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A Comparative Study of Qualitative Analgesia for Postoperative Period between Ropivacaine and Ropivacaine with Clonidine in Epidural Block

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Abstract

Background: *Pain is one of the most emotional sensation known to mankind. It frequently exceeds its protective nature and makes postoperative period a suffering. The pain in the postoperative period demands relief not only on humanitarian ground but also to reduce physical morbidity following the operation. So relief of pain in postoperative period extends the anaesthesiologists interest beyond the confines of the operating theatre.*

Epidural anaesthetic and analgesic techniques are commonly used for various operative procedures, obstetric analgesia, postoperative pain and chronic pain management. Ropivacaine has increasingly replaced bupivacaine because of its similar analgesic properties, lesser motor blockade and decreased propensity of cardiotoxicity. Clonidine has been frequently used as an adjunct to local anesthetics because it improves the quality of anesthesia and analgesia, reduces the dose requirement of the anesthetic agent and provides a more stable cardiovascular course. In this study we included 60 patients undergoing various endoscopic urological surgeries like TURP, URS, OIU and cystoscopy procedures.

Material and Methods: *Patients were randomly divided in two groups.* ***R-Group****: 30 patients received 0.5% ropivacaine 18 ml.* ***RC-Group****: 30 patients received 0.5% ropivacaine 18 ml with clonidine 60 µg . Pre-op and intra-op, haemodynamic parameters and side effects were observed. For postoperative pain assessment, VAS score was used at postoperative 2,4,6,7,8,9,10,12 hour.*

Results: *The objective evidence of block like mean arterial pressure, heart rate showed significant change in RC-group. Pain score(VAS) was significant at 6^{th} hr ,7^{th} hr ,8^{th} hr ,9^{th} hr and at 10^{th} hr postoperative period due to the reduced VAS in RC-Group. Demand of rescue analgesia was more in R-Group. Level of sedation, side effects were not statistically significant.*

Conclusion: *Clonidine as an adjunct to Ropivacaine by epidural injection improves and augments the block, reduces heart rate and blood pressure. It also prolongs the duration and the quality of analgesia in postoperative period with no more side effects like nausea, vomiting and sedation.*

Keywords: *Clonidine, Epidural block, Postoperative pain, Ropivacaine, Urological Surgeries*

I. Introduction

Feeling of pain is one of the most important emotional determinants which dominate the perception of patients who undergo the surgical procedures.[1] The thought of pain creates a lot of fear, anxiety and mental stress in the patients despite administration of adequate treatment. Post-op period can acquire the dimensions of a nightmare once a patient starts experiencing the agony of excruciating pain if not given proper attention.[1]

In postoperative period when the effect of the anaesthesia disappears, the tissue injury persists and pain producing substances which are liberated during the operation greatly reduce the normally high threshold of the nociceptors, so that innocuous stimulation produces pain. Moreover the cut ends of axons further contribute to nociception.[2] Surgical trauma and subsequent postoperative pain, result in a broad range of endocrinologic, immunologic and inflammatory responses, including increased release of catabolic hormones and inhibited secretion of anabolic mediators. To minimize or overcome these adverse effects, the postoperative pain should be optimally treated. Epidural anesthesia and analgesia is widely regarded as a boon for patients as it can provide a relief from pain for a longer duration. Epidural administration of various analgesics gained increasing popularity. An epidural block can be performed at the lumbar, thoracic, or cervical level. Epidural techniques are widely used for operative anesthesia, obstetric analgesia, postoperative pain control, and chronic pain management.

Epidural bupivacaine had been used extensively in the past for providing adequate post-op pain relief in patients. However, in recent years, ropivacaine has increasingly replaced bupivacaine for the said purpose because of its similar analgesic properties, lesser motor blockade and decreased propensity of cardiotoxicity.

