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# The effect of clonidine on peri-operative neuromuscular blockade and functional recovery: a randomized placebo-controlled trial

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## ABSTRACT

**Background:** Alpha-2-agonists are as used adjunct for anaesthesia. We conducted this study with the aim to determine whether the addition of clonidine, an α-2-agonist, decreases the time to recovery from neuromuscular blockade caused by non-depolarising muscle relaxant. Secondary objectives were to know whether clonidine as an adjuvant improves hemodynamic stability, decreases stress hyperglycaemia, pain and time to discharge from Post-Anaesthesia Care Unit (PACU). **Methods:** This placebo-controlled clinical trial, enrolled 64 patients into clonidine (n = 32) or placebo (saline) group (n = 32). Study drug was given 1.5 mcg/kg IV bolus at the time of induction followed by infusion (1.5 mcg/kg/hour) intra-operatively. Extubation was started when train-of-four (TOF) count was ≥ 2. Primary outcome measure was time to achieve TOF ratio of ≥ 70% and ≥ 90%, assessed at 5, 15, 30- and 60-minintervals following extubation. **Results:** 2 patients in each group were excluded due to intra-operative requirement of additional supportive medications, hence in each group 30 were analysed. Significant difference was observed between clonidine and placebo groups in terms of time to achieve TOF ratio ≥ 70% and ≥ 90%, stress hyperglycemia, hemodynamic and pain profile, no statistical difference in the Ramsey sedation score and modified Aldrete score between groups. Patients given clonidine required repeat doses of non-depolarising muscle relaxant at longer intervals, with decrease in total amount administered. Clonidine group had a median time to achieve TOF ratio ≥ 70% at 15 min compared to 60 min in placebo group. **Conclusion:** Clonidine hastens the recovery from neuromuscular block with reduced stress hyperglycaemia and post-operative pain, along with unaffected Ramsey sedation score and modified Aldrete score.

**Key words:** Clonidine and Neuromuscular Recovery, Clonidine and Functional recovery

## INTRODUCTION

In today's era, elective surgeries are planned with early discharge from the hospital. Early return to ambulation could be brought about by such peri-operative anaesthesia that causes faster recovery from neuromuscular blockade, along with adequate analgesia, smooth extubation with minimal stress responses, and decreased incidence of adverse effects[1].

Many anaesthetic adjuncts are often used as a premedication to decrease the dose of anaesthetic agent for faster recovery[2,3]. Alpha-2-agonists are commonly utilized adjuvant because of their analgesic,[4,5] anxiolytic, sedative and anesthetic sparing properties[6–8] along with their ability to blunt the hemodynamic responses to peri-operative stress[9].



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According to Murphy and colleague the neostigmine reversal for Non-Depolarising Neuromuscular Blockade (NDNMB) required more than 10 minutes to recover from NM block[10], thus critical respiratory events were significantly more common postoperatively if the TOFR was < 0.7 in the recovery room[11]. It was also noted by some authors if repeated boluses or an infusion of NDNMBD had been given the incidence of postoperative residual NMB was greater for shorter surgical procedures[12–14].

Therefore, to minimize the repeat boluses of NDNMBDs, we have designed this study with the hypothesis that clonidine as an adjuvant enhanced the neuromuscular block thus reduced boluses were required to provide neuromuscular relaxation. To validate this hypothesis the present study was conducted in a cohort of Indian population to evaluate the time to achieve TOFR) ≥ 70% (as surrogate indicator of adequate reversal[15], also TOFR ≥ 90% which is considered as end point to achieve complete neuromuscular recovery[16,17].

## MATERIALS AND METHODS

### Study Design, Setting and Participants

The study was designed as a randomized, placebo-controlled, double blinded trial conducted as a part of the postgraduate program in the Department of Anesthesiology, Jawaharlal Nehru Medical College, Aligarh Muslim University, India, which is a tertiary care referral centre. The trial was approved by the Institutional Ethics Committee, faculty of medicine, AMU, India.

