Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 10, 2023

"EFFICACY OF CLONIDINE AS AN ADJUVANT TO ROPIVACAINE IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK"

Type of manuscript- original research article

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ABSTRACT-The purpose of the study was to evaluate the effects of clonidine in combination with ropivacaine on peripheral nerves during brachial plexus block. This study was carried out on 60 (18-60 years) patients undergoing elective upper limb surgery. Patients were randomly divided into two groups of 30 each .Group RN patients received 30ml of 0.5% ropivacaine mixed with 0.5ml normal saline and Group RC patients received 30ml of 0.5% of ropivacaine with 30µg of clonidine in supraclavicular brachial plexus block.The results of this study support the use of adjuvant clonidine with ropivacaine for supraclavicular block anaesthesia, as ropivacaine produces good analgesia and motor blockade in supraclavicular brachial plexus block and the addition of clonidine to ropivacaine increases the effect of analgesia and motor blockade significantly. Addition of 75µg of clonidine to ropivacaine, for brachial plexus block, should be considered for prolonged upper limb surgery and decreasing the post-operative rescue analgesic requirement.

Keywords- brachial plexus block, clonidine, ropivacaine

INTRODUCTION

Upper limb surgeries are mostly performed under regional nerve block such as brachial plexus block. Regional nerve blocks not only provide intraoperative anaesthesia but also extend analgesia in the post-operative period without any systemic side effects[(1)]. Local anaesthetics provide anaesthesia and analgesia by blocking transmission of pain sensation along the nerve fibres. Brachial plexus block offers distinct advantage to patient, anaesthesiologist and surgical faculty over general anaesthesia. The anaesthesia is limited to a restricted portion of the body on which the surgery will be performed leaving all other vital centres unaffected and the physiological impact of anaesthesia on the patient will be less than with general anaesthesia. This consideration is important in high risk patients, but these early advantages can be short lived and limited by the relatively brief duration of action of local anaesthetics.

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The supraclavicular block of the brachial plexus has the reputation of providing most complete and reliable anaesthesia for upper limb surgery. However, the duration of analgesia after single injection nerve blocks may not be sufficient for a comfortable transition to oral analgesics[2]. Sometimes the duration falls short of the total duration of surgery in case of long prolonged surgical procedures resulting in the need to convert the procedure to general anaesthesia.

Bupivacaine, an amide local anaesthetic, is most frequently used local anaesthetic but Ropavacaine has also been successfully tried recently. Ropivacaine is less lipophilic than bupivacaine and is less likely to penetrate large myelinated motor fibres resulting in relatively reduced motor blockade. Ropivacaine is an amide local anaesthetic prepared as "S" enantiomer. It is less cardio toxic, less arrhythmogenic, less toxic to central nervous system than bupivacaine, and is also has intrinsic vasoconstrictor property.

There has always been a search for adjuvants to the local anaesthetics that prolong the duration of block but with lesser adverse effects. α-2 adrenergic receptor agonists have been the focus of interest as adjuvants to LA for their sedative, analgesic, perioperative sympatholytic and cardiovascular stabilizing effects with reduced anaesthetic requirements[3,4].

Clonidine, an imidazoline with selective partial agonist activity at α-2 adrenergic receptors has been used for many years as a centrally acting antihypertensive agent and has also been used as an adjuvant with local anaesthetics. The ability of clonidine to reduce the requirements of traditional anaesthetic and analgesic agents is increasingly being used in the perioperative period. Clonidine when combined with a local anaesthetic, has been found to extend the duration of nerve block[5,6,7].

The purpose of the study was to evaluate the effects of clonidine in combination with ropivacaine on peripheral nerves during brachial plexus block in terms of its onset, duration, degree of sensory, motor blockade and to detect any potential complications.

AIMS AND OBJECTIVES

AIM:

To study-

- Onset of sensory and motor block.
- Duration of motor blockade.

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- Duration of sensory analgesia.
- complications

by using 0.5% Ropivacaine(30 ml) + 0.5ml of normal saline and 0.5% Ropivacaine(30 ml) + 0.5ml(75µg) of Clonidine.

OBJECTIVES: .

To compare –

- Onset time of sensory and motor block with 0.5% Ropivacaine (30ml) + 0.5mlof normal saline and 0.5% Ropivacaine (30ml) + 0.5ml of Clonidine
- Duration of sensory and motor block with
- Duration of post-operative analgesia
- Adverse effect if any.

