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COMPARISON OF ATROPINE WITH NEOSTIGMINE AND GLYCOPYRROLATE WITH NEOSTIGMINE FOR REVERSAL OF NON DEPOLARISING MUSCLE RELAXANT

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KEYWORDS :

INTRODUCTION

Anticholinergic drugs like atropine and glycopyrrolate are used for

1. Premedication as antisialagogue and vagolytic.
2. To counteract reflex bradycardia due to vagal stimulation
3. For reversal of residual paralysis along with anti-cholinesterases to prevent muscarinic side effects.

Atropine and glycopyrrolate are commonly used as anticholinergic drugs. Glycopyrrolate is commonly used because of its less side effects compared to atropine.

Non depolarizing muscle relaxants are used during surgical procedures to take control of patient's respiration. They act by interfering with transmission at neuromuscular junction. They compete with acetylcholine for binding at nicotinic receptors. After completion of surgery residual paralysis is hazardous to patients. To reverse this residual paralysis cholinesterase inhibitor – Neostigmine is used. It increases availability of acetylcholine at nicotinic and muscarinic receptors by inhibiting acetylcholinesterase enzyme. Acetylcholine has profound vagal effects like bradycardia, prolongation of QT interval,ventricular escape beats and asystole.[1]

It also causes nausea, vomiting, bronchoconstriction, increased secretions. To reduce or avoid muscarinic side effects of acetylcholine, anticholinergic drugs like glycopyrrolate or atropine are used along with neostigmine. Impaired parasympathetic control of heart rate is associated with increased incidence of cardiac dysrhythmias and ischemia. Anticholinergic drugs suppress parasympathetic control and could be detrimental in the early postoperative period in high-risk patients.

Cardiac arrest and death has been reported following administration of atropine with neostigmine, in most instances where cardiac arrest occurred, the cause may be summation of cholinergic action of neostigmine and central vagal stimulation of atropine [2]. Sudden sympathetic predominance could also be responsible for cardiac arrest [3]

Ovassapian[4] studied that degree and duration of tachycardia was much more when both drugs were used separately. The main disadvantage of atropine is its short duration of action which 60-90 minutes with intravenous route. Hence the chances of late bradycardia are more after reversal with neostigmine when its action wears off.

Glycopyrrolate is a potent long acting anticholinergic agent. Main advantage is its onset of action is similar to that of neostigmine. As it is a quarternary compound it does not cross blood brain barrier[5]. Use of glycopyrrolate was associated with a more stable cardiovascular system, fewer arrhythmias and superior control of oropharyngeal secretions at the time of reversal. [6]

The low dose of atropine administered was associated with parasympathomimetic effects estimated by the slowing of the heart rate and an increase of the mean and beat-to-beat heart rate variability. The bradycardia and increase of heart rate variability following infusion of glycopyrrolate was less marked with glycopyrrolate.[7] Atropine crosses blood brain barrier significantly causing significant postoperative short term memory deficit whereas quarternary amine glycopyrrolate crosses it minimally.[8]

MATERIAL AND METHODS

After approval from ethical committee and written informed consent the study carried out in 60 patients of ASA grade 1 and 2.Age group 20 to 50 years, Weight 30 to 70 kg and ASA grade 1 and2.

Patients are divided into two groups
Group A -30 Patients
Group G -30 Patients.

All patients were between 20 to 50 years of age, and all patients were posted for elective surgery.

Preanaesthetically all patients were thoroughly examined and investigated. Patients were kept nil by mouth for 6 hours. All patients were premedicated with glycopyrrolate 0.004 mg/kg intramuscularly 30 mins before induction of anaesthesia. In the operation theatre, pulse, blood pressure. spo2 sensor and electrocardiography monitoring is attached before induction. All patients monitored from induction to post operative recovery till the study period is over . Inj. midazolam 1 mg IV given. All patients were preoxygenated with 100% oxygen for 1 minute.