The study included patients aged 18–60 years, ASA grade I-II, Mallampati Grade I & II, planned for elective surgery which had an expected duration of surgery < 2 hours. After a thorough pre-anesthetic examination, the clearance for surgery was taken and written informed consent was obtained. Exclusion criteria included patients with major cardiovascular diseases such as coronary artery disease and previous MI, severe or uncontrolled hypertension, Hypotensive patient, severe asthma, COPD, cor pulmonale, neuro-muscular disorder, major hepatic or renal disease, anticipated difficult intubation, diabetes mellitus, history of alcohol or drug abuse, history suggestive of hiatus hernia or GERD, history of allergy to the study medication, previous or current psychiatric illness and morbid obesity.

### Randomization and Blinding

The enrolled patients were randomized into one of the two assigned groups using chit-in-the-box method, and allocation of cases into one group or other was done by an ancillary staff member who was independent from the study team and not involved in the direct care of the patients. Study personnel and patients were unaware of the group assignments for the duration of the study. Double-blinding was ensured by having another nursing staff for preparing and coding of the drug syringes and vials with time, date of preparation and patient identification number. For the placebo group, injections of normal saline were prepared in a manner identical to the active drug preparation. Other investigators, blinded of actual drug composition, administered the drugs and recorded the data. A separate care provider was responsible for the patient care and management. Allocation data was kept concealed from the investigators till the completion of the trial.

### Study Groups

There were only two groups, the clonidine group: Group C and placebo (saline) group: Group S. The study group was given clonidine as an intravenous (IV) bolus in a dose of 1.5 mcg/kg at the time of induction followed by clonidine IV infusion at a rate of 0.5 mcg/kg/hour until extubation. Placebo group was given 0.9% normal saline (N.S.) first as an IV bolus and then as an IV infusion in a manner similar to the study group. Identification of drug group or saline group was not feasible by any of the care providers due the transparent watery physical property of the either group.

### Clinical and Biochemical Procedures

Baseline clinical parameters were assessed prior to surgery. Patients were given oral alprazolam 0.5 mg night prior to surgery. In the operating room, patients were injected with dexamethasone 0.15 mg/kg, midazolam 0.03 mg/kg, tramadol 2 mg/kg and the study drug or placebo saline according to the group allocation as a bolus dose. Patients were induced with propofol at 2 mg/kg in titrated dose. After muscle relaxation with intravenous succinylcholine (1.5 mg/kg), direct laryngoscopy and endotracheal intubation with appropriately sized, cuffed endotracheal tube was done. Subsequently, patients were maintained at 60% $N_2O$ in oxygen along with intravenous vecuronium (0.08 mg/Kg) and isoflurane (0.4–0.6%) intermittently on volume-controlled ventilation mode. The study drug or saline was then administered as an infusion according to the group allocation. Close non-invasive monitoring for vitals and charting was done throughout the surgical procedure and the post-operative period until discharge from PACU.

Twitch recording was done during the perioperative period through Train of Four (TOF) watch to assess the neuromuscular transmission objectively in terms of blockade and recovery[17]. TOF-watch was set in the patients' hand at adductor pollicis muscle. The recording was started from end of injection of vecuronium to all twitch suppression, documented as the onset time of action of relaxant. During intra-operative period to maintain the sustained Neuromuscular Blockade (NMB) the repeat dose of vecuronium was given on getting the two twitches

