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DEATH BY DECIMAL

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CONTENTS

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INTRODUCTION

Medication safety is a crucial part of patient safety in anaesthesia and critical care. Anaesthesia is one of the few specialities where drugs are prescribed, dosages calculated, drawn up and administered by the same person or team of people.[1] Critical care brings different challenges in that patients are on multiple drugs and infusions simultaneously. The drugs administered are frequently of narrow therapeutic index which adds to the need for precision, and therefore the probability of increased chance of drug errors.

INCIDENCE

Drug errors are common in hospitals. A United States study from 2003 found that up to 98000 US deaths annually were attributable to medical errors, a large proportion of these are due to drug errors.[2] The Institute of Medicine (IOM), an agency that investigates the safety of healthcare delivery, reported in 2000 that a total of $29 billion is spent each year on preventable adverse events, and $2 billion of this sum is attributed to adverse drug events (ADEs).[3]

In anaesthesia there is a worldwide problem with drug errors[4]. A new Zealand study found that 89 percent of anaesthesia providers admitted to at least one drug error in their practise and that 12,5 percent of these may have caused some harm to the patient.[5] In South Africa, in a similar study, 39.3 percent of respondents admitted to at least one drug error in their careers.[6] Research done in 3 South African public hospitals revealed a drug error rate of 1 in 247 cases when self-reported by anaesthetists.[7]

When the administration of anaesthesia was independently observed and charts were later reviewed for drug errors (DEs) it was found that about 1 in 20 of all drug administrations contained a DE and or adverse drug event (ADE).[8] This Study by Nanji and coworkers in 2015 is potentially a landmark study as this rate of DEs is much higher than any reported before. 277 operations were observed and 3671 medications were administered. 153 DEs occurred and about one third of these caused an observable ADE. This high error rate found is surprising. First, his could be due to the fact that the errors were observed rather than self-reported or incident reporting. The incidence is likely to be much higher when detected by an observer than through self-reporting. Second, the observers recording the events were experienced anaesthetia care providers. This could be why there is a higher rate compared to other studies. There are many reasons why why DE and ADE rates could be higher at other institutions. The study was done at the Massachusetts General Hospital (Boston, Massachusetts), leaders in medication safety. The institute also uses bar-code-assisted syringe labelling system and electronic information systems that record anaesthesia. The major criticism of the study is that the categorization of events is subjective and still needs to be validated.

DE's are a common source of litigation. An analysis of closed medico-legal claims against Anaesthesiologists showed that 52% of the adverse events resulted from drug-related adverse events.[10]

In critical care medical errors are common ranging from 1,2 to 947 errors per 1000 ICU days with a median of 106 errors per 1000 ICU days[(11)12.] ADE were found in a medical ICU with an incidence of 127,8 per 1000 patient days(13). Another study found the rate of ADE to be higher in medical ICU's than surgical ICU's, 25 versus 14 ADEs per 1000 patient days.[(14)]

As there is no uniformity in methods of reporting, definitions and collection of data, it is very difficult to establish an accurate incidence for DE's. Added to this is the fear of blaming, litigation and defamation.[(15)]

DEFINING ERROR

There are two types of failures that culminate in adverse events

- Active failures – these are unsafe acts committed by individuals who are in direct contact with the patient. They encompass slips, lapses, fumbles, mistakes and procedural violations.
- Latent failures – are the inevitable conditions within a system that lead to errors within the workplace such as time pressure, understaffing, inadequate equipment, inexperience and fatigue.

Managing human error in general has two approaches:

- Person approach – this is focuses on the fallibility of individuals, that would be the tendency to forgetfulness, inattention, or moral weakness.
- System approach – focuses on the conditions under which people work and tries to build defences to avert errors or lessen their effects.