METHODOLOGY

After the institutional ethics committee approval a prospective, randomized, study has been done in sixty patients of either sex, aged between 18 years and 60 years and of physical status ASA grade 1 and ASA grade 2, undergoing elective forearm and hand surgeries. The patients were randomly divided in 2 groups i.e. group RN and RC as per computerized random number table and each group had 30 patients. Written informed consent taken.

Inclusion criteria:

- Patients aged between 18yrs and 60yrs
- Physical status ASA grade 1 and ASA grade 2
- Scheduled for elective forearm and hand surgeries.

Exclusion Criteria:

- Patient‟s refusal
- Traumatic nerve injury
- Patients with medical complications like severe anemia, severehypovolemia, shock, septicemia.
- Abnormal BT, CT or on anticoagulant therapy
- Local infection at the site of proposed puncture
- Known allergy to local anaesthetic agents or study drugs.

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- If supplementation with IV analgesia or general anaesthesia was required due to inadequate/ partial block, the case was not included in study.

OBSERVATION

A randomized, study was done to know the effect of clonidine as an adjuvant to ropivacaine when compared to plain ropivacaine.

Overall 60 patients were studied in age group of 18-60 years in each group RN and RC the youngest patient In our study was 18 and the oldest was 58 years. The mean age of patient in group RN AND RC were 34.80±14.16 years and 33.27±12.3years respectively, while the median age of patients were 34yrs and 32yrs respectively. Mean weight was 61.23± 9.23kg in group RN and 61.37± 10.6kg in group RC and median weight was 60kg and 58kg respectively. Statistically the difference between two groups was not significant ($p>0.05$) with respect to age and weight.

In group RN, there were 19 (63.3%) males and 11 (36.7%) females and in group RC, there were 23 (76.7%) males and 7(23.3%) females. On applying Chi-Square test, the difference between the group was statistically not significant with respect to sex distribution of patients ($p>0.05$).

There was no statistically significant difference between two groups with respect toASA grading of patients ($p>0.05$).

The minimum and maximum duration of surgery in group RN were 105 minutes and 170 minutes respectively and in group RC 100 minutes and 170 minutes respectively. The mean duration of surgery in group RN and RC were 134.83 (± 19.19) minutes and 130.83(±17.72) minutes respectively. The median duration was 130.00 minutes in both the group. The difference between two groups was statistically not significant with respect to duration of surgery ($p>0.05$).

The mean onset time in C5 dermatome in group was RN 7.33 (±1.54) minutes and group RC was 8.1(±1.53), which was statistically comparable($p>0.05$).In dermatome C6, mean onset time was 7.5(±1.54) minutes for group RN and 8.3 (± 1.62) minutes in group RC. The difference was statistically not significant ($p > 0.05$).The mean onset time in C7 dermatome was 8.3 (± 1.52) minutes in group RN and 8.6 (± 1.45) minutes in group RC. This difference was statistically not significant ($p > 0.05$).In dermatome C8 the mean onset time was 12.67 (± 2.54) in group RN and 13.67 (± 2.25) minutes in group RC. This difference was statistically not significant ($p > 0.05$).The mean onset time in T1 dermatome was 13.33 (± 2.54) minutes in group RN and 12.50 (± 2.40) minutes in group RC. This difference was statistically not significant ($p > 0.05$).

The mean time to achieve grade 1 (modified bromage scale for upper limb) motor block was 10 (± 1.86) minutes in group RN and 10.17 (± 0.91) minutes in group RC. This difference was statistically not significant ($p > 0.05$).The mean time to achieve grade 2 motor block was 14.67 (± 3.2) minutes in group RN and 15.17 (± 1.6) minutes in group RC. This difference was statistically not significant ($p > 0.05$). The mean time to achieve grade 3 motor block was 21.67 (± 3.3) minutes in group RN and 22.67 (± 2.86) minutes in group RC. Again, this difference wasstatistically not significant ($p > 0.05$).

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The mean duration of sensory blockade was 523.0 (± 45.72) minutes in group RN and 724.0 (± 36.728) minutes in group RC. This difference was statistically significant ($p < 0.001$).

The mean duration of motor blockade was 456.0(± 38.111) minutes in group RN and 645.0 (± 42.243) minutes in group RC . This difference was statistically significant. ($p < 0.001$).

