 ± 0.44	98.72 ± 0.49	0.83
Just after block	98.74 ± 0.44	98.80 ± 0.45	0.50
1 min after block	98.74 ± 0.48	98.86 ± 0.40	0.18
3 min	98.76 ± 0.43	98.82 ± 0.48	0.51
5 min	98.70 ± 0.50	98.74 ± 0.48	0.68
10 min	98.68 ± 0.51	98.78 ± 0.54	0.34
15 min	98.66 ± 0.59	98.80 ± 0.53	0.20
20 min	98.72 ± 0.49	98.86 ± 0.49	0.16
30min	98.56 ± 0.57	98.78 ± 0.54	0.05
45min	98.68 ± 0.55	98.72 ± 0.53	0.71
60min	98.46 ± 0.61	98.74 ± 0.48	0.93

1.25hr	98.42 ± 0.64	98.66 ± 0.51	0.08
1.50hr	98.00 ± 0.53	98.20 ± 0.53	0.06
1.75hr	98.56 ± 0.57	98.74 ± 0.52	0.10
2.0hr	98.40 ± 0.57	98.62 ± 0.56	0.06
2.25hr	98.76 ± 0.43	98.64 ± 0.59	0.25
2.50hr	98.28 ± 0.57	98.12 ± 0.71	0.22
2.75hr	98.26 ± 0.56	97.98 ± 0.84	0.06
3hr	98.14 ± 0.57	98.48 ± 1.35	0.10
3.5hr	98.46 ± 0.64	98.64 ± 0.59	0.15
4hrs	98.44 ± 0.61	98.62 ± 0.60	0.14
4.5hr	98.40 ± 0.67	98.58 ± 0.60	0.16
5hr	98.50 ± 0.64	98.62 ± 0.56	0.32
5.5hr	98.42 ± 0.60	98.60 ± 0.57	0.13
6hr	98.40 ± 0.69	98.58 ± 0.60	0.17
8hr	98.46 ± 0.64	98.58 ± 0.64	0.35
10hr	98.48 ± 0.61	98.58 ± 0.60	0.41
12hr	98.40 ± 0.60	98.48 ± 0.61	0.51
14hr	98.44 ± 0.67	98.58 ± 0.60	0.27
16hr	98.26 ± 0.77	98.48 ± 0.67	0.13
20hr	98.36 ± 0.72	98.46 ± 0.67	0.47
24hr	98.14 ± 0.75	98.40 ± 0.67	0.07

Spo2 remained stable and comparable in both the groups throughout the study period. (P>0.05). There was no significant difference in sedation score between two groups. Sedation started at 30 minutes of block with maximum sedation score reached between 1.5-2 hours in both group. Sedation score decreased to 0 within 5 hours. At no time, sedation score exceeded 2 and no patient developed signs of respiratory depression.

Table 10
Complications

Complication	Group C		Group D	
	no of patients	%	no of patients	%
Nausea-Vomiting	4	8%	6	12%
Bradycardia	3	6%	1	02%
Hypotension	3	6%	3	06%
Respiratory depression	0	0%	0	0%
Headache	0	0%	0	0%
Neurological complication	0	0%	0	0%

In group C, three patients developed bradycardia and three patients developed hypotension where as in group D, one patient developed Bradycardia and three patients developed hypotension. Four patients (8%) in group C and six patients (12%) in group D experienced nausea and vomiting, which was statistically not significant. No other complication was noted in either group.

Discussion

Dexmedetomidine hydrochloride, a newer agent within the class of α_2 adrenoceptor agonist, delivers clinically effective sedation with analgesic property for use in intensive care unit setting. Additionally, it has an ability to eliminate or reduce the need for other analgesic medications. There is no evidence of respiratory depression with dexmedetomidine. Because of its selective α_2 receptor activity, use of dexmedetomidine has modest and predictable haemodynamic effects, making it a popular sedative and analgesic drug in intensive care unit.[25] Dexmedetomidine is now being used outside the ICU in variety of clinical settings, including sedation and adjunct analgesia in the operating room, sedation in diagnostic procedures and for other applications such as withdrawal/detoxification amelioration in adult and paediatric patients.[25]