Defining error is important as active failures are usually due to individual mistakes (which may be random) and culture of naming and shaming is not conducive to reporting error and finding solutions. Latent failures are more preventable as they are more predictable and changing a system may lessen this type of failure. We can learn from high-reliability organisations such as the military which knows that humans are prone to error and tries to make the systems more robust for error prevention. They assume that humans are variable and that active failures will occur and practise endlessly for emergency situations.[(16)]

Table 1: Definition of medical errors([15])

Medical error	The failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim
Drug error	Any error in the medication process, whether there are any adverse consequences or not
Adverse drug event	Any injury related to the use of a drug. Not all adverse drug events are caused by medical error or vice versa
Preventable ADE	Harm that could have been avoided through reasonable planning or proper execution of an action
Near miss	The occurrence of an error that did not result in harm
Slip	A failure to execute an action due to routine behaviour being misdirected
Lapse	A failure to execute an action due to lapse in memory and a routine behaviour being omitted

TYPES OF DRUG ERRORS

Wrong drug

This may be due to a several factors which complicate the delivery of drugs:

- Look-alike drugs and syringe swaps – there have been several reports in the literature about the wrong drug given due to similar looking ampoules. In New Zealand a doctor was charged with manslaughter for giving Dobutamine instead of Dopram.[17] Thiopentone with its yellowish colour can easily be confused with some of the prophylactic antibiotics given. In one report Thiopentone was given instead of antibiotic prophylaxis[18] and in the NAP5 report on awareness, the antibiotic Cefuroxime was given instead of Thiopentone.[19] In Kwa-Zulu Natal, South Africa, cefazolin and ceftriaxone are presented in very similar vials for reconstitution and colleagues have reported giving the drug ceftriaxone inadvertently for surgical prophylaxis. Although this seems innocuous, it may contribute to antibiotic resistance of an antibiotic frequently used for treatment of infection. In obstetric anaesthesia, the practice of drawing up suxemethonium as an emergency drug has resulted in the drug being given instead of syntocinon, leading to awake paralysis. Fentanyl and Suxemethonium have also been implicated in awake paralysis as they are often drawn up in a 2ml syringe and in the UK have similar looking ampoules.[19, 20]

  With the number of drugs and the number of pharmaceutical companies manufacturing the same drug on an increase, the incidence is likely to increase.[21]

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Figure 1: Unlabelled syringes containing solutions of inj. thiopentone (A) and inj. ceftazidime (B)

Figure 2: Look-alike bottles of inj. metronidazole and inj. Atropine

- Unlabelled syringes(22)

Drug dosage calculation errors – are common causes of drug errors. This is where the topic for this booklet originated and the reports of dosage calculation errors are seen in the media.[(23)]

The dosage calculation ability of doctors in Australia has been found to be less than optimum.[4] The mean score for all levels was 72%. Junior staff (< 3years experience) in hospitals were found to perform worse on drug dose calculation tests than the other clinicians, scoring a mean of 57.8%. Subgroup analyses showed that senior doctors and those in critical care specialties (intensive care, emergency medicine and anaesthesia) achieved significantly higher actual scores than junior doctors and those in non-critical care specialties, respectively.[(19)]

Although doctors in anaesthesia and intensive care scored better, it is important to remember that in South Africa and other developing parts of the world, that junior doctors or interns are frequently asked to perform anaesthesia and manage emergencies or critically ill patients.[(24)]
The most difficult type of drug calculation errors are the percentage and ratio calculations.[(25, 26)] Medical students as well as doctors have the most trouble with these kinds of calculations. The most common agents that are used that require these types of calculations are local anaesthetics, adrenalin and mannitol.

Other common drug calculation errors that are made are those that require infusion (e.g., micrograms per kilogram per minute). The most common place that this has been studied is ICU and common errors are those related to preparation, dose and infusion rate.[27] Acetylcysteine has a complex dosing schedule. Research done in ICU's in the UK showed that 5% of incorrect dosing of acetylcysteine was due to calculation errors.[28]

Intravenous paracetamol has been reported to be involved in drug error. It is presented as a 10mg/ml solution. The dosage is then calculated and administered in millilitres instead of milligrams resulting in a ten-fold overdose.[29]

Errors of omission may be those of omitting to give prophylactic antibiotics which are indicated.

