Editorial

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The use, misuse and abuse of muscle relaxants

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For the sake of humanity and betterment of treatment modalities, researchers in medical field have done tireless job since decades in elevating the level of evidence based medicine. Compared to other medicine and surgical fields, the young anesthesiology science has achieved wonderful advancements mainly due to the efforts of these researchers and also a large contribution by the surgical patients. However, every advancement may also have some inherently associated drawbacks just like shadow parts of the objects which are inseparable.

The most lethal medications which can be potentially misused or abused belong to this wonderful specialty. Besides anesthetics, Muscle Relaxants (MRs) have contributed to a greater extent towards morbidity and mortality associated with their use, misuse and abuse. The misuse and abuse is restricted not only to the four walls of the operation theatre or ICU but also the evidence from the published literature and sporadic reports keeps on bringing the dreaded aspects when MRs gets in hands of non-specialists.

The present editorial aims to highlight those scenarios in which MRs are used, misused and/or possible gets abused and also to adopt some possible measures and precautions so as to bring down their misuse and abuse. The preventive measures discussed though are not comprehensive; they definitely can decrease the morbidity and mortality associated with their misuse and abuse. The reporting of such incidence will not only help in bringing forth the awareness but will also possibly help in modifying the existing and developing the newer measures to stop the misuse and abuse of muscle relaxants.

USES OF MRs

In anesthesia and intensive care, MRs are mainly used for following purposes:

- For accomplishing intubation by paralysis of upper airway muscles so that endotracheal tube can be placed
- For achieving and supplementing surgical relaxation by paralysis of abdominal and thoracic muscles during surgery so that surgery procedure is possible in these areas of powerful muscles.
- For control of ventilation in the ICU when patients are unable to tolerate ventilation[1]

Whenever, MRs are used in above scenarios there is always a likelihood that misuse (overuse/underuse) can occur. It can have frightening outcome and psychological breakdown when a patient is conscious but unable to communicate or not able to move limbs or for that matter any part of the body. This potential awareness during surgery and anesthesia can lead to post-traumatic stress disorders. There have been many audits, reporting and trials on awareness during anesthesia but none of the resulting outcomes have been measured longitudinally.

LEGAL BARRIERS ASSOCIATED WITH USE OF MRs-HISTORICAL ASPECTS

In developing nations such reporting and trials have been underreported but in developed world like US and Canada many lawsuits were filed between 1980-1985 when cardiac anesthesia was in the infant stage using high dose narcotic anesthesia. In these cases, though

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the hemodynamic parameters and clinical condition of the patients remained stable perioperatively, the recall and awareness during surgery led to reporting of mass discomfort postoperatively among majority of the patients. Pancuronium was the muscle relaxant used with high dose narcotics and smaller dose of benzodiazepine. The initial phase of cardiac anesthesia did not live up to the standards of patient comfort as the basic principle of Amnesia was not given weightage in this high dose narcotic anesthesia. Narcotics can provide deep sedation but do not provide complete amnesia and use of MRs in such cases accentuated the awareness phenomenon which led to filing of million dollar lawsuits.

POST-OPERATIVE BLUES

Another grey area leading to abuse and misuse pertains to reversing the effect of MRs at the end of surgery. Throughout globe common medication used is neostigmine and glycopyrrolate/atropine combination for reversing the effect but how many times in clinical practice one observes the following aspects (Table 1)

If the patients are not fully reversed, there always remains the risk of aspiration, pneumonitis, hypoxemia and prolonged stay in hospital. This mainly occurs due to diminished airway reflexes and reduced oesophageal contractility as a result of residual paralysis.

RECITE TRIAL

A large multicentric prospective RECITE trial (Residual Curarization and its Incidence at Tracheal Extubation) was conducted in Canada to investigate the incidence and severity of residual NMB in ASA physical status I-III patients undergoing open or laparoscopic abdominal surgery, and scheduled for general anesthesia with at least 1 dose of a nondepolarizing neuromuscular blocking agent for endotracheal intubation or maintenance of neuromuscular relaxation[2]. Neuromuscular function was assessed using acceleromyography with the TOF-Watch SX. The incidence of residual NMB was 63.5% (95% confidence interval, 57.4%-69.6%) at tracheal extubation and 56.5% (95% confidence interval, 49.8%-63.3%) at arrival at the PACU. In an exploratory analysis, no statistically significant differences were observed in the incidence of residual NMB according to gender, age, body mass index, ASA physical status, type of surgery, or comorbidities (all $P > 0.13$). The results of the study gives a clear message to everyone practicing anesthesia that there always remain the chance of residual neuromuscular blockade despite using qualitative neuromuscular monitoring and the use of neostigmine. The scenario in developing is further gloomy where majority of the operative set-ups don't have/use routine neuromuscular monitoring and solely rely on clinical subjective judgment.

POTENTIAL CAUSES OF ABUSE OF MRs

There is a very thin line and a narrow demarcation between the use, misuse and abuse of MRs but going by the reports, literary evidence and subjective clinical experiences, the potential causes of abuse can be listed as follows:

- Accidental abuse during use.
- Unawareness of pharmacokinetics and pharmacodynamics.
- Drug errors.
- Diversion of muscle relaxants from four walls of OT.
- Deliberate misuse.

