

How to Cite:

Atri, A., & Gupta, S. (2022). Comparison of dexmedetomidine and clonidine with ropivacaine in epidural anaesthesia in vaginal hysterectomies. *International Journal of Health Sciences*, 6(S7), 5551-5562. <https://doi.org/10.53730/ijhs.v6nS7.13283>

Comparison of dexmedetomidine and clonidine with ropivacaine in epidural anaesthesia in vaginal hysterectomies

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Abstract---Background The present randomized double blind prospective study was carried out for Comparison of Dexmedetomidine and Clonidine along with Ropivacaine in epidural anaesthesia for vaginal hysterectomy. Methods: 60 female patients of ASA grade I and II, between the age group of 45 - 60 years were randomly assigned to 2 groups. Group RD: received 17 ml of 0.75% Ropivacaine and 1.5µg/kg of Dexmedetomidine , Group RC: received 17 ml of 0.75% Ropivacaine and 2µg/kg of Clonidine in supine position via epidural catheter. Onset, quality, duration of sensory and motor block and hemodynamic parameters evaluated. Results: Patients from Group RD have fast sensory block onset (i.e. 9.96±0.61min), prolonged two seg. regression time (138.93±4.48) and prolonged Analgesia time ((i.e 353.9±4.03min) as compared to Group RC i.e. (12.4±0.77), (128.8±3.46),(308.06±5.47) respectively. The duration of motor blockade was prolonged in patients of group RD (242.23±5.72min) as compared to the patients in group RC (230.66±5.20min). Patients in group RD were more sedated as compared to the patients in group RC. Initial fall in heart rate was more in patients of RD group as compared to the patients of group RC but later on both the groups showed stable heart rate. Fall in systolic, diastolic and mean arterial blood pressure was more in patients of RD group (during 5 to 50- 55 min of epidural injection) as compared to the patients of group RC. Later on both the groups showed stable systolic blood pressure. Conclusion: Dexmedetomidine is better adjuvant as compared to Clonidine for providing early onset and prolonged intraoperative as well as postoperative analgesia, better sedative property. Both the drugs showed bradycardia and hypotension which was clinically insignificant.

Keywords---dexmedetomidine , ropivacaine, clonidine.

Introduction

Surgical methods and the anaesthetic techniques have evolved and improved drastically over the last two decades. Many techniques and drug regimens, with partial or greater success, have been tried from

time to time to calm the patients and to eliminate the anxiety component during regional anaesthesia.[1-3]

The fear of surgery, the strange surroundings of the operation theatre, the sight and sound of sophisticated

equipment, dynamicity of an 'operation' during regional anaesthesia and the masked faces of so many strange personnel makes the patient panic to any extent.[4,5] The intense sensory and motor block, continuous supine position for a prolonged duration and the inability to move the body during regional anaesthesia brings a feeling of discomfort and phobia in many of the patients.[6] The high cephalic spread of analgesia with local anaesthetics may be significant but still its quality sometimes may not correlate with the level of sensory analgesia.[7] At this stage, the impulsive use of large doses of sedation or even general anaesthesia with mask defeats the novel purpose of regional anaesthesia whereby a continuous verbal contact with the patient is lost.

Sedation, stable haemodynamics and an ability to provide smooth and prolonged post-operative

analgesia are the main desirable qualities of an adjuvant in neuraxial anaesthesia.

α -2 adrenergic agonists have both analgesic and sedative properties when used as an adjuvant in regional anaesthesia.[8-13] Dexmedetomidine is a highly selective α -2 Adrenergic agonist with an affinity of

eight times greater than clonidine. There is no such study which has compared the dose equivalence of these drugs but the observations of various studies have stated that the dose of clonidine is 1.5–2 times

higher than dexmedetomidine when used in epidural route.[14-19] The anaesthetic and the analgesic

requirement get reduced to a huge extent by the use of these two adjuvants because of their analgesic

properties and augmentation of local anaesthetic effects as they cause hyperpolarisation of nerve fibres by

altering transmembrane potential and ion conductance at locus coeruleus in the brainstem.[20-24] The stable

haemodynamics and the decreased oxygen demand due to enhanced sympathoadrenal stability make them

very useful pharmacologic agents.[25,26]

Keeping their pharmacologic interactions and other properties we planned a double blind prospective

randomized clinically controlled study at our institute with an aim to compare the analgesic and sedative

effects of both these drugs when used epidurally as an adjuvant to ropivacaine in patients undergoing vaginal hysterectomy.

Material and methods

After hospital ethics committee approval and written informed consent, 60 female patients of

ASA grades I and II, between 40-60 years of age, and posted for elective vaginal hysterectomy were selected. The patients with haematological disease, bleeding or coagulation test abnormalities, psychiatric diseases, history of uncontrolled hypertension or diabetes, history of drug abuse and allergy to local anaesthetics of the amide type were excluded from the study.