in TOF watch, at which point 25% of an initial bolus dose of muscle relaxant was repeated. At the end of the procedure the study drug or saline infusion was stopped and at TOF count ≥ 2, the endotracheal tube was replaced with Air-Q intubating LMA simultaneously the residual block was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg IV. Thereafter, neuromuscular recovery was assessed using TOF-watch at intervals of 5, 15, 30 and 60 minutes. The time from the administration of reversal agent till the attainment of TOFR ≥ 0.7 and ≥ 0.9 was recorded. The LMA was removed by the patient himself. Systolic, diastolic and mean arterial blood pressures (SBP, DBP and MAP), HR, rate pressure product (RPP) and modified Aldrete score of discharge from PACU were recorded at pre-defined intervals following extubation. Hypotension (decline of SBP > 30 mm Hg from baseline) was corrected with IV fluids and small doses of mephentermine 6 mg IV as and when required. Symptomatic bradycardia was corrected with atropine 0.5 mg IV. In PACU, any untoward event such as coughing, pain, nausea and vomiting were noted. Sedation was evaluated on 6-point Ramsay Sedation Score[18] following extubation at intervals of 5, 15, 30 and 60 minutes. After one hour of stay in the PACU, they were assessed by Modified Aldrete Score[19] for discharge. Capillary blood glucose was assessed: just prior to induction, prior to extubation and following extubation, to assess the effect of study drug on stress hyperglycaemia. Rate pressure product[20], also known as the cardiovascular product, was calculated to determine the effect of the drug on myocardial oxygen demand. No changes to the trial methodology were done after the commencement of the trial.

### Sample Size

Sample size was calculated for the primary outcome variable with appropriate power analysis considering a two-sided alpha of 0.05and an effect size of 0.8. We estimated that 28 patients in each group would yield a minimum statistical power of more than 80%. To account for possible attrition or dropout, 4 additional patients were planned to be included in each group, making the final sample size 64. Our sample allocation ratio was 1.

## STATISTICAL ANALYSIS

Data analysis on completion of the trial was done by an independent investigator, who was not involved in the care of the enrolled patients. Analysis was conducted using an intent-to-treat approach using GraphPad Prism 7. The Time to TOF ratio ≥ 70% & 90%, which was the primary outcome measure, was treated as a categorical variable since TOF could only be recorded at certain pre-defined intervals, which resulted in discrete values. Accordingly, its comparison between active drug and placebo group was done using independent samples Mann Whitney U Test. The continuous variables such as HR, SBP, DBP, MAP and RPP were calculated using Shapiro Wilk test, and other inter-group comparison was done by independent samples t-test, a P value of less than 0.05 was considered as statistically significant.

## RESULTS

Patients were enrolled from November 2014 to October 2016. The trial was stopped when an adequate number of patients had been included. The overview flowchart of the entire clinical trial is presented as per CONSORT flow diagram of the study (Figure 1).

## STUDY SUBJECTS

410 patients were assessed for eligibility during the study period and 346 were excluded due to not meeting the inclusion criteria. Of the 64 patients who were enrolled, 32 were assigned to intraoperative clonidine group and 32 to the placebo group. All enrolled patients received the allocated intervention. No patients were lost to follow up since patients were admitted to the same hospital post-operatively and discharged only after fulfilling the discharge criteria of the day case surgery. However, 2 patients in each group developed complications and had to be given additional medications, and hence they were excluded from the analysis.

Of the 60 patients whose data was analysed, mean age was 35 years (range 32 to 38 years), and 31 patients (51.7%) were male. The most common surgery performed was laparoscopic cholecystectomy, which was carried out in40 cases and remaining 20 patients were undergone lumbar discectomy at L4-5 or L3-4. Comparison of the baseline clinical and demographic data between the clonidine and control groups showed no statistical difference (p > 0.05) in terms of age, weight, heart rate, blood pressure and calculated rate pressure product (Table 1). In each of the two groups, 26 patients were in American Society of Anesthesiologist class I while 4 were class II, no significant difference was found in gender composition of the two groups (M:F ratio in clonidine vs control, 15:5 vs. 16:4).