The mean duration of analgesia was 552± 58.14 minutes in group RN, while it was 765.03 ± 58.95 minutes in group RC. The difference between the two groups was statistically significant.(p value < 0.001).

The mean sedation scores were 2.13 ± 0.35 and 2.93 ± 0.25 in group RN and group RC respectively . The difference between the two groups was statistically significant (p value < 0.001).

The baseline mean heart rate was 83.33 ± 8.45 bpm in group RN and 80.93± 4.79 bpm in group RC and this difference was statistically not significant.There was fall in mean heart rate compared to baseline from 5 min to 180 minutes in group RN.The lowest heart rate was 67.40 ± 6.08 bpm at 90 th min after giving block.However, this fall in heart rate was within physiological range. . None of the patients developed bradycardia (heart rate< 50 bpm).

In group RC also, there was fall in mean heart rate as compared to baseline from 5 min to 180 minutes . The lowest heart rate was 65.50 ± 2.99 bpm at 60thmin after giving block. However, this fall in heart rate was within physiological range. None of the patients developed bradycardia (heart rate< 50 bpm).The difference between the mean heart rate of two groups wasstatistically not significant at all the respective intervals. ($p > 0.05$)

The mean Spo2 was statistically comparable at all the respective intervals betweeen group RN and RC. ($p > 0.05$).

The difference in baseline mean SBP was statistically not significant . (117.7± 7.41mmHg and 118.00 ± 6.76 mmHg in group RN and group RC respectively) ($p > 0.05$).There was fall in mean SBP compared to baseline from 5 min to 180 minutes in group RN .The lowest SBP was 99.90 ± 6.3 mm of Hg at 90th min after giving block.However, this fall in SBP was within physiological range. None of the patients developed hypotension (SBP< 90 mm of Hg).In group RC also, There was fall in mean SBP compared to baseline from 5 min to 180 minutes .The lowest SBP was 100.47 ± 5.44 mm of Hg at 180min after giving block.However, this fall in SBP was within physiological range and none of the patients developed hypotension (SBP< 90 mm of Hg).There was no statistically significant difference in mean systolic blood pressure of the two groups at all the respective intervals.($p s > 0.05$).

The difference in baseline mean DBP was statistically not significant (75.47 ± 6.78 mmHg and 77.27 ± 5.97 mmHg in group RN and group RC respectively) ($p > 0.05$).In group RN, there was fall in mean DBP compared to baseline from 5 min to 180 minutes .The lowest DBP was 62.20 ± 4.82 mm of Hg at 90min after giving block.However, this fall in DBP was within physiological range.In group RC also, fall in mean DBP was observed as

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compared to baseline from 5 mins to 180 mins. The lowest DBP was 61.80 ± 4.72 mm of Hg at 90th min after giving block.However, this fall in DBP was within physiological range.There was no statistically significant difference in mean diastolic blood pressure between group RN and RC at all the respective intervals .($p > 0.05$)

The difference in mean value of basal VNRS was statistically not significant in both groups (2.2 ± 1 and 2.47 ± 0.97 in group RN and RC respectively) ($p > 0.05$) . At incision, at the end of surgey and at 4th hour also the difference was not statistically significant ($p > 0.05$). At 6, 8, 10 and 12 hour the mean values of VNRS in group RN were 0.37 ± 0.56 ,1.5 ± 0.68 , 3.0 ± 0.53 and 3.4 ± 0.5 respectively , while in group RC the values were 0 , 0.7± 0.53, 2.07 ± 0.58 and 3.0 ± 0.59 respectively .The difference was statistically significant at the respective intervals between thetwo groups. ($p < 0.05$).

DISCUSSION

Supraclavicular approach gives the most effective block for all portions of upper extremity and is carried out at the level of trunks of brachial plexus. The plexus is blocked where it is most compact i.e. at the middle of brachial plexus, resulting in homogeneous spread of anaesthetic drug throughout the plexus with a fast onsetand complete block.

Supraclavicular block with local anaesthetics provide excellent operating conditions with good muscle relaxation, but the duration of analgesia is rarely maintained for more than 4-6 hours even with the long acting local anaesthetics (bupivacaine, ropivacaine and levo-bupivacaine). Continuous infusion of local anaesthetics into brachial plexus sheath requires an infusion pump and has potential for cumulative toxicity and unpredictable variability in absorption. Various studies have shown that addition of adjuncts like Clonidine and Dexmedetomidine in local anaesthetic solution in peripheral nerve blocks prolonged the duration of anaesthesia and analgesia. An ideal combination of local anesthetic and adjuvant should provide adequate intra-operative anesthesia, good extended postoperative analgesia without prolonging motor blockade or producing adverse hemodynamic or respiratory consequences.

