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Original Article

Comparison of acceleromyography guided neuromuscular recovery of post cardiac surgery patients with or without using anticholinesterase agent.

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Abstract

Pretext: *Routine reversal of non depolarizing muscle relaxant neuromuscular blockade is common in practice after general anaesthesia. Neostigmine is most commonly used anticholinesterase agent and it has some serious side effects.*

We designed observational study to assess if avoidance of pharmacological neuro muscular reversal agents in post cardiac surgery patients with acceleromyographic neuromuscular monitoring (TOF) guided physiological reversal of neuromuscular block can have better recovery profile.

Methods and Material: *60 patients who were posted for elective cardiac surgery were divided into two groups (Group S: study group and Group C: control group) of 30 patients each. All patients were managed with institutional protocol peri-opertively, except in recovery period at the time when TOF ratio was more than 0.4, group C patients were given fix dose neostigmine/ glycopyrrolate intravenously while Group S patients were given placebo. All patients were extubated when alertness and TOF ratio of 0.9 achieved. Recovery profile of two groups was compared, using standard statistical analysis by paired t test, annova test and Fisher exact test.*

Results: *Extubation time were significantly longer in group S than group C.(Gr.S 22.3 ± 12.4 min, Gr. C 14.7 ± 9.6 min). Patients of group S remained more stable haemodynamically during extubation than group C (p value 0.039). Group C patients had more but statistically non significant new onset arrhythmias post extubation. Other adverse events like nausea, vomiting and respiratory distress were similar in both the groups. None of the patients from any of the group required reintubation. Lengths of stay in recovery as well as length of stay in hospital was not different between the groups.*

Conclusions: *We concluded that with the guidance of objective neuromuscular monitoring we can physiologically reverse neuro muscular blockade and extubate patients without giving anticholinestersase drugs to group of patients with more stable hemodynamics and avoid possible adverse effect of reversal drugs.*

Keywords: *Neuromuscular blocking drug reversal, acceleromyography, neuromuscular monitoring, TOF ratio, post cardiac surgery recovery profile.*

Introduction

There is ample evidence that post operative residual neuro muscular block results in increase postoperative mortality and morbidity[1]. Routine reversal of neuromuscular blockade is common in order to prevent recurarization in many countries after surgery under general anaesthesia[2]. But use of neuro muscular blocking drugs reversal (NMBDR) does not guarantee complete neuro muscular reversal[3]. Not only dosage, but timing of giving NMBDR also affect adequacy of regaining muscle power[4]. These NMBDR agents are also known to have very detrimental side effects. Numerous reports of these adverse events including many incidences of cardiac arrest after NMBDR are published in literature[5]. Recently, guidelines are published with proposal of making objective neuromuscular monitoring mandatory for assessment of reversal of neuromuscular blockade prior to extubation for all cases done under general anaesthesia where non depolarizing muscle relent were used[6]. These guideline suggests to extubate patients only after regaining train of four (TOF) score of 0.9. NMBDR are themselves causes cholinergic muscle paralysis. High-dose neostigmine or unwarranted use of neostigmine may translate into increased postoperative respiratory morbidity. Murphy GS et al[7] concluded that with use of shorter acting neuromuscular agents, cardiac surgical patients can be extubated early after general anaesthesia without using NMBDR. Avoidance of NMBDR might be very helpful in cardiac surgery patients, who are more susceptible for detrimental side effects of NMBDR[8]. We designed a case control prospective study to investigate that with guidance of objective neuromuscular monitoring and avoiding NMBDR drugs after elective cardiac surgery, can better recovery profile (hemodynamic changes, new onset arrhythmias, respiratory complications, post operative nausea vomiting, residual paralysis and incidence of recurarization) be achieved.

Methods

After getting clearance from Institute Ethics Committee and written informed consent, 60 patients planned for elective cardiac surgery with NYHA grade 2 and 3 statuses, with well optimized co morbidity and those who can be extubated early were included in this study. They were divided into two groups (Group S; study group and Group C; control group) of 30 patients each. Under standard and invasive monitoring, patients were induced with 3-5 µg/ kg of fenanyl, 0.05 mg/ kg midazolam, 0.1 mg / Kg vecuronium through intravenous (IV) route. Hypnotic dose of propofol 1-2 mg/ kg was given intra venously (iv) as per response with assisted ventilation. All patients were intubated and ventilated as per institutional protocol. Isoflurane 1% and top up doses of anesthesia drugs was given throughout operative period. Last dose of muscle relaxant was given just prior to shifting to post cardiac surgery recovery unit (PCSRU). In PCSRU, patients were electively ventilated on controlled mode for first hour and ventilator mode was shifted to synchronous mode if all other parameters for weaning from ventilators were normal.