Ropivacaine is a well tolerated regional anaesthetic drug effective for surgical anaesthesia as well as the relief of postoperative and labour pain. Clinically adequate doses of ropivacaine appear to be associated with a lower incidence or grade of motor block than bupivacaine.[3]

Though a slightly larger dose of ropivacaine is required as compared to bupivacaine to achieve the analgesic and anesthetic effects, the addition of an adjuvant can decrease the dose of ropivacaine required, thereby eliminating quite a few side effects associated with larger doses of ropivacaine. Neuraxial adjuvants augment the action of local anesthetics.[4] The addition of an adjuvant has further enhanced the effectiveness of these local anesthetics as they not only help in intensifying and prolonging the blockade effect but also help in the reduction of the dose of local anesthetics. Neuraxial opioids are associated with quite a few side effects so, clonidine is being extensively evaluated as an alternative option as far as opioid-related side effects such as respiratory depression, nausea and pruritis are concerned.[5]

Clonidine is a partial alpha-2 adrenergic agonist. It has been used as an adjuvant to epidural local anesthetics and opioids to improve the quality of analgesia after major abdominal surgeries.[6] It can provide pain relief by an opioid independent mechanism as it directly stimulates pre and postsynaptic alpha 2 adrenoceptors in the dorsal horn gray matter of the spinal cord, thereby inhibiting the release of nociceptive neurotransmitters.

Though at higher doses, it may further reduce the dose of local anesthetic and prolong the analgesic duration, but at the same time can exert its toxic effects resulting in profound hypotension, bradycardia and deep sedation.

Anesthesia for urology surgery poses special problems by way of patient factors and complexity of the procedure. Preoperative optimization of the patients with renal dysfunction and comorbidity; specific complications associated with the operative procedures, such as transurethral resection of prostate, laparoscopy surgery, percutaneous lithotripsy and renal transplantation.[7,8]

II. Methodology

Sixty patients undergoing endoscopic urological surgeries which included TURP, URS, OIU, Cystoscopy etc. procedures were randomly selected for the study. The study was approved by the Hospital Ethics Committee. Patients with ASA grade I, II, age between 20 to 75 years, height between 150 – 180 cm were included for surgery. Patients who denied consent or with bleeding disorders, spinal deformities, neurological deficit, local skin sepsis around the site of needle insertion, co-morbid disease, history of allergy and ASA class III, IV were excluded. After obtaining written informed consent, initial pre-operative counselling and reassurance was done to gain the confidence of the patient. The nature of the procedure was explained.

III. Procedure

In the operation theatre, the heart rate, blood pressure and respiratory rate of the patient were recorded. An intravenous infusion was started and the patients were preloaded with 500 ml of Ringer lactate solution and connected with monitors like pulse oximetry, ECG leads and noninvasive blood pressure monitor. They were put on lateral or sitting position. Under all aseptic precautions 2% lignocaine plain injected locally in the desired area, epidural space was found with 18 G tuohy needle at L3 – L4 space by loss of resistance using air injection technique.

In first group, 18 ml of 0.5% ropivacaine was injected slowly after the aspiration of syringe & in the second group 18 ml of 0.5% ropivacaine with 60mcg of clonidine mixture was injected slowly after aspiration of syringe. After injecting the drug the tuohy needle was taken out & dressing applied over that area.

All the patients were continuously monitored for heart rate, blood pressure, respiratory rate and oxygen saturation and recorded in the anaesthesia chart for every 5 min for first half an hour and every 10 min till the end of the surgery. Intraoperative hypotension was treated with IV fluids, oxygen supplementation and titrated doses of mephentermine 3-6 mg intravenous. Bradycardia was treated with injection atropine. No sedatives or narcotics were administered intravenously preoperatively. Pre-op and intra-op, haemodynamic parameters and side effects was observed and recorded. Post operative assessment of intensity of pain was done by visual analogue scale, later intended study drugs were given when the visual analogue pain score touched the 3 cm mark.

R-Group: 30 patients received 0.5% ropivacaine18 ml.
RC-Group: 30 patients received 0.5% ropivacaine18 ml with clonidine 60 μg.
In the post-operative period the following parameters were studied:

A. Visual analogue scale -

For postoperative pain assessment, VAS was used (VAS: 0-10; 0: no pain, 10: worst pain imaginable).[9] The VAS scores of the patients at postoperative 2,4,6,7,8,9,10,12hr.After obtaining written informed consent, initial pre-operative counselling and reassurance was done to gain the confidence of the

patient. In the visual analogue scale the patients were shown a scale of 10 cm length. Zero end of the scale was taken as 'No pain' and 10 cm mark as 'Maximum pain'. Intensity of pain increases gradually from '0' to '10'. Patients were instructed to point the intensity of pain on the scale.