Different studies have shown that perineural administration of clonidine is better than subcutaneous or i.m. injections, signifying that the local anaesthetic- enhancing effect of clonidine is possibly mediated at the neuron. This explains the difference in response to different types of nerve blocks probably related to the rate and extent to which the injected anaesthetic solutions penetrate into the nerve. It is highly lipid soluble; easily crosses the blood-brain barrier to interact with alpha-2 adrenergic receptors at both spinal and supraspinal sites within the CNS producing its analgesic effect. These receptors are located on primary afferent terminals(both peripheral and spinal endings),on neurons in superficial lamina of spinal cord and within several brain stem nuclei, implicated in analgesia, supporting the possibility of analgesic action at peripheral, spinal and brainstem. Clonidine possibly enhances or amplifies the sodium channel blockade action of local anaesthetics by opening up the potassium channels resulting in membrane hyperpolarisation, a state in which the cell is unresponsive to excitatory input. Peripheral

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antinocicpetion induced by clonidine has also been related to a 2-adrenoceptor-mediated local release of enkephalin-like substances.

Various authers have used different doses of clonidine from 30µg to 300µg in combination to local anaesthetic, **Bernard et al.,** in their study used 30µg, 90µg & 300µg of clonidine in combination to 400mg of mepivacaine and reported that small dose of clonidine enhances the quality of block with minimum side effects[7]. **Buttner et al.,** compared 120µg & 240µg of clonidine in combination to 400mg of lidocaine and reported dose dependent prolongation of anaesthesia and analgesia with no significant difference in onset of action[8]. **AH El Sayed** studies the same result by adding 150µg of clonidine to 40ml of 0.75% ropivacaine[9]

The two groups were comparable with respect to age, weight, sex, distribution and ASA status, the mean age being 34.80 +- 14.16 years and 33.27 +- 12.30 years in group RN and RC respectively. The mean weights of patients were 61.23+- 9.23 kg in group RN and 61.37+- 10.59 in group RC. The differences in all the demographic parameters are statistically not significant including the gender and ASA grading. In the study of **Patil KN, Singh ND et al**, the demographic data in terms of age (38.10 and 43.33), sex (19:11 and 18:12), weight (57.03 and 59.87), ASA physical status were comparable in both groups. Our study was comparable to this study[10]. **ZanzmeraVatsal et al,** demographic data can also be compared to our study with mean age (35.68 and 36.45), sex (39.21 and 43.17), weight (57.76 and 58.45), and ASA grading (47.13 and 49.11)[11].

In the present study, the onset of sensory block was studied at various dermatomal levels. Sensory block onset time was defined as the time from the completion of injection of study drug to first loss of pinprick sensation in any of dermatome. The mean onset time of sensory block was 7.33 (±2.54) in RN group when compared to RC group which is 8.1 (± 1.53), though there is a slight delay in the onset time of sensory block in group RC but it is not statistically significant.

This has also been seen in the study done by **Patil KN, Singh DM,** who compared two groups of 30 patients each: Group I: 30ml 0.75% ropivacaine + 1ml normal saline. Group II: 30ml of 0.75% ropivacaine + 1µg/kg body weight clonidine. There was similar onset time of sensory block with clonidine[10]. In another study conducted by **Qazi Ehsan Ali et al.,** showed that the onset time ofsensory block in both the groups similar to our study(8.05±3.21 in RN group and 9.1±3.16 in RC group)[12]. **Buttner et al.**, compared 120µg and 240µg of clonidine with ropivacaine and concluded that there was no influence of clonidine on onset time of sensory block [8].The study done by **Usha Bafna et al.,** using 2µg/kg clonidine added to 28ml of 0.5% ropivacaine showed that there is a delay (11.4±3.4 min)in the onset of sensory block as compared to our study showing that with a higher dose, the onset time of the sensory block increased[13]. **Rajmala Jaiswal et al** conducted a study with similar drugs in axillary plexus block, they have used 35ml of ropivacaine 0.5% + 1ml of clonidine (150µg) and found that the mean onset time of

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sensory block was much delayed 26.48±7.88 min when compared to supraclavicular approach[14]. This abnormality might be because of lesser rate and extent of penetration of drug into the nerve fibre in axillary plexus block. This suggests that the onset time of sensory block not only depends on the clonidine added to ropivacaine but also depends on dose and technique used.

