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Original Research Article

Effects of addition of different doses of clonidine to intrathecal ropivacaine in lower limb and subumbilical surgeries

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Abstract

Aim and Objectives: The present study was undertaken to compare the quality of subarachnoid block and vital parameter changes by addition of different doses of clonidine to intrathecal 0.5% isobaric ropivacaine in sub umbilical surgeries.

Methods: The study enrolling 135 patients of either sex (age 20-50 years), ASA grade I & II were randomly allocated into three groups of forty five each. Group I received 15 mcg clonidine + 3.2 ml of 0.5% ropivacaine + 0.2 ml normal saline, group II received 30 mcg clonidine + 3.2 ml of 0.5% ropivacaine + 0.1 ml normal saline and group III received 45 mcg clonidine + 3.2 ml of 0.5% ropivacaine. Characteristics of spinal block, vital parameter changes and level of sedation were recorded.

Results: We found no significant effect on onset and quality of sensory and motor block by using different doses of clonidine. Group II and group III had prolonged duration of sensory and motor block as compared to group I. There were no significant differences in maximum level and time to reach maximum level of sensory block in all three groups. Time for two segment regression was significantly prolonged in group II and group III as compared to group I. The incidence of hypotension, bradycardia and level of sedation score was higher in group III as compared to group I and II.

Conclusion: Addition of 30 mcg of clonidine to intrathecal ropivacaine is safe and likely to be as effective as higher doses in prolonging duration of sensory and motor block and having minimum side effects and hence seems to be optimum.

Keywords: Intrathecal, Ropivacaine, Clonidine, Block characterstics, Sub umbilical surgeries.

1. Introduction

Due to significant progress in the safety of anesthesia, intubation, low intra-operative blood loss, and continued analgesia in the post-operative period, spinal anesthesia and other regional techniques are frequently used in sub umbilical surgeries like lower extremity orthopaedic, arthroscopic, lower abdominal surgeries[1]. Spinal anaesthesia is a popular anesthetic technique that is widely used across the world [2] and produced fastest, predictable and reliable form of anaesthesia for sub umbilical surgeries [3]. Local anaesthetics such as lignocaine and bupivacaine had been used for spinal anesthesia since many years. But as lignocaine is having more neurotoxic effects and bupivacaine having cardio-toxic effects, local anaesthetics with fewer side effects like ropivacaine and levobupivacaine have been introduced for spinal anesthesia [4].

Ropivacaine is a long-acting amide local anaesthetic agent and first produced as a pure enantiomer. Early report suggests that the agent is less toxic to the central nervous system and the cardiovascular system and is widely used as an alternative to bupivacaine[5]. It was presented as producing equivalent spinal anesthesia with a faster recovery period than that of bupivacaine and provides effective spinal anaesthesia for patient's well being and surgeons work as well as provides some pain relief in initial postoperative period. The level of motor block is similar to bupivacaine, but with a later onset of motor block and a little shorter duration [5]. The quality of intraoperative analgesia and muscle relaxation was significantly lower with ropivacaine. Solution to this is to maintain the advantage of ropivacaine while improving quality and duration of spinal anaesthesia and intra-

operative analgesia could be the use of an analgesic adjuvant.

Clonidine is a partial agonist of the α2-adrenoreceptor and acts as an analgesic and a sedative. Literature reviews obvious that intrathecal clonidine is being extensively evaluated as an alternative to other adjuvants for improving quality and prolongation of spinal anaesthesia with minimal effects on vital parameters. It was found that addition of clonidine as adjuvant in spinal anesthesia, leads to decrease the time to onset of block, increase its depth and increase duration of anaesthesia, decrease the amount of bleeding from the surgery field, lower the dose of local anesthetic, reduce systemic absorption and therefore prevent side effects.

Hence the present study envisaged with an intention to test the association of the α2-adrenergic agonist clonidine with ropivacaine, also to assess clinical effects of adding different doses of clonidine to intrathecal isobaric ropivacaine to study characteristics of spinal block and vital parameter changes in patients undergoing sub umbilical surgeries.