Induction was achieved with injection propofol 2 mg/kg intravenously and injection scholine 1.5 mg/kg IV is given as a muscle relaxant. After complete relaxation intubation with appropriate sized cuffed endotracheal tube was performed. Anaesthesia to be maintained with O2+N20 (50:50) and isoflurane as an inhalational anaesthetic agent and vecuronium as muscle relaxant. Pulse, blood pressure, spo2%, ETCO2 and isoflurane concentration will be monitored throughout the procedure.

Patients were infused with IV fluids and blood as appropriate. Throughout the procedure pulse rate, blood pressure, spo2 and ECG monitored. Isoflurane concentration is adjusted as per haemodynamics and discountinued approximately 10-15 minutes before expected time for completion of surgery. Last dose of vecuronium was administered at least 15 minutes before completion of surgery. N2O was continued till administration of reversal agents. Thorough suction of oropharynx was done before administration of reversal drugs.

Group A was given injection atropine 0.02 with inj.neostigmine 0.04mg/kg and Group G was given inj.glycopyrrolate 0.008mg/kg and inj. Neostigmine 0.04mg/kg, slowly over 1-2 minutes.

To ensure adequate oxygenation and carbon dioxide elimination controlled ventilation was continued throughout reversal. Pulse, blood pressure, spo2, end tidal CO2 and isoflurane concentration

were recorded before reversal, every minute for 1st 5 minutes, at 10 mins, 15 mins, 30 mins, 45 mins and 60 mins. Tracheal extubation was done when respiratory attempts and reversal of neuromuscular blockade was adequate. Oropharyngeal suction was done thoroughly before extubation and after extubation.

Heart rate was monitored closely after administration of reversal agent.

Patient shifted to recovery room and following parameters were monitored.

1. Changes and trends in pulse rate.
2. Changes and trends in blood pressure
3. Changes in spo2
4. Changes in end tidal carbon dioxide.
5. Changes in isoflurane concentration.

Changes in pulse rate and blood pressure between group A and group G were analysed. Changes in pulse rate and blood pressure in each group were analysed.

Value of P less than 0.05 taken as statistically significant.

DISCUSSION

Anticholinergic drugs atropine and glycopyrrolate are used for multiple medical conditions. In General anaesthesia, non depolarizing muscle relaxants are used for better maintenance of patient's haemodynamics. After completion of procedure this residual curarisation is detrimental to patient. So a cholinesterase inhibitor neostigmine is used to reverse this residual curarisation, but it acts on both nicotinic and muscarinic receptors. These muscarinic side effects are detrimental to patient, so to prevent these side effects anticholinergic drugs are given along with cholinesterase inhibitor.

In our study, we divided patients in 2 groups of 30 patients each. Group A, received 0.02 mg/kg of atropine and 0.04 mg/kg neostigmine,
whereas

Group G received 0.008 mg/kg glycopyrrolate with 0.04 mg/kg neostigmine.

Physical characteristics:

In our study, mean age of patients in Group A (Atropine with Neostigmine group) was 35.1 years and those in Group G (Glycopyrrolate with neostigmine group) patients was 35.77 years and in group A patients mean weight was 52.53 Kg and mean weight in Group G patients was 55.47 kg.

Mean pulse rate:

Table : maximum and minimum pulse rate of patients at different intervals in both the Groups.

Study	Max pulse rate		Time (in min)		Minimum pulse rate	
	Group A	Group G	Group A	Group G	Group A	Group G
Present study	105.27± 5.5	90.1±4.5	3	3	70.4±5.4 at 60min	85.7±3.8 at 60min
Mirakhur et al	-	-	2.6	3	-	-
Heinonen et al	-	-	-	-	50 at 12 min	50 at at 60 min

In our study, mean pulse rate till 10 minutes of post reversal is higher in group A patients than group G patients and Lower pulse rate is observed in group A patients than group G patients at the end of the post reversal duration. This is in concordance with study conducted by Ostheimer, Mirakhur[2] who found that glycopyrrolate is better drug for counteracting neostigmine induced bradycardia during reversal, there is less tachycardia and arrhythmias with this drug as compared to atropine. Baraka concluded that glycopyrrolate is a better drug with more stable heart rates particularly useful when tachycardia is undesirable. Bali also found that glycopyrrolate was associated with less initial tachycardia and minimal arrhythmias. Wong found that atropine and glycopyrrolate give equal protection against neostigmine induced bradycardia but incidence of arrhythmias were greater with glycopyrrolate group which is discordance with present study.