In the present study the mean duration of sensory block was 523 (± 45.72) min in group RN and 724(±36.73) min in group RC. There was statistically significant difference among two groups (P< 0.01). This difference is because of clonidine which exerts its local anaesthetic prolonging effect directly on the nerve fibre, as the result of the complex interaction between clonidine and axonal ion channels. Similar increase in duration of sensory block observed in the study conducted by **Patil KN, Singh ND**, who compared 30ml of 0.75%ropivacaine +1µg/kg of clonidine with a control group of 30ml of 0.75%ropivacaine+1ml of normal saline. The duration of sensory block in the group with clonidine was 703.83±42.90 This was comparable to our study though we used similar dose of clonidine and lesser concentration of ropivacaine[10]. In the study of **AH El Saied et al,** they used 40ml of 0.75% ropivacaine plus 150µg of clonidine in group A and 1ml of normal saline added to local anesthetic in group B for axillary brachial plexus block. Duration of sensory block was 489 min in group B and 628 min in group A, This shows even with higher volume of ropivacaine and increased dosage of clonidine in axillary approach of brachial plexus block compared to supraclavicular approach there was significant decrease in duration of sensory block[9].

Similar observations were made by **Shivinder Singh and Amitabh Agarwal,** in their study by comparing 40ml of 0.25% of bupivacaine plus 150µg of clonidine with 40ml of 0.25% of bupivacaine plus 1ml of normal saline in supraclavicular brachial plexus block. They observed no recovery of sensation in both groups upto two hours. From 2-4 hours 28% of patients of the control group had recovery of sensation while none of the patients of the clonide group had recovery of sensation[15]. The difference was statistically significant (p<0.05). Between 4 and 8 hours, 72% of the patients of the control group had recovery of sensation as compared with 44% of patients of clonidine group, the comparision being statistically significant (P < 0.05). In a majority of patients (56%) of the clonidine group, recovery of sensation occurred after 8 hours whereas in the control group, all patients had recovered sensations by 8 hours, and the difference was statistically significant (P<0.05), showing a prolongation of block in the clonidine group.

By this it is evident that clonidine enhances the sensory block duration of local anesthetic. Duration of sensory block depends on dosage of clonidine, volume and concentration of ropivacaine and the technique employed. Hence by increasing clonidine dose the concentration and volume of ropivacaine can be decreased and there by chances of side effects which occur with ropivacaine like nausea, vomiting, headache, fever can be decreased.

In the present study motor block onset time was defined as the time from the completion of injection of study drug to first loss of motor power of any of the four nerves graded

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with modified bromage scale for upper extremity. The mean onset time for motor block was 10 (± 1.86) min in group RN and 10.17 (±0.91) min in group RC. Though the onset of motor block was faster in group RN, but this difference was statistically not significant. Similar results have been observed in the study of **Patil KN and Singh ND,** in which they used 30ml 0.75% ropivacaine + 1µg/kg of clonidine.they observed the mean onset time of motor block was 9.83 min in clonidine group[(10)]. When the drug used in the axillary plexus block by **Rajmala Jaiswal et al,** they observed the mean onset of motor blockade was 37.04±14.18 minutes, the volume and concentration used being 35ml of 0.5% ropivacaine plus 1ml(150µg) of clonidine when compared to our study though they used higher dose of clonidine and higher volume and ropivacaine there is much delayed onset of motor blockade with axillary approach, this may be due to more precise identification of brachial plexus through supraclavicular approach[(14)].

The onset time of motor block therefore depends not only the volume and concentration of ropivacaine, dosage of clonidine but also the approach used for brachial plexus block. By observing various studies it is evident that there is contrary results in onset time of motor block by clonidine in combination with ropivacaine it needs to have further studies of greater number of patients for evaluation.