### Primary Outcome

Time taken to achieve a ratio of ≥ 70% of train-of-four (TOF), was found to be lower in the clonidine group as compared to placebo (Table 2). The difference was highly statistically significant as per Mann-Whitney U test (U value = 187.5, P value = 0.001). Median time to attain (TOF) ratio ≥ 70% was 15 minutes in clonidine group and 60 minutes in the placebo group. A greater proportion of people achieved TOF ratio ≥ 70% in clonidine group compared to placebo group at

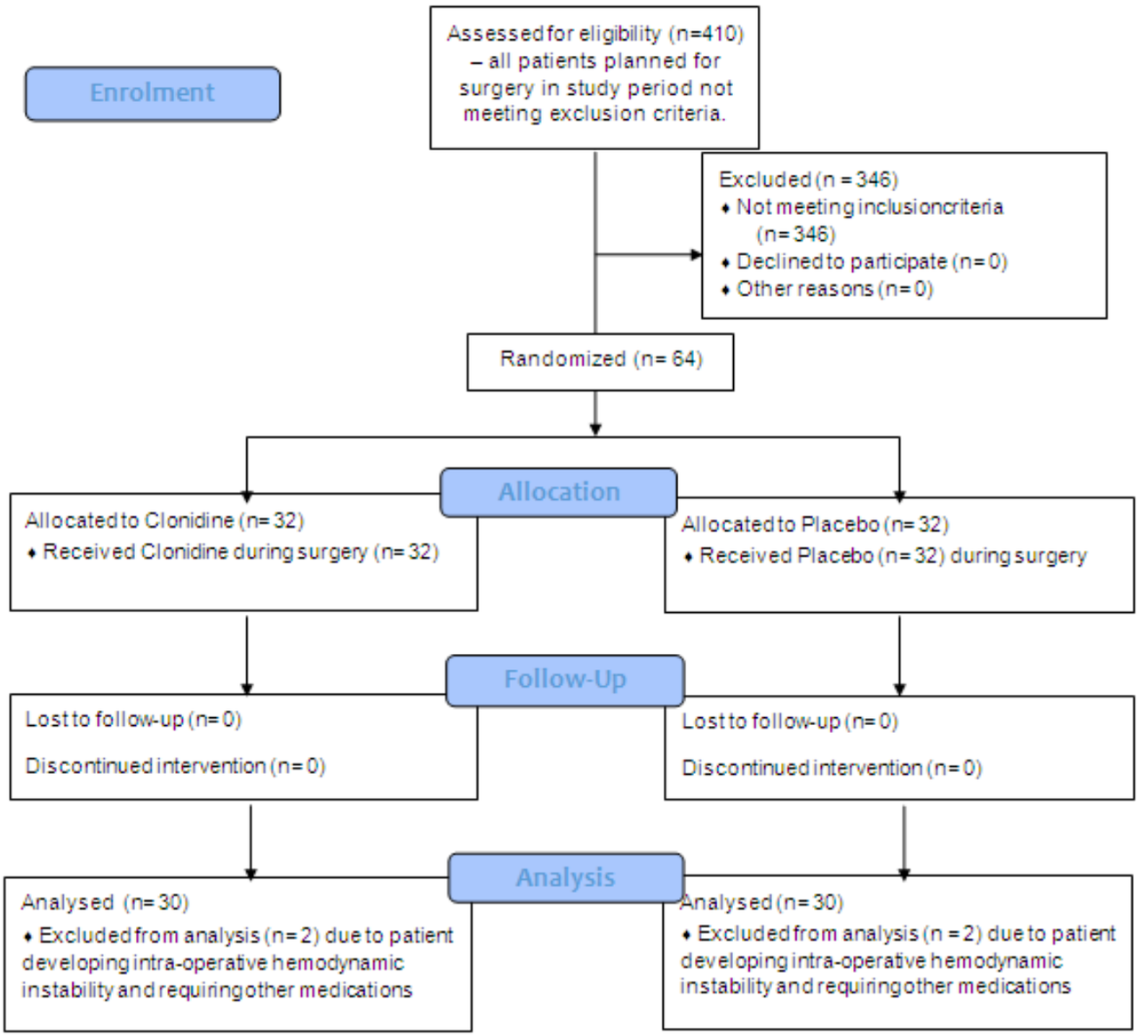


**Figure 1.** CONSORT flow diagram of study.

**Table 1: Baseline demographic and clinical characteristics of two groups**

| Baseline Parameters | Clonidine (mean ± SD) | Placebo (mean ± SD) | 95% CI | P value |
|---|---|---|---|---|
| Age | 35.67 ± 11.56 | 34.67 ± 12.57 | –5.24 to 7.24 | 0.75 |
| Weight (kg) | 55.30 ± 13.26 | 57.43 ± 11.62 | –8.58 to 4.31 | 0.51 |
| Base line HR(beats/min) | 78.47 ± 11.75 | 80.17 ± 6.92 | –6.68 to 2.28 | 0.50 |
| Systolic BP (mmHg) | 123.97 ± 12.49 | 122.67 ± 13.03 | –5.29 to 7.89 | 0.69 |
| Diastolic BP (mmHg) | 78.97 ± 9.15 | 77.70 ± 7.19 | –2.99 to 5.52 | 0.55 |
| Rate Pressure Product (RPP) | 9705.8 ± 1665.3 | 9824.4 ± 1248.2 | –879.2 to 641.9 | 0.76 |

SD is standard deviation; CI, confidence interval of the difference; $p > 0.05$ is not significant statistically

| Table 2: Time to achieve specified TOF ratio amongst the two groups | | | | | | |
|---|---|---|---|---|---|---|
| Parameters | Proportion of patients with TOF ratio ≥ 70% | | | Proportion of patients with TOF ratio ≥ 90% | | |
| | Clonidine | Placebo | 95% CI (P value) | Clonidine | Placebo | 95% CI (P Value) |
| At the time of replacement of ETT with Air-Q LMA | 0% | 0% | 0 (0) | 0% | 0% | 0 (0) |
