Introduction

The National Coordinating Council for Medication Errors Reporting and Prevention defines a drug error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of health care professional, patient or consumer. Such event may be related to professional practice, health care products, procedure and system, including prescribing, order communication, product labeling, packaging and nomenclature, compounding, dispensing, distribution, administration, education, monitoring and use ***(Nwasor et al., 2014).***

Drug error was distinguished from the adverse drug event that was defined as any injury resulting from medical intervention related to a drug, and from the adverse drug reaction that was defined as any response to a drug which is noxious and unintended which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or for modifications of physiological functions ***(Hakkarainen et al., 2012).***

Drug errors were the fourth most common category of adverse drug events (10, 8%) resulting in permanent disability in 17% and death in 8%. Worse 51% of the events were considered to be preventable. Moreover the

voluntary reporting which is most commonly used in the study of medication errors underestimates the actual incidence of errors due to fear of legal action and fear of reporting to national monitoring agencies that may hinder some reporting of errors ***(Cooper and Nossaman, 2013).***

Administration of a drug during anesthesia is a highly complex procedure often taking place under conditions of stress, haste and fatigue. Each drug administration can be associated with up to 40 component steps, therefore it's not surprising that errors can and do occur. Errors tend to occur in recurrent patterns and similar circumstances often precipitate similar errors, effective risk management requires a reporting culture so that latent errors present in anesthesia delivery system can be identified and eliminated ***(Abeysekera et al., 2005).***

Drug errors are a common occurrence during the conduct of anesthesia (one in every 113-450 anesthetic administered). Several factors contribute to drug errors in anesthesia including experience of the anesthesia provider, severity of comorbidities and type of procedure ***(Cooper et al., 2012)***.

Outcomes of drug errors reported to The Australian Anesthetic Incident Monitoring Study were minor morbidity in 11.7% of incidents, major morbidity in 4.7%

of incidents, death in 0.3% of incidents, unplanned high dependency care in 2.2% of incidents, prolonged hospital stay in 2.8% of incidents, awareness in 4.4% of incidents, no harm in 73.5% of incidents and a non specified outcome in 0.3% of incidents ***(Abeysekera et al., 2005).***

Drug errors in anesthesia context can be classified as syringe or drug preparation errors, equipment misuse or malfunction, route of administration errors, dose errors and communication errors ***(Raw, 2014).***

The rate of drug errors was reduced to one in every 625 anesthetic administered after implementation of Anesthesia Patient Safety Foundation recommendation concerning standardization of high alert drugs, using technology and establishment of a reporting culture ***(Cooper and Nossaman, 2013).***

Aim of the Study

The aim of this study is to highlight the prevalence and incidence of drug errors in anesthetic practice, address the types of errors, search among the reported incidents for the laid out guidelines of management of errors and to repeat the previously published strategies for prevention of drug errors.

Incidence and Outcomes of Drug Errors in Anesthesia

Medication errors in anesthesia are mainly those of drug administration and not prescription because in the operating theaters, the anesthetist select, prepare, label and administer all the drugs needed for the procedure. Anesthetists are unique in that a single practitioner is usually responsible for all parts of the process often without any formal checking maneuvers required. In other areas of medical practice, several individuals may be involved and checking mechanisms are usually more robust ***(Nwasor et al., 2014).***

The management of anesthesia has become safe with the advent of newer safe anesthesia drugs, good quality equipments and high standard of monitoring, but the practice of polypharmacy, complex working conditions and involvement of multilevel medical and paramedical staff expose this area to potentially life threatening medication error at some point of the treatment process. The Institute of Medicine (IOM) report highlights that 44000-98000 patients die each year as a result of medical errors, a large portion of these being medication related. Surprisingly 30% of members of Canadian Society of Anesthesiologists

admitted to experience at least more than one in their lifetime ***(Kothari et al., 2010).***

Incidence of drug errors in anesthesia:

Anesthesia medication errors occur in one in 10 anesthetic cases in prospective studies that used voluntary reporting. Prospective studies suggest that general medication errors occur in the administration of one in every 133 injections. When retrospective adverse anesthesia events are analysed, the rates are reported as being anywhere from one in 5000 to one in 1300 anesthetics. Thus prospective volunteer studies are more meaningful than retrospective adverse event studies ***(Raw, 2014).***

Risk factors:

Critical incidents occurred most commonly during middle of the anesthesia (42%), frequently during induction (28%) and at the beginning of the procedure (17%). Human errors were believed to be a factor ranging 65-87% for deaths during anesthesia in several studies. Lack of staff, overtime and odd working hours, inattention, poor communication, carelessness, haste and fatigue are the common factors related to medical and paramedical personnel ***(Kothari et al., 2010).***

Haste and distraction may occur at any time, especially during emergency cases when pressure to proceed may lead to short cutting of usual checking routines. Anesthetic techniques and equipments have undergone significant safety improvements over the last years, however, filling syringes ,mixing drugs and administration techniques are similar to those used 100 years ago ***(Abeysekera et al., 2005).***

Complex surgical procedures and patients with significant comorbidities often require therapeutic interventions with infrequently used medications utilized under dynamic conditions, all contributing to higher medication error rates when compared with cases with lower surgical complexity. Adult surgical cases had higher American Society of Anesthesiologist (ASA) scores, required more multiple drug infusions and typically required medications infrequently used. Incorrect dosage errors in pediatric surgical cases were found to be the most common reported event due to the frequent need for weight adjusted dosage ***(Cooper et al., 2012).***

The anesthesia provider- in- training reported a twofold increase in errors with the most frequently reported errors being incorrect dose and swap errors. The inexperience of trainees in the specialty may also lead to a higher frequency of medication errors in teaching

programs, yet there are few data to support this claim ***(Cooper et al., 2012).***

Outcomes of drug errors in anesthesia:

The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) realized the need for a standardized categorization of errors. This council adopted a medication error index that classified errors according to the severity of outcome ***(Kothari et al., 2010).***