Most of the clinical experience gained in the use of intrathecal α_2 adrenoceptor agonist has been described with clonidine. The use of intrathecal clonidine has well established synergistic effect with local anaesthetic. Clinical studies in surgical patients show that the intrathecal clonidine increases the duration of sensory and motor spinal block when added to spinal local anaesthetics and this effect of clonidine is dose dependent[26-30] and doses of >75µg intrathecal clonidine is accompanied by excessive sedation, hypotension and bradycardia. The clinical studies about the use of intrathecal dexmedetomidine in surgical patients are limited in the literature. Kanazi et al[30] found that 3 µg dexmedetomidine is equipotent to 30 µg clonidine in prolonging duration of sensory and motor block with minimal side effects when added to 15 mg spinal bupivacaine for urology surgery. From Kanazi's study and animal studies, we assumed that 3-5µg dexmedetomidine would be equipotent to 30-45 µg clonidine.

Present study showed that the supplementation of 12.5 mg of spinal bupivacaine with 30 µg clonidine or 5 µg dexmedetomidine did not show significant difference in the time for onset and peak of sensory blockade. But addition of 5 µg dexmedetomidine showed significantly prolonged two segment regression (147.04±32.09 min) and total duration of sensory blockade (325.76±38.49 min) as compared to clonidine where time for two segment regression and total duration of sensory blockade was (120.9±24.61 min) and (264.8±38.87 min). Dexmedetomidine also showed longer postoperative analgesia period of 9 hours as compared to 7 hours in clonidine group. In this study, the addition of 5 µg dexmedetomidine to intrathecal bupivacaine also did not show significant difference in time for onset of motor block but showed prolonged duration of motor block when compared with 30 µg clonidine intrathecally with bupivacaine. Findings of this study are similar to the findings reported by G.E. Kanazi et al[30], Rampal Singh et al[31] and Solanki S L et al[32] where Kanazi et al and Rampal Singh et al concluded that there was no significant difference in onset of sensory and motor block. Rampal singh et al also concluded that total duration of sensory and motor block was prolonged with dexmedetomidine as compared to clonidine. Solanki S L et al concluded that addition of dexmedetomidine to intrathecal bupivacaine produces longer post operative analgesia than clonidine. Yaksh et al[33] has shown that the intrathecal $\alpha_2$adrenoceptor agonist can cause dose dependant decrease in motor strength in animals and prolongation of motor block

of spinal anaesthetics due to addition of α_2 agonist may result from their binding to motor neurons in dorsal horn.

In this study, addition of dexmedetomidine did not cause significant fall in blood pressure intraoperatively and postoperatively. Three patients in dexmedetomidine group and three patients in clonidine group developed hypotension which responded to intravenous fluid therapy and is statistically not significant. Intrathecal local anaesthetics block the sympathetic outflow and reduce the blood pressure. Intrathecally administered α_2 adrenoceptor agonists have a dose dependent sedative effect.[5,21-24,29] The dose of dexmedetomidine and clonidine selected in this study did not produce excessive sedation, as at no time, sedation score exceeded two and no patient developed respiratory depression or fall in SpO_2. In fact, the sedation produced by dexmedetomidine and clonidine was found to be desirable as all the patients remained calm and quite in intraoperative and postoperative period. The only side effect noted was nausea and vomiting but it was not clinically and statistically significant and its incidence was comparable in both the groups.

Conclusion

Dexmedetomidine in the dose of 5μg added to 15 mg bupivacaine in subarachnoid block for gynecological vaginal surgery provides comparable onset for sensory and motor blockade but significantly prolonged duration as compared to 30μg of clonidine. Longer duration of postoperative analgesia with dexmedetomidine makes it superior to clonidine in respect to post-operative analgesia. Both the drugs produce desirable level of intraoperative and postoperative sedation, stable haemodynamics and minimal side effects. There was no significant difference in level of sedation in both groups. Haemodynamics and SpO_2 remained within normal limits and were comparable in both the groups.

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