Errors of wrong route may also occur with disastrous consequences – when epidural/peripheral nerve catheter local anaesthetic infusions are given intravenously[30] and when intravenous drugs such as vincristine are given intrathecally.[31]

ICU

The same types of drug errors that occur in the ward are commonplace. The administration of a single dose of any drug to the patient in critical care requires at least 80 - 200 individual steps at different stages.

The frequency with which drug errors occur at each step is written in brackets:

- Prescription (17%)
- Transcription (11%)
- Preparation (14%)
- Dispersion
- Administration (53%)

ICU errors also occur when patients are discharged to other wards and unnecessary prescriptions are continued or the patients usual chronic medications are not given.[15]

Never events

'Never events' are defined as 'serious, largely preventable patient safety incidents that should not occur if relevant preventive measures have been put in place'.[32]

Many of these never events relate to the perioperative period and the ones related to drug errors are listed below:

- Wrongly prepared high-risk injectable medication
- Maladministration of potassium-containing solutions
- Wrong route administration of chemotherapy
- I.V. administration of epidural medication
- Maladministration of insulin -
- Overdose of midazolam during conscious sedation
- Opioid overdose in an opioid-naıve patient
- Wrong gas administered

RISK FACTORS FOR DRUG ERRORS

Doctors asked what the causes were for their drug prescribing errors on the wards cited business, fatigue, being interrupted, poor knowledge of a particular drug or were confused by looking after other patients teams.[33]

Cooper and colleagues[34] asked doctors what risk factors were associated with drug errors during anaesthesia specifically. They found that inadequate experience and unfamiliarity with equipment were the most common reasons for drug errors. Other risk factors were haste, inattention, carelessness and odd working hours.

Fatigue

Fatigue is common in modern day shift workers and likely contributes to drug errors. The effects on the cognitive function of the anaesthetist are summarised in table 2.[35] A review of the first 10 years of the Australian Incident
Management System reported that 2.7% of severe incidents were fatigue related. Additionally, the most common errors reported were drug errors which were four times more likely to occur if fatigued.[36] A survey of New Zealand Anaesthetists reported that up to 86% of respondents had made a medical error that they ascribed to fatigue.[37]

Decreased vigilance
Impaired memory and learning
Delayed reaction times
Loss of pro-activity and decreased decision-making
Increased risk taking and tolerance of error
Decreased psychomotor performance
Increased lethargy
Disregard of non-important information
Inefficient communication

Table 2: Cognitive effects of chronic sleep loss and fatigue

Environmental risk factors

It is suggested that more errors may be made during the night when healthcare workers are tired or busy with emergency cases but evidence shows that the risk of drug error is higher during the day time.[38]

ICU's are busy, stressful places to work and patients often have many drugs by single dose and infusions prescribed.

PREVENTION OF DRUG ERRORS

The cause of drugs error is multi-faceted; so many different interventions may be beneficial. These interventions should be systematic and based on the available evidence. Unfortunately the available evidence is based on evidence which is largely expert opinion. This is the lowest level of evidence, but Merry and colleagues[39] have tried to rank this evidence to see which expert opinions are more common. They arrived at 5 recommendations for the injection of intravenous drugs in anaesthesia:

1. The label on any drug ampoule or syringe should be read carefully before a drug is drawn up or injected
2. The legibility and contents of labels on ampoules and syringes should be optimised according to agreed standards
3. Syringes should (almost) always be labelled
4. Formal organisation of drug drawers and workspaces should be used
5. Labels should be checked with a second person or a device before a drug is drawn up or administered

These 5 recommendations were also applied to drug errors or near misses to see if they were validated. They also identified further recommendations, based on reported incidences that would not have been prevented by the above 5 steps.