B. Side effects: nausea, vomiting, hypotension

C. Sedation score:

The sedation levels of the patients would be defined in accordance with the Ramsay Sedation Scale,[10] Graded from 1 to 6

1. Deep sleep – Does not respond to verbal commands.
2. Sleepy – Responds to verbal commands.
3. No complaint or body movement – Calm.
4. Complaints with body movement – But Calm.
5. Substantial complaining and body movement – Not Calm.
6. A great degree of complaining and body movement, accompanied by some excitement.

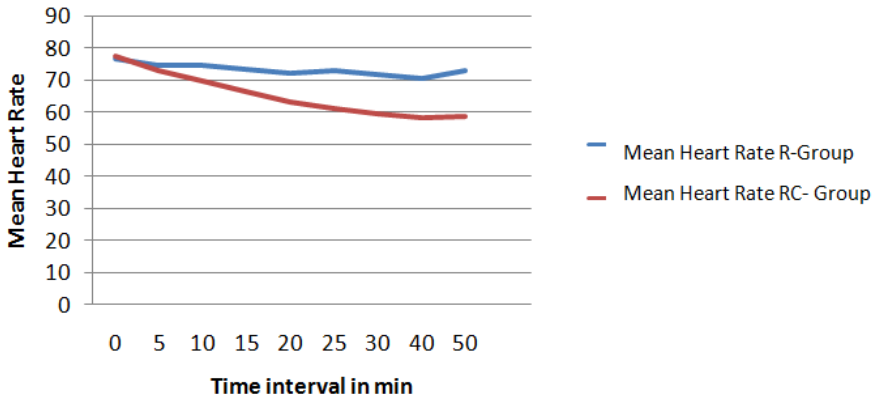
D. Rescue analgesia

This was calculated from the time when the first dose was given, postoperatively and followed up till the patient complained of pain. Time at which patients complained of pain more than 3 cms on the VAS scale was noted. That point was taken as the end of fair analgesia.

Table –1: Mean of mean heart rate in between R-Group and RC-Group

Time interval in min	HR				Significance
	R-Group		RC-Group		
	Mean	SD	Mean	SD	
0	76.67	7.29	77.73	7.44	0.5770 NS
5	74.77	6.75	73.37	7.02	0.4343 NS
10	74.53	6.22	70.00	6.17	0.0063 S
15	73.23	6.11	66.77	6.25	0.0002 HS
20	72.17	5.32	63.17	5.40	0.0000 HS
25	72.80	4.90	61.13	5.62	0.0000 HS
30	71.73	5	59.43	6.13	0.0000 HS
40	70.55	5.69	58.37	5.10	0.0000 HS
50	73	7.01	58.60	4.33	0.002 S

SD: Standard deviation, NS: Not Significant, HS: Highly significant, S: Significant



Variation of heart rate was studied at different time intervals up to 0 to 60 min. There was significant change in the heart rate at 10 min to 40 min in compare to R-Group which is statistically significant (P<0.000) [Table no – 1]. It shows Ropivacaine with Clonidine has decreased the heart rate more when compared to Ropivacaine alone.

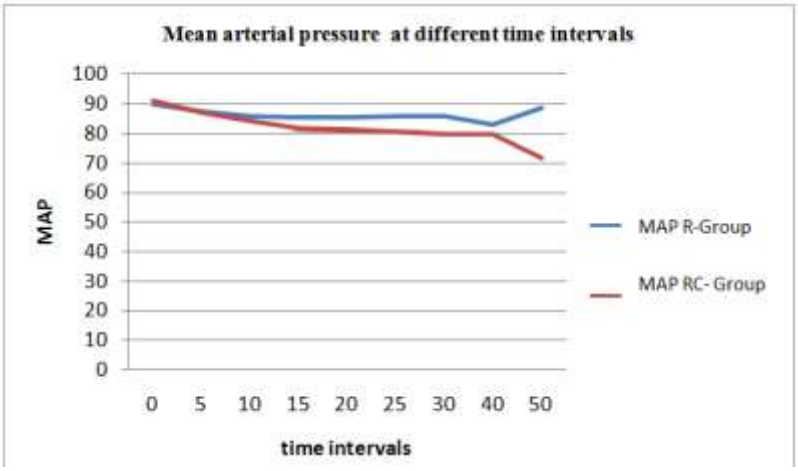
Table –2: Mean of mean arterial pressure in between R-Group and RC-Group at different time intervals

Time interval in min	MAP				Significance
	R-Group		RC-Group		
	Mean	SD	Mean	SD	
0	89.71	3.86	90.96	4.62	0.2623NS
5	87.28	3.55	86.78	4.60	0.6390NS
10	85.88	3.70	84.02	4.47	0.0851NS
15	85.42	3.74	81.71	4.35	0.0008S