| 5 minutes post extubation | 26.7% | 3.3% | 5.07 to 41.3 (0.012)* | 3% | 0% | –8.6 to 16.1 (0.34) |
| 15 minutes post extubation | 70.0% | 20.0% | 25.1 to 66.9 (0.001)* | 43.3% | 6.67% | 15.0 to54.8 (0.0011) |
| 30 minutes post-extubation | 86.7% | 46.7% | 16.3 to 58.3 (0.0011)* | 66.7% | 23.3% | 18.2 to 61.5 (< 0.001) |
| 60 minutes post-extubation | 100% | 93.3% | –5.68 to 21.3 (0.154) | 100% | 93.3% | –5.68 to 21.3 (0.154) |

TOF, train-of-four; CI, confidence interval of the difference; * p < 0.05: statistically significant

5 minutes (95% CI = 5.07 to 41.3, P-value = 0.012), 15 minutes (95% CI = 25.1 to 66.9, P-value = 0.001) and 30 minutes (95% CI = 16.3 to 58.3, P-value = 0.001).

### Secondary Outcome Measures

In the 60 patients analysed, heart rate (HR) of all remained above the bradycardia threshold during the entire duration of surgery. Cases administered clonidine had lower HR and Mean Arterial Pressure (MAP). We found the difference in HR to be statistically significant only up till 5 minutes post-extubation while the difference in the MAP was significant only at 10 minutes, 45 minutes and 60 minutes and 60 minutes post-extubation (Table 3). We also found no difference in clonidine group in their values of SBP 15 minutes prior to extubation and 1-minute post-extubation (95% CI = –12.5 to 1.51, P-value = 0.120), while a statistically significant difference in placebo group in the same parameters was present (95% CI = –21.9 to –0.94, P-value = 0.034). At all times post-extubation, the calculated rate pressure product was significantly lower in clonidine group as compared to the placebo, indicating a lower myocardial oxygen demand in patients given clonidine.