No muscle relaxant drugs were given. Patients (Pt's) were put initially on 1 mg/ kg/ Hr infusion of propofol which was titrated according to Ramsay sedation score of 5. Intravenous paracetamol was given for analgesia and to tolerate endotracheal tube. Those patients who required muscle relaxants or opioids due to any cause were excluded from study.

Patients were reassessed for extubation after 4 hours (hr.) of shifting to recovery and when they fulfilled the criteria for weaning, propofol infusion was discontinued. Patients were examined for alertness, muscle power, return of reflexes, verbal command following. They were assessed for acceleromyographic train of four (TOF) score (TOF Watch S organon), Ireland)and after confirming TOF score more than 0.4,they were given pre filled 10 syringe which either contain 2.5 mg neostigmine with 0.04 mg glycopyrrolate

(group C)or 0.9% normal saline (group S) and this time was noted as reversal time (Trev).

Acceleromyographic neuromuscular monitoring was done every 10 min from this time till TOF ratio of more than 0.9 was achieved. Pt's were extubated and time was recorded as extubation time (Text.). Haemodynamic events were recorded along with rhythm changes, respiratory discomfort, nausea and vomiting. Change of more than 20% from base line in heart rate and mean blood pressure was considered as significant haemodynamic change. Time of shifting to step down recovery (LOS recovery) and discharge from hospital (LOS hospital) were recorded which were done as per institutional protocol (Appendix 1). Any complication related to extubation like re-intubation, arrhythmias, AV block, bronchospasm and re curarization were also included in post operative adverse event. Statistical analysis was done using "paired t test" and "annova test" and ci for two proportions "fisher exact test". Suitable analysis with Pad InStat 6.0 programme (Graph Pad Software, SanDiego, CA, USA).

Results

Table 1: Demographic data (± mean values)

variable	Group c (n=30)	Group s (n=30)	P value
Age	59.4 ± 12.9 yrs	63.7 ± 17.2 yrs	0.27
Weight	63.6 ± 19.8 kg	69.2 ± 15.3 kg	0.22
Sex (M:F)	18:12	16:14	0.27
Diabetic	14:30	9:30	0.4
Smoker	18: 30	14:30	0.66
Hypothyroid	9:30	5:30	0.38
Surgery	cbag16:valve14	12:18	0.30
Duration of surgery Tind.-Tshf.	254 ± 119 min	276 ± 109 min	0.45

(Tind. Induction time, Tshf: shifting from ot time)

Table 2: Peri operative data (± mean values)

Total drug used	Group c (n=30)	Group s (n=30)	P value
Propofol	239± 67.94 mg	254 ± 64 mg	0.38
Fentanyl	565 ± 95.39 µg	543 ± 58 µg	0.28
Midazolam	5.5± 0.82 mg	5.9 ± 1.2 mg	0.13
Vecuronium	20.2 ± 2.8 mg	19.1 ± 3.2 mg	0.20
Reversal time from Last dose (Trev)	346.2 ± 69.2min	358.5 ± 78.4 min	0.52
Extubation time from reversal (Text)	**14.7 ± 9.6 min**	**22.3 ± 12.4 min**	**0.01**

Table 3: Post operative Complication

variable	Group c n=30	Group s n=30	P value
Hemodynamic changes > 20% Base	**19**	**11**	**0.039**
A-V block	2:28	1:29	1
New Arrhythmias	7:23	4:26	0.50
Respiratory distress	1:29	1:29	1
ponv	5:25	2:28	0.43
Post extubation ventilatory support	0:30	0:30	1
LOS recovery	4±1 day	4±1 day	1
LOS hospital	7±2 day	7±2 day	1

Analysis of Results

Both the groups were comparable in terms of demographic data, co-morbidity nature and duration of surgery. (table 1). There was no statistically significant difference in amount of anaesthesia drugs used during perioperative period (Table 2). All patients were electively ventilated for first 4 hours as per PSCRU protocol and weaning started after they fulfilled surgical criteria of stability. All patients regained consciousness and responded to verbal commands with comparable time interval, but extubation time

were significantly longer in group S than group C.(Gr.S 22.3 ± 12.4 min, Gr. C 14.7 ± 9.6 min) (Table 2). It was observed that only 11 out of 30 patients in group S have hemodynamic changes more than 20% of base line in comparison to 19 patients in control group during extubation. Patients of group S remained more stable haemodynamically during extubation than group C (p value 0.039). Group C patients had more but not statistically significant new onset arrhythmias post extubation in comparison to Group S. Other adverse events like nausea, vomiting and respiratory distress were similar in both the groups. None of the patients from any of the group required reintubation, which reflects that both the strategy are safe. Length of stay in PCSRU as well as length of stay in hospital was not statistically different between the groups. (Table 3)