DELIBERATE MISUSE

Anaesthetics and muscle relaxants have been used for:

- Euthanasia.
- Suicides.

Table 1: Common scenarios observed during reversal

• Whether the patient has been fully reversed?
• Whether the dose of reversal was correct?
• Was the timing of the administration of reversal was correct?
• Which types of risks are involved if reversal is given in less than the ideal dose?
• Whether the syringes were labeled correctly?
• Whether the expiry date was checked thoroughly along with identifications of correct vials?

- State executions.
- In homicides by the criminals.

In all homicidal poisonings medicines account for 65% of all cases. Worst scenario develops when criminals come to know their potential misuse[3]. Exact incidence of MRs abuse is not known but from sporadic case reports it can be estimated somewhere between 2-3% in cases of homicide and suicides. Though anesthesiologists are not directly involved in the admission of poisoning cases in the hospital, the increasing abuse of anesthetics and MR's have compelled the authorities to recognize a greater role of anesthesiologist in evaluating, investigating and prosecution of such cases.

ACCIDENTAL ABUSE DURING USE

In clinical practice many instances can be traced where accidental abuse of MRs has occurred and will keep on recurring if specific precautions are not fully exercised. The combination of basic (eg.,: Thiopentone) and acidic drugs (eg., including Sch, Rocuronium, Atracurium, Pancuronium, Vecuronium can be detrimental sometimes especially in cases of emergency securing of airway, trauma and rapid sequence induction. There can be precipitation of drugs if drip is not running freely and/or flushing method is not used after each injection. The precipitate will not allow the effect of the MRs and intubation can fail. There have been reports when in cases of trauma and shock, intravenous (I.V.) line secured with difficulty can get dislodged and it is difficult to find the I.V. line again. This has resulted in either inability to give rapid I.V., administration of MRs or delaying the supplementation of dose. Absence of neuromuscular monitoring also indirectly contributes in indiscriminate use

UNAWARENESS

This one of the common causes at entry level in the specialty when people start learning the skills of the anesthesia

- Unawareness of pharmacokinetics of MRs (linear vs non-linear).
- Unawareness of pharmacodynamics (changing P over time such as phase-II block with repeated administration of Sch).
- Recovery characteristics vary among MR's.
- Rapid distribution (Cp) to shallow elimination phase. That is just akin to moving from vast sea to a narrow tunnel.

ABUSE IN ICU

In recent years there have been reports of prolonged neuromuscular blockade in patients being treated with nondepolarising Neuromuscular Blocking Agents (NMBA) including pancuronium, vecuronium and atracurium. Metabolism of these drugs might be reduced leading to increased plasma levels which may persist for up to two weeks after discontinuing the drug. An abnormal decrease in compound muscle action potential amplitudes with slow repetitive stimulation has been demonstrated (decremental response) in such cases. Concomitant use of aminoglycosides and polypeptide antibiotics increases the neuromuscular block. Latent myasthenia gravis may be unmasked. Neuromuscular transmission dysfunction generally coexists with neuropathy or muscle dysfunction and thus might be overshadowed by the features of neuropathy or myopathy. NMBAs and steroids should be used in minimum required doses and regular monitoring of CK should be done[4,5].

PRECAUTIONS TO BE TAKEN IN ICU TO PREVENT MISUSE AND ABUSE

The use of MRs can be made judicious by observing the following precautions. (Table 2)

Many of the sedatives, anesthetics, antibiotics and steroids have additive and synergistic effect with MRs. Therefore choice of MRs should be prudent to avoid interaction with other drugs.

Present day legal and non-friendly attitude towards physicians keeps these wonderful specialists out from the protective cover of socio-behavioral and clinico-legal umbrella. Such incidents keep on happening frequently in our vicinity and cast a dark shadow on the grace of our specialty. "A little knowledge is a dangerous thing" is perfectly true regarding the clinical profile of drugs used in anesthesia including MRs. This is more apt a statement for those physicians who are not well trained in the science and skills of resuscitation. This "little knowledge" can contribute directly or indirectly to the misuse and abuse of MRs. Therefore, every specialist from anesthesiology should keep in mind the potential causes of misuse and abuse of MRs for the safety and comfort of the patients as well as of their own safety.

Table 2: Precautions during use of muscle relaxants	
1	**Sedation should be used adequately to avoid awakening psychosis**
2	**Neuromuscular monitoring equipment should be available**
3	**The ventilatory support should also be appropriate and adequate**
4	**Every paramedical staff should be taught about the pharmacokinetics, pharmacodynamics and clinical profile of MRs**
5	**Ventilator should be properly calibrated and circuits should be checked for any leakage or obstruction.**
6	**MRs should be chosen on the basis of following:** . Onset time and speed . CVS/ANS/CNS effects . Metabolism and clearance . Histamine release . Cumulative effects . Ease of reversal . Ease of administration by infusion . Effect on hepatic enzymatic system . Effect of intermediate and active metabolites . Cost factor especially in developing nations.

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