These are:

1. Error during administration should be reported and reviewed. This has to do with changing from a culture of blame to a culture of safety. This is where reporting of errors is encouraged so that solutions can be found to problems. Humans are prone to error and it is usually the systems which we work in which are faulty (latent errors).
2. Management of inventory should focus on minimising the risk of drug error. (e.g. a drug safety officer and/or a pharmacist should be appointed for the operating theatres and any changes in presentation should be notified ahead of time).
3. Look-alike packaging and presentation of the drug should be avoided where possible.
4. Drug should be presented in prefilled syringes rather than ampoules – this means that pharmacists would draw up the drugs. There is still a risk of error but it is less as the pharmacist is usually not distracted, has someone double checking with them and draws up several of the same drugs at the same time.
5. Drug should be drawn up and labelled by the anaesthesia provider himself/herself.
6. Colour coding by class of drugs should be according to an agreed national or international standard.
7. Coding of syringe according to position or size should be done.

Figure 3. Standard colours of induction agents (yellow), non-depolarising neuromuscular blockers (red) and hypnotics(orange)

Physicians
• Awareness of risk factors*
• Medication reconciliation† (resulted in 57% RR reduction in discharge orders being changed) [40]
• Pharmacology education[41]
• Prescribing vigilance among physicians caring for patients with renal or liver failure*
• Good handover technique*
Nurses
• Awareness of risk factors
• Pharmacology education
• Second check*
• Good handover technique*
Pharmacists
• Medication reconciliation† (resulted in 1 medication order being changed for every 2.5 patients admitted)
• Satellite pharmacy[42]
• Support for dose adjustments for patients with renal or liver failure*
Unit directors
• Elimination of extended physician work schedules† (resulted in a 17% reduction in serious medication errors)[43]
• Computerized physician order entry (effect on medication error in the ICU unclear [RR 87% to > 450%]; no evidence of improved patient outcomes)14–16
• Clinical decision support systems17 (improved practitioner performance in 19 of 29 drug dosing or prescribing system studies‡)
• Computerized intravenous devices18,19 (no effect on serious medication errors [RR 1.19] or adverse drug events [RR 1.04])
• Pharmacists' participation in rounds (reduces rate of adverse drug events due to prescription errors by 66%)20
• Standardized protocols (protocol-specific errors reduced to 0%–1%)22,23
• Screening programs for psychological distress33
• Bar code technology74–76
• New staff orientation (including residents)77–85
• Adequate nurse staffing86–89
• Intensivist staffing90
• Adequate working conditions and caregiver fidelity*
Organization
• Culture of safety91–93
Note: RR = relative risk.
*No clear evidence.
†Prevention methods identified in articles that satisfied our search criteria included a summary of effect estimates.
‡Computerized decision support system effect estimate from Garg et al.94

Table 3: Strategies for preventing medication errors in the intensive care unit (ICU)

CLOSED LOOP SYSTEMS – THE WAY FORWARD?

We have seen the use of closed loop systems used in neonatal temperature control but the applications of closed loop systems(CLS) to sedation, anaesthesia, medication delivery, haemodynamic management and ventilation control.[44]

The application of these systems to medication delivery is particularly interesting as it may eventually decrease the amount of drug errors. Anaesthesia is a busy environment where lots of decisions and titrations of drug doses need to be made in ill patients. Multitasking has been shown to cause lapses in adherence to protocol in trauma resuscitation, regardless of vigilance or intent[45], and this can likely be extrapolated to anaesthesia. The use of computers to give the anaesthetist more time to make the critical clinical decisions may also be of benefit.