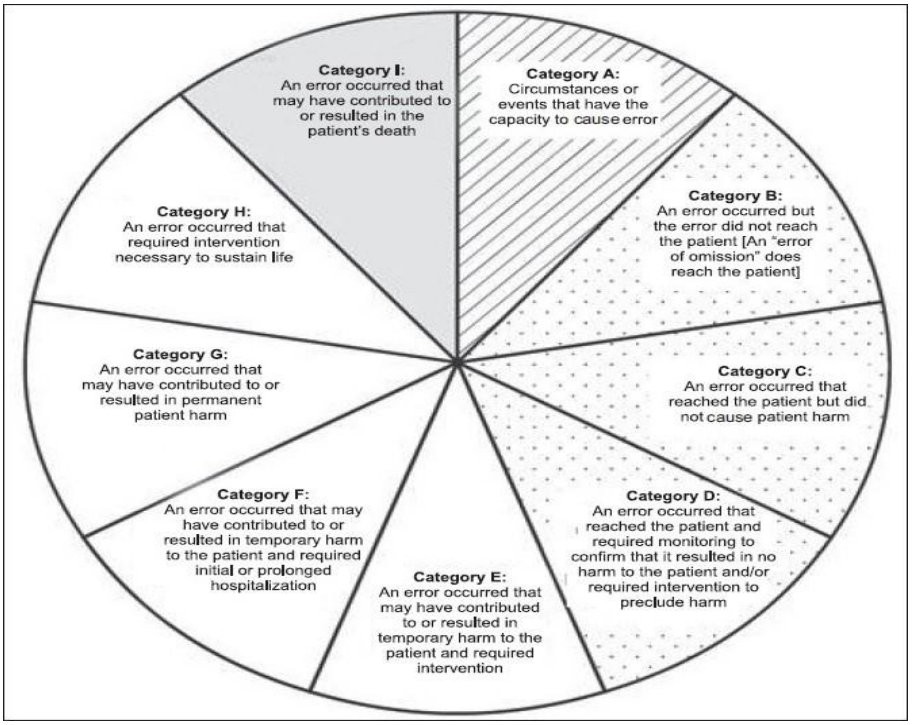

Figure (1): NCC MERP medical error index ***(Kothari et al., 2010).***

No anesthetist will complete his or her career without making a drug error at some stage. Most errors are of minor consequence, however, serious morbidity and mortality resulted from clearly preventable events. Some of the errors were classified as dangerous with the potential to cause serious hemodynamic or neurological damage. For example, one patient suffered a cardiac arrest due to wrongful administration of adrenaline instead of oxytocin during a cesarean section. In the patient whom there was a medication error, untoward sequelae ranged from a brief apnea, sedation, tachycardia and cardiac arrest to delayed recovery from anesthesia ***(Nwasor et al., 2014).***

It is recognized that drug errors are causing a substantial global problem as many results in harm to patients and increased cost to health care providers and anesthesia is not an exception to it. Medical errors erode not only a patient's but a family's confidence in health care organizations, public confidence also suffers due to these errors. The error of one moment becomes the sorrow of whole life hence, memory of errors can haunt the provider for years. Anesthesiologists have been charged for manslaughter and homicide ***(Kothari et al., 2010).***

Types of Drug Errors in Anesthesia

Drug error is a major cause of morbidity and mortality in medical profession, and anesthesia is not an exception to it. Man, medicine, machine and modus operandi are the main contributory factors to it ***(Kothari et al., 2010).***

I-Syringe or drug preparation errors:

The most important feature in this error was the large number of errors involving drugs in syringes of similar size and drug preparation error, suggesting that these errors occur frequently and the need to re-evaluate our drug administration routines to avoid these harmful occurrence. There are four groups which are analysed together as syringe or drug preparation errors for both contributing factors and suggested corrective strategies ***(Abeysekera et al., 2005).***

1-Syringe swaps:

A syringe swap occurred when a drug was given from a syringe whose contents were correctly labeled, but the drug was not the one intended. The main drugs involved in syringe swaps were opioids, neuromuscular blocking agents, reversal agents, benzodiazepines, vasopressors, and local anesthetics ***(Abeysekera et al., 2005).***

The low incidence of medication errors in early reports may be related to the study design, the retrospective nature of studies or the fact that minor errors were underreported. Of the six studies since the Webster study in 2001, the reported incidence of medication errors, type of error and the drugs involved in errors were found to be similar and unchanged among all of the international studies over an eleven years period ***(Cooper and Nossaman, 2013).***

2-Syringe label error (Drug swap):

A wrong drug ampoule labeling error occurred when the contents of the syringe were different to that indicated on the label or to what was expected to be in the drug ampoule used. This error occurred when the drug was prepared, either due to drawing up from an incorrect ampoule or mislabeling the syringe once it was drawn up . Inconsistency among drug manufacturers in drug containers and labeling remains a well known risk and has been a long standing point of controversy. Although some have advocated that all ampoules should be identical to ensure that the label is read carefully, it is recognized that human tend to see what he expect to see and words are not usually recognized by what is written but by their shape (The Poggenorf effect). Drugs involved in ampoule labeling

errors were similar to those involved in syringe swaps ***(Abeysekera et al., 2005)***.