20	85.52	3.29	81.13	4.29	0.0000HS
25	85.82	3.53	80.42	3.85	0.0000HS
30	85.82	3.21	79.91	3.49	0.0000HS
40	83.04	16.12	79.78	3.20	0.2807NS
50	88.39	4.64	71.45	2.4	0.1123NS

SD: Standard deviation, NS: Not Significant, HS: Highly significant, S: Significant

Variation of MAP in both groups was compared at different time intervals up to 0 to50 min. There was significant change in the MAP at 10 min to 30 min which is statistically significant [Table no – 2]. It shows ropivacaine with clonidine has decreased the MAP more compared to ropivacaine alone.



Epidural clonidine decreases blood pressure at a brainstem level and by inhibiting sympathetic spinal cord outflow.[11,12] Sympathetic reflexes are diminished, while baroreceptor responses are unaltered. Hypotension results primarily from a reduction in systemic vascular resistance, with little change in cardiac output. Clonidine reduces heart rate by direct and central mechanisms [13], and in some human studies, epidural administration has significantly reduced heart rate.[11,13]

We observed that nausea, vomiting hypotension were not significant in both groups. The groups did not differ statistically concerning PONV and antiemetic drug consumption. Sedation is a side effect frequently associated with the use of clonidine but the low dose of clonidine used here does not contribute to much sedation. Ruth Landau et al in 2002, found that sedation has been reported to occur as soon as 15 to 60 minutes after doses of 120 μg of clonidine [14] and 60 to 120 minutes after 150 μg of clonidine or 75 μg of clonidine with 50 μg of fentanyl.[15] In our study we got less side effect with low dose of clonidine.

Table – 3: Comparison of VAS in between R-Group and RC-Group

Time interval in hour	R-Group		RC-Group		Significance
	Mean	SD	Mean	SD	
2	0	0	0	0	
4	0	0	0	0	
6	0.97	0.18	0	0	0.0000HS
7	2.40	0.56	0.37	0.49	0.0000HS
8	3.43	0.68	0.93	0.25	0.0000HS
9	3.67	0.55	1.57	0.50	0.0000HS
10	3.03	0.18	2.17	0.38	0.0000HS
12	3	0	3.03	0.41	0.6607NS

SD : Standard deviation, NS : Not Significant, HS: Highly significant, S:significant

As seen from table 3 pain score (VAS) was compared between the two groups at different time interval for the first 12 hrs. It was found that VAS was significant at 6^{th} hr ,7^{th} hr ,8^{th} hr ,9^{th} hr and 10^{th} hr in postoperative period. This was due to the reduced VAS in RC-Group when compared to R- Group.

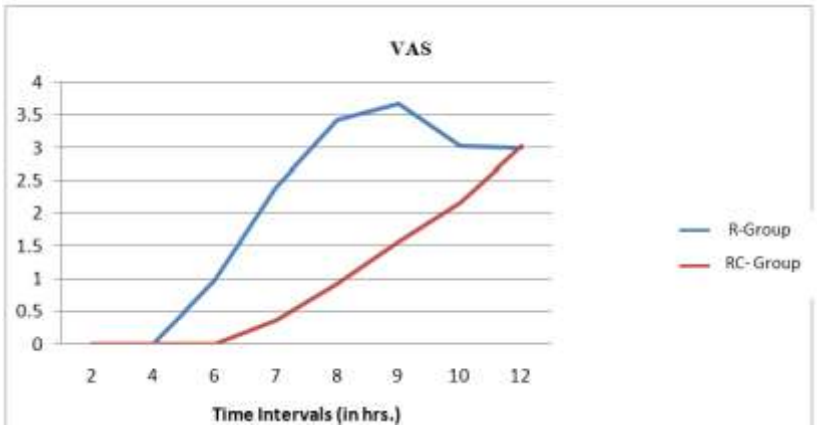


Table – 4 : Rescue analgesia total doses taken in 24 hour

No. of patients	R-Group	RC-Group	Significance
Mean ± sd	2.10± 0.40	1.03 ±0.18	0.0000HS

SD: Standard deviation, NS: Not Significant, HS: Highly significant, S: Significant

Demand of rescue analgesia more in R-Group then in RC-Group. This is Statistically Significant.