As assessed using Mann Whitney U test, patient-provided score on Numerical Rating Scale for pain was significantly lower in the clonidine group than in the placebo group at 5 minutes (P < 0.001), 15 minutes (P < 0.001), 30 minutes (P < 0.001) and 60 minutes post-extubation (P = 0.002), indicating a better pain profile in cases given clonidine. However, no such difference at any of above time intervals was found with regards to Ramsey Sedation Score (Table 4). We also found no statistically significant difference in the Modified Aldrete score of the two groups at 1-hour post-extubation.

Both the clonidine and the placebo groups had comparable blood sugar levels prior to induction and prior to extubation. The levels of capillary blood glucose rose in both groups post-extubation. However, the mean blood glucose post-extubation was significantly lower in the clonidine group (118.87 ± 16.04) than in placebo (139.20 ± 34.79). The difference was highly significant (95% CI = –34.33 to –6.33, P-value = 0.0052), indicating the lower stress hyperglycemia in patients administered clonidine (Table 5).

### Exploratory Analysis

Time to achieve TOF ratio ≥90% was also determined and found to be significantly lower in the clonidine group as compared to the placebo group at 15 minutes (95% CI = 15.0 to 54.8, P value = 0.0011) and at 30 minutes (95% CI = 18.2 to 61.5, P value = 0.001)

## DISCUSSION

In this trial, we evaluated the effect of clonidine on functional recovery following intra-operative neuromuscular blockade. In our study, both the clonidine and placebo groups had a similar intensity of clinical effect of vecuronium when they were extubated. This was assessed by the TOF count ≥ 2 when extubation was done. To find out the adequate NM recovery we have taken two parameters the TOFR 0.7 and 0.9. At ≥ 70%, one can able, to protect the airway after tracheal extubation[15] TOFR ≥ 90% is indicator of complete neuromuscular recovery[16,17]. We found, recovery of NDNM blockade was faster in group C (Table 2) than group S. However, we found no difference (P value > 0.05) in the level of sedation and time to discharge in two groups post-extubation (Table 4).

We found a significant reduction in rate-pressure-product and thereby myocardial oxygen demand in patients given clonidine at all recorded times post-extubation (Table 3). Clonidine was also found to improve the peri-operative pain profile[21]. Clonidine attenuates the hemodynamic stress responses encountered during the peri-operative period[22].

Pharmacokinetic interaction of clonidine and nondepolarizing muscle relaxants is not very clear, and conflicting reports are available in the literature. It was found that after oral clonidine administration, the vecuronium-induced muscle