2. Material and Methods

After obtaining institutional ethics committee approval and written informed consent from all patients, this prospective, randomized controlled double blinded study was conducted in 135 patients of either sex, ASA grade I and II, aged between 20-50 years and were scheduled for elective sub umbilical surgeries, requiring the duration of more than half an hour. Patients having hypertension, long standing uncontrolled diabetes mellitus, bleeding tendencies, disorders of cardiovascular system, respiratory system and neuromuscular system, liver diseases and psychiatric disorders, patients with severe anaemia, spinal deformities and emergency hypovolemic patients and local infections at the site of lumber puncture were excluded from the study. Patients were randomly allocated into three groups of forty five each. Group I received 15 mcg clonidine + 3.2 ml of 0.5% ropivacaine + 0.2 ml normal saline, group II received 30 mcg clonidine + 3.2 ml of 0.5% ropivacaine + 0.1 ml normal saline and group III received 45 mcg clonidine + 3.2 ml of 0.5% ropivacaine intrathecally. The total volume injected was 3.5ml in all groups. A detailed history and a thorough general and systemic examination and all relevant investigations were done for all the patients. All the patients were starved overnight and they received oral diazepam 5mg in the night prior to surgery.

In the operation theatre standard monitoring devices NIBP, ECG, pulse oximeter, temperature were applied to the patient and baseline parameters like systolic/diastolic/mean BP, heart rate, SPO_2, along with respiratory rate & temperature were recorded. Patients preloaded with 500ml of Ringers Lactate solution. Patients were placed in left lateral position on the operation table and with strict aseptic precaution; midline approach, subarachnoid block was achieved in L3-L4 space with 25 G Quinkes spinal needle. Drug was injected after free flow and clear aspiration of CSF. Patients were immediately placed in the supine position slowly. The person giving the spinal block and the person who was observing intra-operative and postoperative parameters and the patients were unaware of the drug given. The time of injection of drug was noted.

Sensory onset was subjectively studied by pin prick method with sterile needle & asking patients about tingling or any sensation of warmness. Feeling of tingling or any sensation of warmness noted as time of onset of sensory block. The patients were tested every 30 seconds at one fixed dermatome level L1. Then highest dermatomal level of analgesia was noted. By same response to pin prick the time for two segment regression from highest level was also noted. Time required for regression of level to S2 was taken as total duration of sensory block. Motor blockade was assessed at every minute after giving the drug intrathecally by straight leg raising while lying supine and was graded according to modified bromage scale Bromage 0: patients is able to move hip, knee & ankle, Bromage 1: patients is unable to move hip, but able to move knee & ankle, Bromage 2: patient was unable to move hip & knee but able to move ankle, Bromage 3: patient is unable to move hip, knee & ankle. The time taken for the onset of motor blockade and the duration of motor blockade was noted. The time required for raising of the ankle to the time of injection of drug was taken as duration of motor blockade.

Heart rate, blood pressure & respiratory rate & oxygen saturation were monitored immediately after injection and then after every 5 minutes for first 30 minutes and then every 10 minutes thereafter throughout the surgery and till the complete recovery from block. The anaesthesia record was maintained and changes in heart rate, blood pressure, respiratory rate & SPO_2 were noted. In present study, hypotension was defined as a decrease in systolic blood pressure by 20% from baseline value and was treated with small incremental doses of mephenteramine 6mg and dopamine drip (200mg in 500 ml 0.9% Normal saline) was started if B.P. did not improve even after 3 doses of mephenteramine. Also Bradycardia was defined as heart rate less than 60 beats per minutes and was treated with incremental doses of atropine 0.3 mg. Mainly sedation was studied as the central effects. The time of onset of sedation after injection of drug was noted and the sedation was graded as-Grade 0: fully conscious, Grade I: mild drowsiness, Grade II: A sleep but arousable, Grade III: unarousable with loss of

verbal contact. Patients were observed for perioperative complications like hypotension; bradycardia, nausea and vomiting, shivering, dryness of mouth, urinary retension, and any neurological sequelae till their discharge from the hospital & inadequate block requiring supplementation with general anaesthesia.