Patients were randomly allocated to one of the following two treatment groups in a double blinded fashion based

on a computer-generated code

Group RC received 17 ml of 0.75% ropivacaine and 2 µg/kg of clonidine. Patients in group RD were administered 17 ml solution of 0.75% ropivacaine and 1.5 µg/kg of dexmedetomidine. Both groups were administered tablet Ranitidine 150 mg as premedicant a night before and on the morning of the surgery. Preoperatively patients were taught to analyse pain according to VNRS (0-no pain to 10- worst imaginable pain)

In the operation theatre, a good intravenous access was secured and monitoring devices were attached which included heart rate, electrocardiograph (ECG), pulse oximetry (SpO₂), non-invasive blood pressure

(NIBP), respiratory rate and the baseline parameters were recorded. The drug syringes were prepared by

an anaesthesia technician who was unaware of the proceedings. Patients were administered epidural

block with 18 gauge Touhy needle and a catheter was secured 3-4 cm into epidural space and a test dose

of 3 ml of 2% lignocaine hydrochloride solution containing adrenaline 1:200,000 was injected. After

4–6 minutes of administering the test dose, the drug solution was given.

The bilateral pin-prick method was used to evaluate and check the sensory level while a modified Bromage scale (0 = no block, 1 = inability to raise extended leg, 2 = inability to flex knee and 3 = inability to flex ankle and foot) was used to measure the motor blockade. Both sensory and motor blockade was checked at 5, 10, 15, 20, 25 and 30 minutes intervals after the epidural administration of the drugs. The surgical position

was made approximately after 25–30 minutes of epidural administration of drugs in every patient after

complete establishment of sensory and motor block.

The following block characteristics were observed and recorded:

Onset and highest dermatomal level of sensory analgesia, complete motor blockade, time to two segment regression, sensory level regression to S1 and motor regression to bromage 1

Grading of sedation was evaluated by ramsay sedation score. Sedation scores were recorded just before the initiation of surgery and thereafter every 20 minutes during the surgical procedure. Cardio-respiratory parameters were monitored continuously and recordings were made every 5 min until 30 min and at 10 min interval, thereafter up to 60 min and then at 15 min interval for next hour and finally at 30 min in the third hour. Hypotension (defined as systolic arterial pressure falling more than 20% mmHg) was treated with inj. Mephenteramine 3–6 mg in bolus doses and heart rate <50 beats/min was treated with 0.3 mg of inj. atropine. Intravenous fluids were given as per body weight and operative loss requirement. During the surgical procedure, adverse event like anxiety, nausea, vomiting, pruritis, shivering, etc. were recorded. Nausea and vomiting were treated with 6 mg of intravenous ondansetron.

All the vital and haemodynamic parameters were recorded in the recovery room also at 1, 5, 10, 20

and 30 min interval. The onset of pain was managed by top-up doses of 8 ml of 0.2% ropivacaine after

operation. At the end of study, all the data was compiled systematically and analyzed using 'Analysis

of variance and chi-square test. Statistical package for social science (SPSS) version 10.0 for windows,

Chicago III was used to compare the continuous variables between the two groups. Value of $P < 0.05$

was considered significant and $P < 0.0001$ as highly significant.

Results

The demographic profiles of the patients in both the groups were comparable with regards to age, weight and body mass index. The distribution as per ASA status was similar in both the groups and mean duration of surgery was comparable in both the groups and statistically non significant ($P > 0.05$) [Table 1].

Table 1

Demographic profile of both the groups			
Demographic characteristic	Group RD	Group RC	P value
Age	50.37±8.65	53.06±5.36	0.66
Weight	54.84±12.52	58.26±6.74	0.72
Body mass index	27.04±4.46	29.32 ± 3.08	0.92
ASA	21/4	20/5	0.81
Mean duration of surgery	96.34 ± 14.58	99.78 ± 13.68	0.26

Sensory and motor block characteristics

Addition of dexmedetomidine to ropivacaine as an adjuvant resulted in an earlier onset (8.52 ± 2.36 min)

of sensory analgesia at T10 as compared to the addition of clonidine (9.72 ± 3.44 min). Dexmedetomidine not

only provided a higher dermatomal spread but also helped in achieving the maximum sensory anaesthetic

level in a shorter period (13.14 ± 3.96 min) compared to clonidine (15.80 ± 4.86 min). Modified Bromage

scale 3 was achieved earlier (17.24 ± 5.16 min) in patients who were administered dexmedetomidine as

adjuvant. All these initial block characteristics turned out to be statistically significant values on comparison ($P < 0.05$) [Table 2.]