**Table 3: Effect of clonidine on Hemodynamics**

| Parameters | Heart Rate | | | MAP Pressure | | | Rate Pressure Product | | |
|---|---|---|---|---|---|---|---|---|---|
| | Clonidine (mean ± SD) | Placebo (mean ± SD) | 95% CI (P Value) | Clonidine (mean ± SD) | Placebo (mean ± SD) | 95% CI (P Value) | Clonidine (mean ± SD) | Placebo (mean ± SD) | 95% CI (P Value) |
| Pre-extubation | 78.47 ± 11.75 | 87.70 ± 18.02 | 17.10 to -1.37 (0.02)* | 91.43 ± 14.40 | 97.27 ± 15.37 | -13.53 to 0.86 (0.135) | 10172 ± 2008.1 | 11416 ± 3225.0 | –2632 to 144.67 (0.078) |
| 1 min post-extubation | 89.13 ± 16.05 | 97.17 ± 17.72 | –16.77 to 0.70 (0.08) | 91.40 ± 16.56 | 99.33 ± 18.51 | –17.01 to 1.14 (0.085) | 10916 ± 2462.9 | 13166 ± 3763.5 | –3894 to –606.8 (0.008)* |
| 3 min post-extubation | 80.53 ± 16.08 | 91.07 ± 18.08 | –19.38 to –1.69 (0.02)* | 86.83 ± 9.82 | 91.83 ± 12.93 | –10.93 to 0.93 (0.097) | 9473.1 ± 2096.4 | 11758 ± 3956.6 | –3921 to –648.8 (0.007)* |
| 5 min post-extubation | 78.73 ± 16.50 | 88.40 ± 18.37 | –18.69 to –0.64 (0.04)* | 86.63 ± 8.88 | 8.88 ± 14.82 | –12.32 to 0.32 (0.062) | 9150.1 ± 1913.9 | 10955 ± 3032.4 | –3116 to –495.3 (0.008)* |
| 10 min post-extubation | 77.83 ± 14.85 | 83.57 ± 14.98 | –13.44 to 1.97 (0.14) | 84.57 ± 9.70 | 91.57 ± 12.01 | –12.64 to –1.36 (0.016)* | 8827.8 ± 1573.8 | 10282 ± 2733.5 | –2607 to –301 (0.014)* |
| 15 minutes post-extubation | 76.53 ± 16.70 | 82.67 ± 15.43 | –14.44 to 2.18 (0.14) | 86.00 ± 11.11 | 88.47 ± 14.41 | –9.12 to 4.18 (0.461) | 8823.73 ± 1919.8 | 10186 ± 2720.5 | –2579 to –145.81 (0.029)* |
| 30 minutes post-extubation | 74.67 ± 14.85 | 80.00 ± 14.38 | –12.89 to 2.22 (0.16) | 85.57 ± 9.21 | 88.43 ± 11.84 | –8.35 to 2.62 (0.299) | 8542.5 ± 1433.8 | 9748.2± 2415.4 | –2232 to –179.16 (0.022)* |
| 45 minutes Post-extubation | 75.17 ± 12.16 | 78.13 ± 11.81 | –9.16 to 3.23 (0.34) | 84.00 ± 10.25 | 90.73 ± 10.95 | –12.22 to –1.25 (0.017)* | 8490.1 ± 1302.6 | 9510.3 ± 1924.4 | –1869 to –170.91 (0.019)* |
| 60 minutes post-extubation | 74.87 ± 12.97 | 77.17 ± 11.79 | –8.71 to 4.11 (0.47) | 83.30 ± 9.69 | 88.67 ± 10.80 | –10.67 to –0.06 (0.047)* | 8467.8 ± 1379.9 | 9262.9 ± 1953.6 | –1669 to 78.98 (0.074) |

TOF, train-of-four; CI, confidence interval of the difference

**Table 4: Effect of clonidine on pain profile and Sedation**

| Scores | Numerical Pain Rating Score | | | Ramsey Sedation Score | | |
|---|---|---|---|---|---|---|
| | Clonidine (Median, IQR) | Placebo (Median, IQR) | P value (U value) | Clonidine (Median, IQR) | Placebo (Median, IQR) | P Value (U Value) |
| 5 minutes post-extubation | 1, 2 | 2, 1 | < 0.001 (158) | 2, 1 | 2, 1.25 | 0.33 (384) |
| 15 minutes post-extubation | 1, 1 | 3, 1 | < 0.001 (157) | 2, 0 | 2, 1 | 0.30 (380) |
| 30 minutes post-extubation | 1, 1 | 2, 1 | < 0.001 (186.5) | 2, 1 | 2, 1 | 0.38 (390) |
| 60 minutes post-extubation | 1, 1 | 2 ,2 | 0.002 (239) | 2, 1 | 1, 1 | 0.12 (345) |

P value < 0.05 indicates insignificant difference statistically between two groups; IQR, Inter-Quartile Range; U value, Mann-Whitney U test;