3. Observations and results

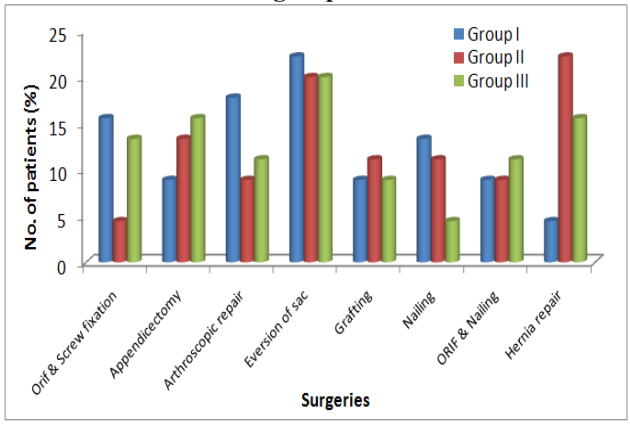
A total of 135 patients who underwent sub umbilical surgeries were enrolled for the study and were randomly allocated into 3 groups of 45 patients each. The demographic profiles of the patients were comparable in all the three groups and difference was statistically not significant, (Table 1).

Table 1: Demographic profile of patients

Parameters	Group I	Group II	Group III	P value
Age (years)	36.02 ± 6.40	34.67 ± 5.33	35.27 ± 4.94	0.517
Weight (kg)	65.09 ± 5.32	63.16 ± 6.77	64.67 ± 6.71	0.314
Height (cm)	162.84 ± 5.54	163.64 ± 5.43	163.8 ± 6.02	0.693

Types of surgeries in all three groups were similar, eversion of sac was the commonest surgery and next common surgeries performed were hernia repair, arthroscopic repair and appendicectomy. Other surgeries being performed were O.R.I.F and screw fixation, nailing, O.R.I.F. and nailing, grafting. All the operative procedures were comparable shown in figure 1.

Figure 1: Comparison of type of surgeries in three groups



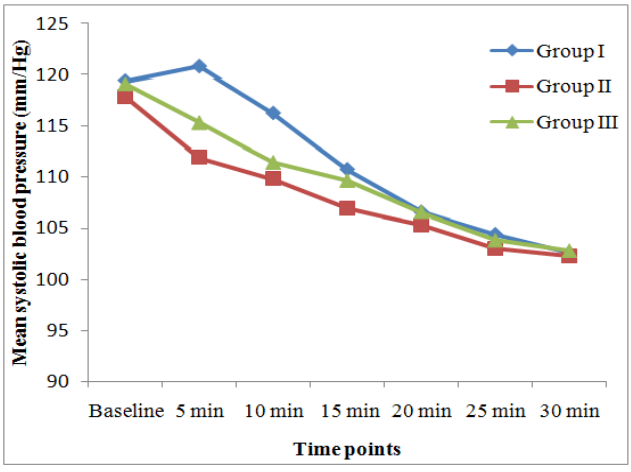
We found no significant effect on onset and quality of sensory block by using different doses of clonidine. In spite of using different and increasing doses of clonidine, time of onset of motor block and grade of motor block were almost similar in between all groups. The duration of sensory and motor block were significantly prolonged in group II and group III as compared to group I. The maximum level reached in group I was T6 in 31.11% patients followed by T8 and T10 in 20% patients. Maximum level reached in group II was T6 in 40% patients followed by T7 and T8 in 17.78% patients and maximum level reached in group III was T6 in 33.33% patients followed by T10 in 22.22% patients and T8 in 20% patients. We used constant volume intrathecally in present series and maximum height being comparable in all three groups. There were no significant differences in maximum level and time to reached maximum level of sensory block in all three groups in spite of using different and increasing doses of clonidine. Time for two segment regression was significantly prolonged in group II and III as compared to group I (Table 2).