Table 2 : Comparison of initial block characteristics in both the groups

	Group RD	Group RC	P value
Onset time of sensory block at T10 (in	8.52 ± 2.36	9.72 ± 3.44	0.032

minutes)			
Maximum sensory block level	T5-T6	T6-T7	
Time to reach maximum sensory block level (in minutes)	13.14±3.96	15.80±4.86	0.018
Time in minutes for complete motor block (in minutes)	17.24 ± 5.16	19.52±4.06	0.041

$P < 0.05$ significant (s)

Mean sedation scores were significantly higher in RD group compared to RC group as 36% patients in group RD had a sedation score of 3 as compared 16% in group RC ($P < 0.0001$). Only 16% of the patients in the RD group had sedation scores of 1 compared to 32% wide and awake patients in RC group, which was a highly significant statistically ($P < 0.0001$)

Table 3: Comparison of intraoperative sedation scores in patients in both the groups

Sedation score	Group RD (no. of patients)%	Group RC (no. of patients)%	P value
1	4(16)	8(32)	<0.0001
2	12(48)	13(52)	0.65
3	9(36)	4(16)	<0.0001
4	0	0	
5	0	0	

$P < 0.0001$, highly significant (HS)

The findings of Table 4 reveal statistically significant values on comparison of post-operative block characteristics among the two groups. Dexmedetomidine provided a smooth and prolonged post-operative analgesia as compared to clonidine. The evidence was very much visible in the prolonged time to two segmental dermatomal regression (136.46 ± 8.12 min) as well as return of motor power to Bromage 1 (246.72 ± 30.46 min). As a result the time for rescue analgesia was comparatively shorter (310.76 ± 23.75 min) in the patients who were administered clonidine ($P < 0.05$). The superior block characteristics by the addition of dexmedetomidine were clearly evident from the lesser dose consumption (68.54 ± 16.84mg) of ropivacaine for post-operative analgesia for the next 24 hours ($P < 0.05$).

Table 4: Comparison of post operative block characteristics in both the groups

value	Group RD	Group RC	p
Mean time to two segmental regression (in minutes)	136.46 ± 8.12	128.08 ± 7.54	<0.05
Mean time for motor regression to bromage 1 (in minutes)	246.72 ± 30.46	228.44 ± 27.18	<0.05
Mean time for sensory regression to S1 (in minutes)	316.64 ± 40.36	296.72 ± 35.52	<0.05
Time to first rescue top up (in minutes)	342.88 ± 29.16	310.76 ± 23.76	<0.05
Total dose of ropivacaine used (mg)	68.64 ± 17.42	82.52 ± 20.82	<0.05

Table 5 shows the comparative incidence of various side effects in both the groups which were observed in the intra-op and post-op period. The incidence of dry mouth was significantly higher in both the groups but it was statistically non-significant on comparison ($P > 0.05$). The incidence of other side effects like nausea, vomiting, headache, shivering and dizziness were comparable in both the groups and statistically non-significant. We did not observe any respiratory depression in any patient from either group.

Table 5: Comparison of side effects between both the groups

Side effects	Group RD	Group RC
nausea	4 (16)	3(12)
vomiting	1(4)	1(4)
shivering	1(4)	2(8)
Headache	1(4)	1(4)
dizziness	3(12)	2(8)
Dry mouth	6(24)	7(28)
Respiratory depression	0	0

Figures in parentheses are in percentage

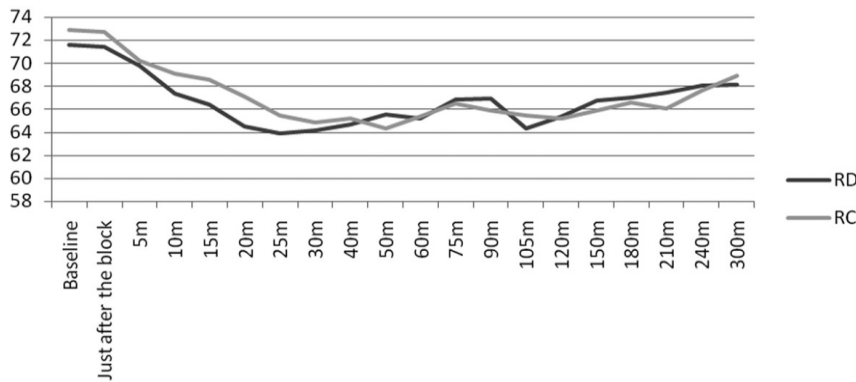


Figure 1: Comparison of heart rate in the group RD and RC covering the pre-op, intra-op and post-operative period.