In our study there is a statistically significant (p value < 0.001) increase in the mean duration of motor blockade in Clonidine group645 (± 42.24) minutes as compared to RN which is 456.0(± 38.11) minutes. This increase in the duration of motor blockade has also been observed by a meta-analysis conducted by **Daniel M. Popping et al.,** on various studies where in Clonidine was added in the doses ranging from 90 to 150 µg to various local anaesthetics (mepivacaine, lidocaine or ropivacaine) in brachial plexus block[(6)]. He found that average duration of motor block was 405 min (range, 122-728) in control group. Clonidine significantly prolonged the duration of block to 546 min in clonidine group. Similar results were observed by **El Saied AH et al**., in their study they compared efficacy of clonidine (150µg) when added to 40ml of 0.75% ropivacaine with 1ml of normal saline added to 40ml of 0.75% ropivacaine in axillary brachial plexus block and observed that clonidine increases the mean duration of motor block (552 min to 721 min)[(9)]. When compared to our study duration of motor block was higher in this study this may be because of higher volume of ropivacaine and higher dose of clonidine they used.

In the present study the difference in mean value of basal VNRS of both the groups was statistically not significant (2.2 ± 1 and 2.47 ± 0.97 in group RN and RC respectively) (p > 0.05) . At time of incision, at the end of surgery and at 4th hour also the difference was statistically not significant (p > 0.05). At 6, 8, 10 and 12 hours the VNRS was significantly low in group RC as compared to group RN. The mean values of VNRS at 6,8,10 and 12 hours in group RN were 0.37 ± 0.56 ,1.5 ± 0.68 , 3.0 ± 0.53 and 3.4 ± 0.5 respectively, while in group RC the values were 0, 0.7± 0.53, 2.07 ± 0.58 and 3.0 ± 0.59 respectively. The difference is statistically significant at the respective Intervals between the two groups (p< 0.05). In the present study, duration of post-operative analgesia was taken till the time patient asked for rescue analgesia (VNRS >3). The mean duration of analgesia was 552.00

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± 58.14 minutes in group RN ,while in group RC it was 765.03 ± 58.95 minutes and the difference was statistically significant between the two groups($p < 0.001$). Thus Clonidine significantly lowered the VNRS pain score and increased the duration of analgesia when added to ropivacaine.

In the study of **Singelyn et al.,** where he compared 8 groups with increasing doses of clonidine(0,0.1,0.2,0.3,0.4,0.5,1 and 1.5%) added to 40ml of 1% mepivacaine and reported that a minimum dose of clonidine(0.1µg/kg) added to mepivacaine prolongs the duration of analgesia and found no added advantage by exceeding the dose to 1.5µg/kg body weight[16]. **Murphy BD et al.,** in their "systemic review on novel analgesic adjuvants for supraclavicular brachial plexus block" observed that addition clonidine (up to 150µg) appears to have significant analgesic benefit in brachial plexus block[17].

A Meta-analysis was conducted by **Daniel M. Popping et al,** on various studies doses ranging from 90 to 150µg in supraclavicular brachial plexus block. He found the duration of postoperative analgesia for group with local anaesthetic alone was 461 min whereas in Clonidine group it was significantly increased to 584 min[6]. Similarly **KN Patil, NoopurDasmit Singh.,** Observed the mean duration of analgesia the group without clonidine(30ml of 0.75%ropivacaine+1ml of NS) was 613.10±51.80 and in the group with clonidine(30ml of 0.75% ropivacaine+ clonidine 1µg/kg of body weight) was 878.33±89.96[10]. When compared to our study though there was slight decrease in duration of motor blockade in this study, there is significant increase in duration of analgesia. It has also been shown in the study of **Zanzmera Vatsai et al.,**in their study duration of analgesia was prolonged with addition of clonidine to ropivacaine[11]. Mean duration of analgesia was 584.17min in the group with 30ml of 0.5% ropivacaine plus 0.6ml of normal saline and 799min in the group with 30ml of 0.5% ropivacaine plus 0.6ml clonidine(90µg) . They suggested that there is no need of using higher doses of clonidine above 90µg as there is no improvement in analgesia with higher doses. When compared to our study in this study with 0.1% increase in clonidine concentration there was significant increase in duration of analgesia.

In the above studies **Murphy et al** observed clonidine has significant beneficial effect upto 150µg and **Zanzmera et al.,** observed no beneficial effect over 90µg hence it require further studies for evaluation[17,11].

The baseline mean heart rate was 83.33 ± 8.45 bpm in group RN and 80.93± 4.79 bpm in group RC and this difference was statistically not significant($p > 0.05$) There was fall in mean heart rate compared to baseline from 5 mins to 180 minutes in group RN .The lowest heart rate was 67.40 ± 6.08 bpm at 90th min after giving block. In group RC also, there was fall in mean heart rate as compared to baseline from 5 mins to 180 minutes .The lowest heart rate was 65.50 ± 2.99 bpm at 60th min. However this fall in heart rate was within physiological range in both the groups. None of the patients developed bradycardia (heart rate< 50 bpm) The difference between the mean heart rate of two groups was statistically not significant at all the respective intervals ($p > 0.05$).