Table 2: Summary of results regarding characteristics of subarachnoid (spinal) blockade

Characteristics		Group I	Group II	Group III	P-value
Onset of sensory block (sec.)		38.95 ± 20.94	40.04 ± 19.66	46.89 ± 23.34	0.166
Onset of motor block (sec.)		132.58±56.93	149.11±56.96	148± 58.09	0.314
Quality of sensory block (%)	II	11.11	6.67	2.22	0.239
	III	88.89	93.33	97.78	
Quality of motor block (%)	II	13.33	6.67	2.22	0.128
	III	86.67	93.33	97.78	
Duration of sensory block		354.29±15.39	428.22±18.62	437.31±21.09	0.001
Duration of motor block		247.04±16.34	324.96±33.35	334.87±27.48	0.001
Time to reach max level (min.)		24.16±4.11	22.89±3.52	22.33±3.46	0.061
Time for 2 segment regression		84.76±5.91	117.04±7.23	120.53±8.38	0.001

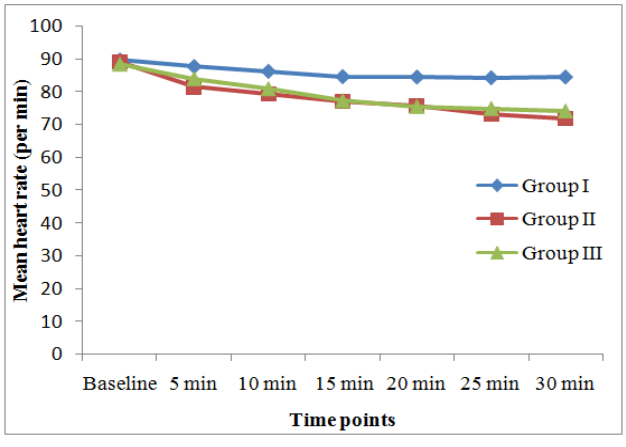
Figure 2 Show the comparison of SBP in three groups. We observed that in group III, 8.89% patients had hypotension and required treatment with injection mephentermine, none of the patients required treatment with dopamine.

Figure 2: Comparison of SBP in three groups



Bradycardia was recorded in two cases (7.5%) in group II and eight (17.78%) patients of group III, the requirement of injection atropine was higher in group III. Thus incidence of bradycardia was increased with increasing doses of clonidine. Figure 3 show the comparison of heart rate in three groups.

Figure 3: Comparison of Heart Rate in three groups



In group I sedation score was nil. In group II 97.78% cases had no sedation score whereas only 2.22% cases had sedation score of 1. Similarly in Group III, 86.67% cases had no sedation score, 2.22% cases had sedation score of 1 whereas 11.11% cases had sedation score of 2. Difference between these groups was statistically significant (p=0.02). Other side effects like nausea and vomiting was reported in 8.89% cases in group III. In 2.22% cases of group II only vomiting was recorded whereas in group I both these symptoms were not reported.

4. Discussion

The present randomized controlled study was undertaken with the combination of isobaric ropivacaine 0.5% and different doses of clonidine (15mcg, 30mcg, 45mcg) consisting of 3 different groups, to find out the optimum dose of clonidine to be added intrathecally for subumbilical surgeries. The demographic data such as age, sex, height and weight being comparable and seems that it has no influence on outcome of the study. Types of surgeries in all three groups were similar and were comparable amongst three groups.

Time of onset of sensory and motor block as well as quality of sensory and degree motor block was clinically and statistically insignificant in between all the three groups by using different and increasing doses of clonidine. This means by increasing dose of clonidine, it did not change the onset and quality of sensory and onset & degree of motor blocks. Our findings correlated with different studies [6,7]. In the present study time required for regression of senory level to S2 was taken as total duration of sensory block. Duration of sensory and motor block was significantly prolonged in group II and group III as compared to group I. By increasing the dose of clonidine intrathecally prolongs the duration of sensory and motor block but increase in duration of sensory and motor block after increasing dose of clonidine from 30 mcg to 45 mcg was comparatively insignificant. The observation of Gonul Sagiroglu *et al*[8] regarding the duration of blocks was not comparable with present study; difference in observation may be due to different amount of doses of ropivacaine used. The current study has supported the finding of De Kock *et al*[6] and Cemile *et al*[7] and confirmed the same efficacy of group II and group III for prolonging the duration of sensory block as compared to group I which had shorter duration of sensory block as compared to other two groups. Whereas findings regarding duration of motor block was comparable with the findings of Sethi *et al*[9] and Wu *et al*[10]. We found no significant differences in maximum level of sensory block and time required to reach maximum level in all three groups in spite of using different and increasing doses of clonidine, this was comparable with various studies[7,8]. The duration of two segment regressions goes on increasing after increasing doses of clonidine but increase was not significant when the dose was increased to 45 mcg from 30 mcg, our finding has supported the finding of Wu *et al*[10].