Discussion

Pharmacological reversal of neuromuscular blocking drugs is always remaining matter of investigation[9]. Since inception of muscle relaxant drugs this controversy still exists.Neostigmine is most commonly used NMBDR agent which by inhibiting cholinesterse enzyme in nicotinic end plate reduces degrdadation of acetyl-choline thus increases its concentration which results in facilitated muscular contraction thus also known as anti-cholinesterase drug. Because neostigmine can also induce bradycardia, increased bronchial and pharyngeal secretions, and bronchospasm by muscarinergic effects, it is coadministered with an antimuscarinergic drug to attenuate such side.Only giving fix dose of NMBDR is not assurance of complete neuromuscular reversal, but timing of administration is also important[10]. The use of anticholinesterases to reverse residual neuromuscular block is efficacious only if recovery is already established. Dose and time for extubation after giving NMBDR depends on the TOF score. It is recommended now to give NMBDR after fourth twitch reappeared[11]. Kirkegaard et al[12] reported study on the timing and likely outcome of reversal from various TOF counts which undermine the fact that early use of NMBD during deep block may result in delayed reversal. This observation supports our concern that even after giving NMBDR risk of incomplete reversal and risk of re curarization exists. There are numerous publications in literature confirming this phenomenon. To optimize dose drug schedule and to reduce risk of residual neuromuscular block recent recommendations proposed to make use of neuromuscular monitoring mandatory for confirmation of adequate NMBDR state and to extubate only after achieving TOF ration of 0.9. Murphy GS[13] published study on NMBDR and concluded acceleromyography monitoring reduces muscle weakness and improves quality of recovery in the early postoperative period.

As NMBDR are themselves causes cholinergic muscle paralysis, high-dose neostigmine or unwarranted use of neostigmine may translate to increased postoperative respiratory morbidity[14]. Study published by Sasaki N[15]concluded that neostigmine reversal did not affect oxygenation but was associated with increased atelectasis. Eikermann et al[16] found unwarranted use of NMBDR can impair genioglossus and diaphragm muscle function, increase upper airway collapsibility and impair upper airway dilator muscles activity.

Goyal S *et al*.[17] concluded that anticholinesterases agents can be avoided safely if objective neuromuscular monitoring is used. Complete recovery from the neuromuscular blockade can be ensured without possible adverse effects of anticholinesterases. In our study we found that patients those were not given NMBDR, remain more haemodynamically stable during extubation and have less but not statistically significant new onset arrhythmias post extubation in comparison to patients who received NMBDR. These finding were in favour of conclusion made for post cardiac surgery patient's by Hemmerling T M[18]. Possible explanation is that gradual physiological reversal of neuro muscular receptor without affecting muscarinic and cholinergic antagonism produces more haemodynanmic stable

environment in comparison to patients those received NMBDR-anticholinergic combination. Other adverse events like nausea, vomittings and respiratory distress are similar in both the groups. None of the patients from any of the group require reintubation, which reflects both the strategy were safe. This is because all the patients were extubated under acceleromyographic neuro muscular monitoring after achieving recommended TOF ration of more than 0.9. Length of stay in PCSRU as well as length of stay in hospital was not statistically different between the groups. Thus interpretation can be made that avoidance of NMBDR does not prolonged recovery period and stay in hospital.

Conclusion

Our results were in accordance of our hypothesis that with the guidance of objective neuromuscular monitoring we can safely reverse neuro muscular blockade and extubate patients without giving anticholinestersase drugs. In this study observation was made that more stable haemodynamics were achieved in post cardiac surgery patients by avoiding NMBDR.