- ***Intrathecal injection of a wrong drug as a drug swap error:***

Spinal anesthesia is relatively safe with few complications that can be easily managed. Opioids or clonidine can be added to local anesthetics to improve the quality of the block. Major complications that has been attributed to human errors like lake of vigilance, wrong labeling or presentation of syringes and ampoules or underestimation of the double checking concepts were reported ***(Antwi-kusi et al., 2013).*** Accidental intrathecal injection is a catastrophic event that when it happens, the anesthesiologist have to manage it. Unfortunately no unique clinical guideline for management was proposed. The outcome from this medical error varies from transient neurological symptoms to permanent neurologic damage and death ***(Ali et al., 2014).***

Accidental intrathecal injection of trenaxemic acid (TA) :

TA is generally used in the treatment of excessive bleeding. It is a synthetic lysine analogue that has strong antifibrinolytic activity. Plasminogen binds to fibrin to form plasmin which in turn degrades fibrin into fibrin

degradation products. TA blocks the lysine binding sites on plasminogen and prevents interaction with fibrin ***(Sabzi et al., 2009).***

Little is known about the effect of direct intrathecal administration of TA in humans. Wong et al. reported the first case of inadvertent intrathecal injection of 75mg TA in an 18 years male scheduled for appendicectomy. He developed clonic convulsions that progressed to a generalized seizure which treated with IV diazepam and the patient recovered without any sequalae. De leede et al have reported a case of 68 years old man who accidentally received an intrathecal injection of 50 mg TA, immediately after injection he developed status epilepticus, the outcome was complicated with hypotonic paresis of all four limbs, which resolved but resulted in residual bilateral peroneal palsy. Yeh et al reported that seizures and refractory ventricular fibrillation after accidental intrethacal injection of 500 mg of TA were associated with fatal outcome ***(Butala et al., 2012).***

Massive inadvertent intrathecal injection of TA was found to trigger myoclonic jerks, refractory ventricular arrhythmia and cardiovascular collapse that did not respond to resuscitation ***(Raghu et al., 2013).*** The exact mechanism by which TA induces seizures or ventricular fibrillation is unknown. Topical application of TA to the cerebral cortex

produces seizures. Myoclonus could arise from cerebral cortex, brain stem, spinal cord, peripheral nerve and spinal roots, some authors have linked it to cerebellar dysfunction. There are two types of myoclonus arising from the spinal cord; spinal segmental myoclonus and propriospinal myoclonus. The first muscle activated is usually from the thoracic cord, with upward and downward spread resulting in generalized myoclonus. TA induced seizures result either from direct cerebral ischemia secondary to decrease in regional and global cerebral blood flow or blockage of gamma-aminobutyric acid (GABA)-A receptors that govern opening of chloride channels causing reduced excitability blockage and neuronal hyperpolarization. TA results in lowering of depolarization threshold and enhanced excitotoxicity. In an experimental study, the drug caused intracranial and systemic hypertension and epilepsies. Very high doses of the drug would cause massive sympathetic discharge as evidenced by initial hypertensive response and subsequent ventricular arrhythmias reported in some patients. The treatment should include administration of anticonvulsants, intensive hemodynamic monitoring and possibly, cerebrospinal fluid (CSF) lavage ***(Butala et al., 2012).***

Accidental intrathecal injection of atracurium:

Neuromuscular blockers' (NMBs) effect in the CSF is unknown, although several observations have indicated that NMBs are not inert, when injected to the CSF, resulting in adverse reactions like hemodynamic changes and muscle relaxation. NMBs may activate or inhibit subtypes of nicotinic acetylcholine receptors in central nervous system (CNS). The important difference between central and neuromuscular receptors is that the brain subtypes of nicotinic acetylcholine receptors are seven times as permeable to calcium as neuromuscular junction receptors. Non-depolarizing NMBs are highly ionized, more lipophobic and rarely cross the Blood–brain barrier (BBB). Direct or accidental brain injections of NMBs such as gallamine or tubocurarine have been associated with convulsions and neuronal damage. The evidence showed that NMBs causes excitement and seizures when administered to the CNS. Autonomic dysfunction, weakness, neuromuscular blockade and neuronal death have been also observed. Salihoglu et al described generalized hypotonia, tachycardia, hypotension, diplopia and general discomfort after an accidental subarachnoid injection of atracurium. Hemodynamic changes were thought to be due to direct histamine releasing actions related to the intrathecal atracuruim injection and this idea was supported by the short duration of hemodynamic changes ***(Zirak et al., 2011).***