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Similar results were found by **KN Patil, Noopur Dasmith Singh**, mean heart rate in control group was 76.77 ±8.76 and
76.10 ±8.91 in clonidine group. This difference was statistically not significant[10].

Sidharth Sraban Routray et al. observed the mean heart rate in the group with ropivacaine alone was 79.2 ±14.4, and in the group with clonidine was 80.4 ±13.8[18]. this difference was also statistically not significant. Similarly in the study by **ShivinderSingh and Amitabh aggarwal.,** they observed the perioperative and post-operative heart rate was variable at each time interval and was also lower in the clonidine group in comparision with the control group; however, the difference was also not significant ($p>0.05$)[15]. In an other study conducted by **Zazmera Vatsal et al.,** observed bradycardia in 2 patient out of 30 patients who reseived 90µg of clonidine with 30ml of 0.5% ropivacaine, this may be because of higher doses of clonidine causes presynaptic mediated inhibition of norepinephrine release at the neuroreceptor junction and partly by vagomimitic effect[11].

Most studies used between 100-150µg of clonidine, with higher doses showing side effects including sedation, bradycardia and hypotension. In this study we tried to evaluate the results by adding 75µg of clonidine to lesser volume (30ml) of ropivacaine. Haemodynamic effects of clonidine after neuraxial or systemic administration begin within 30 min, reach maximum within 1-2 h, and last approximately 6-8 hrs after a single injection. The difference in baseline mean systolic blood pressures of two groups was statistically not significant (117.7± 7.41mmHg and 118.00 ± 6.76 mmHg in group RN and group RC respectively) p (>0.05). There was fall in mean SBP compared to baseline from 5 mins to 180 minutes in group RN .The lowest SBP was 99.90 ± 6.3 mm of Hg at 90th min after giving block. However, this fall in SBP was within physiological range. None of the patients developed hypotension (SBP< 90 mm of Hg) In group RC also, there was fall in mean SBP compared to baseline from 5 min to 180 minutes .The lowest SBP was 100.40 ±.5.24 mm of Hg at 150th min after giving block. However, this fall in SBP was within physiological range and none of the patients developed hypotension (SBP< 90 mm of Hg) There was no statistically significant difference in mean systolic blood pressure of the two groups at all respective intervals.($p > 0.05$). Similar results observed by **KN Patil, Noopur Dasmith Sing,** In their study baseline mean systolic blood pressure in control group was 120.67±9.32 and in the clonidine group was 120.87±9.3 and they observed no significant difference in mean SBP between the groups at various time intervals[10].

Sidharth Sraban Routray et al., observed mean systolic blood pressure in the group without clonidine was 126.0± 8.9 and in the group with clonidine was 124.4±9.1, there was also no statistically significant difference between the groups during intra operative and post operative period[18].In the periphery, clonidine action on presynaptic ά2 – adrenoceptors at sympathetic terminals reduce the release of norepinephrine causing vasorelaxation and reduced chronotropic drive. By moderate doses clonidine these brainstem and peripheral effects of ά2 - adrenoceptor stimulation are counterbalanced by direct peripheral vasoconstriction through its action on ά1- adrenoceptors from circulating

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 10, 2023

concentrations of Clonidine.The difference in baseline mean diastolic blood pressures of two groups was statistically not significant (75.47 ± 6.78 mmHg and 77.27 ± 5.97 mmHg in group RN and group RC respectively , p >0.05). In group RN, there was fall in mean DBP compared to baseline from 5 min to 180 minutes .The lowest DBP was 62.07 ± 4.69 mm of Hg at 150th min after giving block. However, this fall in DBP was within physiological range. In group RC also, fall in mean DBP was observed as compared to baseline from 5 mins to 180 mins. The lowest DBP was 61.80 ± 4.72 mm of Hg at 90th min after giving block. However, this fall in DBP was within physiological range. There was no statistically significant difference in mean diastolic blood pressure between group RN and RC at all the respective intervals .(p >0.05).