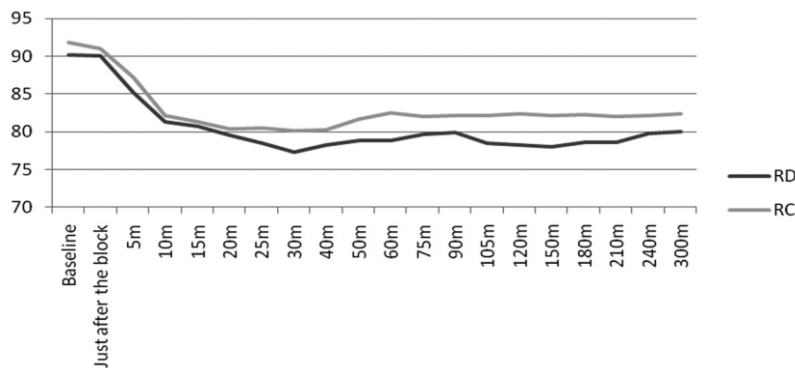


Figure 2: Comparison of mean arterial pressure in the group RD and RC covering the pre-op, intra-op and post-operative period.

Discussion

Epidural anaesthesia is a safe technique that provides surgical anaesthesia and post-operative pain control. Addition of adjuvant to local anaesthesia helps in providing better surgical anaesthesia and post-operative analgesia, with very little adverse effects.(14).

The use of neuraxial opioids is associated with quite a few side effects, so various options including α -2 agonists are being extensively evaluated as an alternative with emphasis on opioid-related side effects such as respiratory depression, nausea, urinary retention and pruritis.[15-17] The pharmacologic properties of α -2 agonists have been extensively studied and have been employed clinically to achieve the desired effects in regional anaesthesia.[8,9,12,13] Epidural administration of these drugs is associated with sedation, analgesia,

anxiolysis, hypnosis and sympatholysis.[10,11] Clonidine has been used successfully over the last decade for the said purpose and the introduction of dexmedetomidine has further widened the scope of α -2

agonists in regional anaesthesia.[18, 19] The faster onset of action of local anaesthetics, rapid establishment

of both sensory and motor blockade, prolonged duration of analgesia into the post-operative period,

dose-sparing action of local anaesthetics and stable cardiovascular parameters makes these agents a very

effective adjuvant in regional anaesthesia.[20-24] The present study was undertaken to compare the

analgesic efficacy, peri-operative and post-operative, as well as sedation effects of α -2 agonists. The

demographic profile of our patients was comparable with respect to mean age, body weight, body mass

index, ASA grade and duration of surgery. The results of the study has shown that the addition of either

1.5 μ g/kg dexmedetomidine or 2 μ g/kg clonidine as adjuvant to epidural ropivacaine not only prolongs

the duration of analgesia but also provides a good sedation level during the surgical procedure.

Dexmedetomidine has a visible edge over clonidine as it enables an earlier onset and establishment of

sensory and motor block. Further, addition of these two adjuvants promotes faster onset compared to

established time of onset of sensory analgesia with ropivacaine alone.(25,26).

The results of our study clearly indicate the effectiveness of epidural dexmedetomidine as it produced profound sedation in 36% of the patients, who were arousable by gentle tactile stimulation compared to achievement of similar sedation level in just 16% of the patients in clonidine group.

Thirty-two percent of the patients remained awake but calm in clonidine group compared to 16% in dexmedetomidine group who were equally cooperative and calm. Overall, the sedation scores were highly significant statistically with administration of dexmedetomidine. The RD group showed visible superiority over RC group in various post-operative block characteristics like the weaning of sensory and motor block, prolonged post-operative analgesia and a lesser amount of total ropivacaine used post-operatively. The cardiorespiratory parameters, as is evident from Figures 1 and 2, remained stable throughout the study period

which reaffirms the established effects of α -2 agonists in providing a haemodynamically stable peri-operative

and post-operative period.[25] Although a slight decrease in heart rate and mean arterial pressure was

observed in both the groups, it never fell down to more than 15% of the baseline values. The side effect profile

of both these drugs was quite favourable as none of the patient in either group had profound deep sedation

or respiratory depression which correlates very well with other studies.[28, 29, 30] Although we observed a little

higher incidence of dry mouth and nausea in both the groups, it was only mildly discomforting to the patients

and was mainly observed in the post-operative period and non-significant on statistical comparison.

Conclusion

We conclude that dexmedetomidine is a better adjuvant than clonidine in epidural anaesthesia as far as patient

comfort, stable cardio-respiratory parameters, intraoperative and post-operative analgesia is concerned.

Overall the experience with dexmedetomidine was quite satisfactory as compared to clonidine because of

its superior sedative and anxiolytic properties during the surgical procedure under regional anaesthesia.

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