**Table 5: Effect of Clonidine on blood glucose and stress hyperglycemia**

| | Clonidine (mean ± SD) | Placebo (mean ± SD) | 95% Confidence Interval | P value |
|---|---|---|---|---|
| Pre-Induction | 92.57 ± 10.57 | 102.17 ± 43.35 | –25.91 to 6.71 | 0.24 |
| Pre-extubation | 115.53 ± 18.99 | 125.53 ± 27.31 | –22.16 to 2.16 | 0.11 |
| Post-extubation | 118.87 ± 16.04 | 139.20 ± 34.79 | –34.33 to –6.33 | 0.0052* |

* Statistically significant (P value < 0.05).

relaxation was enhanced by 26.4% during anesthesia[23], and even the rocuronium-induced neuromuscular block was boosted in patients with prolonged clonidine pre-treatment[24]. Others found that oral clonidine administration does not alter Vecuronium-induced neuromuscular blockade[25]. Contrary to above studies, the pre-operative intravenous clonidine infusion decreased the vaporizer dial concentration of sevoflurane significantly, with haemodynamic stability under minimal anaesthetic drug requirement and without any adverse effects[26].

Present study utilized the clonidine in an intravenous continuous infusion from the time of induction till extubation and recorded observations similar to those of Pathak et al[26]. That means, the clonidine group had a lesser activity of muscle relaxant at the time of extubation. In presence of clonidine, lesser repeat doses of vecuronium was needed to maintain the muscle relaxation, and hence, the extubation time was found shortened as compared to the placebo group. Therefore, considering a similar level of drug clearance in both groups, it follows that patients given clonidine had lower levels of vecuronium at the time of extubation while they had clinical signs of similar neuromuscular block. We termed this phenomenon as the 'pseudo-neuromuscular blockade' since there was possibly a lower level of muscle relaxant in circulation yet the identical effect was maintained in the clonidine group. This anaesthetic sparing effect is said to be due to the suppression of central catecholamine release along with pre-junctional mechanisms involved in neuromuscular transmission[27]. The "the presynaptic Alpha-2 autoreceptors located on noradrenergic (NA) cell bodies, terminals or dendrites, lead to inhibition of NA cell bodies in the locus coeruleus and inhibition of NA release. The, Mu-Receptors and GABA receptors inhibit NA cell bodies and NA release: asynergy exists between opiates, benzodiazepines, and alpha-2 agonists to inhibit the NA system"[28]. Thus, the requirements of the opiates and benzodiazepines are reduced when alpha-2 agonists are used as second-line agents/adjuncts. Conversely, when alpha-2 agonists are used as first line agents, opiates or benzodiazepines are to be used at reduced dosage (50% to 80%). They have been shown to inhibit adenylyl cyclase, and in turn reducing the levels of cyclic adenosine monophosphate and causing hyperpolarization of noradrenergic neurons[9,28]. As cyclic adenosine monophosphate is inhibited, potassium efflux through calcium-activated channels prevents calcium ions from entering the nerve terminal, leading to a suppression of neural firing[9]. This suppression inhibits norepinephrine release and reduces activity of the ascending noradrenergic pathways, resulting in hypnosis and sedation[8]. Activation of this negative feedback loop may also produce reductions in heart rate and blood pressure and attenuation of the sympathetic stress response.

In view of interesting favourable observations after use of clonidine as an anaesthetic adjunct, it would be exciting to assess the functional recovery with the newer drug dexmedetomidine which has better alpha-2 agonistic activity and fewer side effects and is strongly recommended.

## CONCLUSIONS

Clonidine hastened recovery from neuromuscular block with reduced stress hyperglycaemia and post-operative pain, along with unaffected Ramsey sedation score and modified Aldrete score. Therefore, Clonidine is recommended for its use in the day case surgery as an anaesthetic adjunct in order to reduce anaesthetic dose, to achieve pseudo-neuromuscular blockade byond actual block and better post-operative outcome.

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Nil

## CONFLICT OF INTEREST

None declared

The authors declare that there exist NO affiliations with or involvement in any organization or entity with any financial or non-financial interest.

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