KN Patil, Noopur Dasmith Singh.,found mean diastolic blood pressure in control group was 76.47±6.07 and in the clonidine group was 77.63±6.85 and there was no significant difference in mean DBP they observed between the groups at various time interval[(10)]. Similarly **Sidharth Saraban Routry et al.** observed no significant difference in base line and perioperative mean diastolic blood pressure in both the groups[(18)].In the study of **Popping DM et al** baseline haemodynamic parameters were comparable in both groups. Systolic and diastolic blood pressure were found to be significantly lower than baseline from 30 to 120 min in Group with clonidine as compared with Group without clonidine (P<0.001)[(6)]. No treatment was required for this fall in blood pressure. The haemodynamic parameters were comparable at the end of 180 min. **Sivender Singh and Amitabh Aggarwal,** used 150µg of clonidine in combination to 40 ml of 0.25%bupivacaine and observed the maximum fall in systolic and diastolic blood pressure in the clonidine group at 60min[(15)]. however this was observed at 10min for systolic and 30min fir diastolic blood pressure respectively. The pre- and post-operative blood pressure was variable at each time interval in both groups and was statistically insignificant.

In the present study in group RC observed high sedation scores(2.93 ±0.25) than in group RN (2.13 ±0.35). Sedation was assessed by MODIFIED RAMSAY SEDATION SCORE. It may be due to systemic absorption of clonidine and produce sedation by inhibition of substance P release in nociceptive pathway at the level of the dorsal root neuron and by activation of α2 adrenoceptors in locus coeruleus. In the study conducted by **Zanzmera et al.,** where she used 90µg of clonidine with 30ml of 0.5% ropivacaine in comparision to 0.6ml of normal saline with 30ml of 0.5% ropivacaine, they observed that there was statistically significant increase of sedation scores(2) in clonidine group compared to normal saline group (1)[(11)]. In other study conducted by **Qazi Ehsan Ali et al.,**using75µg of clonidine with 0.5% 30ml of ropivacaine, 4 out of 30 patients had post operative sedation but this difference was not statistically significant[(12)]. Similar results observed in the study conducted by **Usha Bafna et al.,** where they used clonidine 2µg/kg body weight with 28ml of 0.5% ropivacaine, there were 4 patients complained mild sedation[(13)]. In study by **Patil et al.,** they used 1µg/kg body weight of clonidine with 0.75% of ropivacaine and they observed no sedation[(10)]. By comparing above studies observed that there is significant increase in sedation with 75 µg or above clonidine with ropivacaine in supraclavicular brachial plexus block. In other study done by **Shingelyn et al** using doses of clonidine ranging from 0.1µg to 1.5µg/kg body weight with 40ml of 1%

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 10, 2023

mepivacaine, there was no increase in sedation scores even with higher doses (1.5µg)[16]. In other study conducted by **Chakraborty et al,** there was increased sedation scores were observed with 30µg of clonidine where it is added to 25ml of 0.5% bupivacaine in supraclavicular brachial plexus block[19].

Hence the sedation caused by clonidine may be not only depends on dosage of clonidine but may also depends on the local anaesthetic used, this requires further studies for evaluation.

Most of the studies conducted using clonidine in regional anaesthesia did not report any adverse effects. Similarly in the present study, no side effects were observed in both the clonidine and control groups throughout the study period. **Singh S et al** compared the effects of Clonidine (150µg) added to bupivacaine with bupivacaine alone in supraclavicular brachial plexus block[15]. No side-effects were observed. However studies by **Buttner et al.,** and **Bernard et al.,** reported the incidence hypotension and bradycardia with the use of clonidine[8,7]. **Chakraborty et al.,**reported that clonidine in combination with bupivacaine dose not produce any clinically important adverse reaction other than sedation[19]. A meta analysis of randomized trails by **Popping DM et al** concluded that clonidine added to local anaesthetic prolongs the duration of analgesia and motor block with increased risk of hypotension, bradycardia and sedation[6]. This may be because of higher dose clonidine they used or faulty technique they employed.

Clonidine has been used as an adjuvant to local anaesthetic in peripheral nerve block in different doses ranging from 30µg to 300µg. Many studies concluded that there was no beneficial effect with more than 90µg of clonidine, and increased risk of side effects like bradycardia hypotension and sedation. So in the present study we used Clonidine (75µg). A volume of 30 ml of

- % ropivacaine was taken as this volume was associated with a more complete spread for brachial plexus block without any risk of local related systemic toxicity.

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