Blood pressure was recorded at different time intervals 5, 10, 15, 20, 25 and 30 minutes after spinal anaesthesia. The SBP at baseline and fall in BP at 15 min, 20 min, 25 min and 30 min were statistically insignificant in all three groups. However at 5 min and at 10 min SBP was significantly lower in group II than in group I and it was statistically significant in group III as compared to group I and group II. In group I and II fall in blood pressure was statistically significant but it was not clinically significant as it was not considered as

hypotension to treat because the fall was less than 20%. Whereas in group III fall in blood pressure was statistically and clinically significant as it was considered as hypotension to treat because fall was more than 20% and 4 patients (8.88%) required treatment with injection mephentramine. Thus administration of low dose of clonidine 15 mcg and 30 mcg associated with minimal risk of hypotension but addition of 45 mcg clonidine associated with high risk of statistically and clinically significant episodes of hypotension but no patient required dopamine. This findings were comparable to finding stated by various authors [6,7,10-12]. Mean heart rate at baseline were statistically insignificant in all three groups however at other time points heart rate was significantly lower in group II as compared to group I and also heart rate was lower in group III than group I. In group III, 8 (17.7%) patients out of 45 patients required injection atropine for treatment i.e. minimum heart rate reached to value of 53 beats/min. incidence of bradycardia was increased with increasing doses of clonidine. Our findings were correlates with other studies [8,10,12,13].

Respiratory rate and oxygen saturation was recorded at different time intervals in all three groups intraoperatively and there were no statistically significant changes observed as compared to baseline values in all three groups. Respiratory rate and oxygen saturation was normal intraoperatively in all patients [8]. In present study sedation was dose dependant and confirmed efficacy of higher doses of clonidine (45 mcg) for increasing incidence of sedation of patients in subumbilical surgeries. Thus, total number of patients with sedation was increased with increasing clonidine doses, this finding supported the finding of previous work [6,8,13].

None of the patients in group I and II had hypotension but 4 patients in group III had hypotension and required treatment with injection mephentermine as it was clinically significant. None of the patients in group I, 2 patients in group II and 8 patients in group III had bradycardia. Patients with bradycardia required treatment with injection atropine. None of the patients in group I, 1 patient in group II and 4 patients in group III had vomiting. While none of the patients in group I, group II had nausea as compared to group III and 4 patients in group III had nausea. None of the patients in all three groups had urinary retention & supplementation with general anaesthesia[7,13].

4. Conclusion

The present study demonstrated that addition of intrathecal clonidine as an adjuvant to ropivacaine in the dose of 30 mcg (group II) significantly increases the duration of sensory and motor block use intrathecally. This dose of 30 mcg of clonidine have an minimal effect on sedation level, heart rate and mean arterial pressure and oxygen saturation which does not require any significant therapeutic intervention as compared to group III (45 mcg clonidine) patients. Increasing the dose of clonidine from 30 mcg to 45 mcg as an adjuvant to be used intrathecally increases the rate of intraoperative complications like bradycardia hypotension & vomiting. Thus the result of our study show that addition of 30 mcg of clonidine to intrathecal ropivacaine is safe and likely to be as effective as higher doses in prolonging duration of sensory and motor block and having minimum side effects and thus seems to be the optimum dose of clonidne to be used intrathecally.

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