IV. Discussion

In our study variation of heart rate in RC-Group was studied at different time intervals up to 0 to 60 min. There was high significant change in the heart rate at 10 min to 40 min compare to R-group heart rate. This was statistically significant (P<0.000). It shows that Ropivacaine when combined with Clonidine results in more reduction of heart rate when compared to Ropivacaine alone. Variation of MAP in RC-Group was studied at different time intervals up to 0 to 50 min. There was high significant change in the MAP at 10 min to 30 min compare to R-Group MAP. This was statistically significant. It shows ropivacaine with clonidine has decreased the MAP more when compared to ropivacaine alone. Epidural clonidine would produce prolonged analgesia from local anesthetics and opioids and would allow a local anesthetic sparing effect. The optimal epidural dose would lie between 60 μg to 75 μg, a dose lower than 60 μg is ineffective, whereas a dose larger than 100 μg induces sedation and hypotension.

Sukhminder Jit Singh Bajwa, et al in 2010**,** showed that RC group required lesser doses of local anesthetic top-up doses as compared to that required by R group patients. The frequency of top up doses increased, duration of analgesic period decreased while total dose consumption of ropivacaine increased in the R group as compared to RC group.[4] In our study we also found similar results.

Pain score (VAS) was compared between the two groups at different time interval for the first 12 hrs. It was found that VAS was significant at 6^{th}hr ,7^{th}hr ,8^{th}hr ,9^{th}hr and 10^{th}hr. This was due to the reduced VAS in RC-Group when compared to R-Group.The demand for rescue analgesic was more in R-Group then in RC-Group. This was statistically significant.

J. G. Forster et al in 2004, in this study, clonidine augmented analgesia after TKA when added to a continuous low dose epidural infusion of ropivacaine and fentanyl.[16] Compared with the control group, patients in the clonidine group received, on average, smaller doses of epidurally infused drugs. At the same time, they required significantly less rescue medication. Enhanced analgesia was also reflected by the observation that in the clonidine group patients suffered less frequently from episodes of marked pain (VAS 4–6) and of breakthrough pain at rest (VAS 7–10). Nevertheless, pain relief was acceptable also in the control group; that is rescue pain medication was adequate, and patient satisfaction was good to excellent in both groups. Although statistically significant, the small difference in VAS scores at 24:00 in favor of the clonidine group is of limited clinical importance.

In a more recent study, clonidine was caudally administered with bupivacaine 0.125% in a group of children aged 1–10 yr undergoing ureteroneocystostomy. Patients in the clonidine–bupivacaine group required significantly less i.v. morphine during the initial 24 hr postoperative period (0.02 mg kg^{-1} in PACU and 0.1 mg kg^{-1} on first postoperative day) than those receiving bupivacaine alone (0.05 mg kg^{-1} in PACU and 0.2 mg kg^{-1} on first postoperative day).

In a similar study, the addition of clonidine 2 μg kg^{-1} to bupivacaine 0.25% (1 ml kg^{-1}) significantly improved caudal analgesia compared with that provided by bupivacaine alone, without an increase in the incidence of side-effects in children undergoing orthopaedic surgery.

Ruth Landau, et al, postulated that adding clonidine to ropivacaine for epidural analgesia during labor should allow good analgesia with minimal motor block. The purpose of this prospective, randomized, double blinded study was to examine whether 75 µg of clonidine increases the analgesic properties (intensity and duration) of an initial ropivacaine dose and produces dose sparing of ropivacaine. In our study we found adding of clonidine prolong the postoperative analgesia and decrease the demand of rescue analgesia.

We observed that nausea, vomiting hypotension was not significant in both groups. The groups did not differ statistically concerning PONV and antiemetic drug consumption.[17] Sedation is a side effect frequently associated with the use of clonidine in postoperative analgesia, often in conjunction with opioids. Probably the low dose of clonidine used here does not contribute to sedation.

Addition of Clonidine to Ropivacaine by epidural injection improved the onset of block, reduced the heart rate and blood pressure more in compare to ropivacaine plain, prolonged post operative analgesia in duration and quality with no more nausea, vomiting and sedation.

V. Conclusion

Addition of Clonidine as an adjunct to Ropivacaine by epidural injection improves and augments the block, reduces heart rate and blood pressure more in compare to ropivacaine alone. It also prolongs the duration and the quality of analgesia, with no more side effects like nausea ,vomiting and sedation.

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