Blood pressure:

In our study, no significant change in both systolic and diastolic blood pressure is observed in either group A or Group G patients, which is comparable with studies done by Ostheimer , Mirakhur[2], Cozantis et al. Bali found that atropine was associated with major falls in blood pressure which was discordance with present study.
Comparison of SPO2:

Miroslav et al in their study mentioned that administering neostigmine combined with glycopyrrolate was followed by significant bronco dilatation and bronco constriction associated with neostigmine is prevented by simultaneous administration of anti cholinergic drugs.

Bourgain et al in their study found that by using neostigmine and atropine combined to reverse neuromuscular blockade in patients with or without COPD total respiratory resistance was not altered significantly. Similar observation, reflected by lack of significant ($p>0.05$) change of mean SPO2 percentage in post reversal interval from that of the before reversal values in both group A and G, is observed in present study.

ETCO2

In our study there was no significant ($p>0.05$) difference of ETCO2 before reversal to that of the ETCO2 at different interval in both groups which shows that there is similar effect on lung dynamics by both atropine and glycopyrrolate.

Isoflurane concentration:

Baurain et al in their study of isoflurane effect, observed that discontinuing isoflurane anaesthesia for 15 minutes improves reversal of vecuronium paralysis. Hence, in our study, isoflurane concentration had discontinued approximately 10-15 minutes before expected time for completion of surgery in both group so that statistically there was no significant ($p>0.05$) difference of isoflurane in between the Group A and Group G in post reversal period.

CONCLUSIONS

Group A patients who were reversed with inj. Atropine and inj. Neostigmine were not cardio-stable causing early tachycardia and delayed bradycardia.

Group G patients who were reversed with inj. Glycopyrrolate and inj. Neostigmine shows cardio-stability, caused less tachycardia and provides more protection against neostigmine induced bradycardia .

Changes in systolic, diastolic blood pressure and mean arterial pressure were insignificant in both groups. There was no significant changes in blood oxygen saturation SpO2 in both groups. There was no significant change in end tidal CO2 in either group. There was significant change in isoflurane concentration in either groups but There was statistically no significant ($p>0.05$) difference of mean Isoflurane concentration in between A and G Group during

References

1. Bjerke R, Mangione M. Asystole after intravenous neostigmine in a heart transplant recipient ;Canadian journal of anaesthesia 2001; vol48; (3): 305-307
2. Mirakhur RK, Dundee JW, Clarke RSJ. Glycopyrrolate neostigmine for antagonism of neuromuscular block: Comparison of atropine neostigmine mixture .british journal of anaesthesia1977; 49 :825.
3. Jones RE, Deutsch S, Turndorf H. Effects of atropine on cardiac rhythm in conscious and anaesthetized man. Anaesthesiology 1961;22: 67
4. Ovassapian Andranic.effects of administration of atropine and neostigmine in man. Anaesth.Anlg.1979;48:219.

5. Proakis AG, Harris GB. Comparative penetration of glycopyrrolate and atropine across the blood brain and placental barriers in anaesthetized dogs. Anaesthesiology 1978; 48:339.
6. Kongsrud Sponheim S.A comparison of atropine and glycopyrrolate in anaesthetic practice.ActaanaesthesiologicScandinavica1982 vol: 26, (6): 620-5
7. Ali-Melkkilä T, Kaila T, AntilaK ,et al. Effects of glycopyrrolate and atropine on heart rate variability ActaAnaesthesiolScand 1991; vol 35 : 436-441
8. Simpson K, Smith R, Davies. Comparison of the effects of atropine and glycopyrrolate on cognitive function following general anaesthesia. British journal of anaesthesia 1987; vol: 59(8) : 966-969