References

1. Farhan H, Moreno-Duarte I, McLean D, Eikermann M. Residual Paralysis: Does it Influence Outcome After Ambulatory Surgery?. Curr Anesthesiol Rep. 2014; 4 (4):290-302.
2. Glenn S. Murphy, M.D.; Aaron F. Kopman, M.D. To Reverse or Not To Reverse?": The Answer Is Clear Editorial Views Anesthesiology 2016, Vol.125, 611-614.
3. Srivastava A, Hunter JM. Reversal of neuromuscular block.Br J Anaesth. 2009 Jul;103(1):115-29.
4. NielsenHK, May O ET AL :The optimal administration time for neostigmine following atrauronium blockade. Kinetics of antagonists. Anaesthesist. 1994 Aug. 43 (8):528-33.
5. Bertolizio, Gianluca et al. Cardiac Arrest and Neuromuscular Blockade Reversal Agents in the Transplanted Heart. Journal of Cardiothoracic and Vascular Anesthesia ,2013 ;27 (6) , 1374 – 1378
6. Naguib, Mohamed B. et al Consensus Statement on Perioperative Use of Neuromuscular Monitoring. Anesthesia & Analgesia. 2018;127. 71-80.
7. Murphy GS, Szokol JW et al Impact of shorter-acting neuromuscular blocking agents on fast-track recovery of the cardiac surgical patient., Anesthesiology. 2002 Mar;96(3):600-6.
8. Pani, Nibedita et al. "Reversal agents in anaesthesia and critical care" Indian journal of anaesthesia 2015; 59,(10) ,664-669.
9. Sorin JB,Aaron FK Current Status of Neuromuscular Reversal and Monitoring: Challenges and Opportunities Anesthesiology 2017, (126), 173-190.
10. Thilen, S. R., & Bhananker, S. M. (Qualitative Neuromuscular Monitoring: How to Optimize the Use of a Peripheral Nerve Stimulator to Reduce the Risk of Residual Neuromuscular Blockade. Current anesthesiology reports, 2016; 6, 164-169.
11. Doanti F neuromuscular monitoring more than meets the eye anesthesiology 2012 :117, 934-6.
12. Kirkegaard H, Heier T et al Efficacy of tactile-guided reversal from cisatracurium-induced neuromuscular block. Anesthesiology. 2002 Jan;96(1):45-50.
13. Murphy GS, Szokol JW et al Residual neuromuscular blockade and critical respiratory events in the postanesthesia care unit. Anesth Analg. 2008 Jul;107(1):130-7
14. Sharma R Muscle paralysis with an accidental overdosage of neostigmine. Acta Anaesthesiol Scand. 2008 Nov;52(10) 1437

15. Sasaki N, Meyer MJ et al Effects of neostigmine reversal of nondepolarizing neuromuscular blocking agents on postoperative respiratory outcomes: a prospective study. Anesthesiology. 2014 Nov;121(5):959-68.
16. Eikermann M, Fassbender P Unwarranted administration of acetylcholinesterase inhibitors can impair genioglossus and diaphragm muscle function. Anesthesiology. 2007 Oct;107(4):621-9.
17. Goyal S, Kothari N et al Reversal agents: do we need to administer with neurom-uscular monitoring – an observational study IJA 2018, 62 (3) 219-224
18. Hemmerling T M, Russo Gianluca, Bracco David Neuromuscular blockade in cardiac surgery: An update for clinicians. (review article): Annals of card. Anesth.2008; 11 (2): 80-90.

Appendix 1: The following criteria were adapted as institutional protocol

Criteria for Weaning Mechanical Ventilatory Support

- Hemodynamic stability
- Absence of uncontrolled arrhythmias
- Central temperature greater than 36.0°C
- Chest tube drainage less than 100 ml in the past 2 h
- Arterial oxygen tension greater than 60 mmHg with a oxygen fraction less than 0.5
- *p* H greater than 7.32

Criteria for Tracheal Extubation

- All of the criteria for weaning ventilatory support met
- Negative inspiratory force greater than −20 cm H^20
- Patient responsive to simple commands
- No neurological defecit.
- Stable hemodynamic on minimal ventilator support.
- TOF Ratio > 0.9.

Criteria for post cardiac surgery recovery Unit Discharge

- Patient alert and cooperative
- No inotropic support
- No significant arrhythmias
- Arterial oxygen saturation greater than 97% with inspired oxygen fraction less than 0.4
- Stable hemodynamics and Invaise monitoring not required.
- Mobilized well with support, can take care of him for daily activity.

Criteria for Hospital Discharge

- Stable hemodynamics and cardiac rhythm.
- Post cardiac surgery day 6 labs and echo chest xray normal.
- Clean incisionsites and absence of elevated temperatures.
- NYHA status of 2 or less with incentive spirometry of 900ml and more.
- Independent ambulation and personal care.
- Able to do active chest physiotherapy