Four different examples of drug CLS highlight the possible benefits:

- Phenylephrine has been used in a CLS for treatment of hypotension during spinal anaesthesia for caesarean birth. The main benefit is less intensive therapy from the anaesthetist and the authors found that there was less nausea and vomiting. Systolic blood pressure was maintained in at a mean of 7.0% below baseline, with 2.5% fluctuation.[46]
- Norepinephrine weaning in ICU using a CLS incorporating fuzzy logic decreased the weaning time significantly.[47]
- Glucose control in ICU has shown benefits in tight control but the risks of hypoglycaemia are higher. A CLS with continuous glucose monitoring and Insulin infusion (which has proved itself on an outpatient basis) may be the answer to the avoidance of hypoglycaemia in intensive insulin administration.[48]
- Anaesthesia can be provided with closed loop systems. Propofol has been used together with BIS for sedation and general anaesthesia and has proven effectiveness in different patient populations. Propofol in a CLS provides a higher level of predictability than with hand titration alone and target levels are achieved with greater precision.[49]

Limitations and considerations in the use of CLS in general:

- Regulatory problems – large investments are necessary before a return is seen on these systems.
- Technical problems – Physiological systems are extremely complicated. They have intrinsic feedback systems which are difficult to predict and produce noise that monitors can misinterpret.
- Risk transfer function. See figure

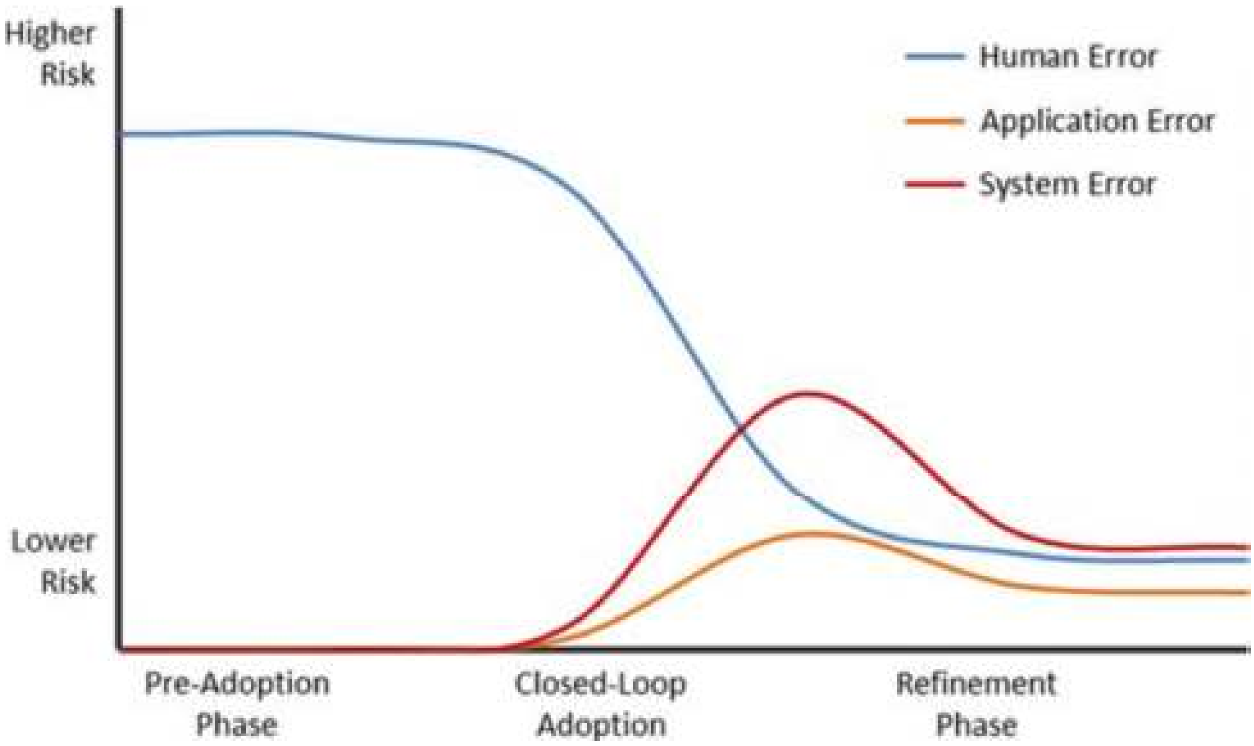

Figure . The risk-transfer function with introduction of closed-loop control. The preadoption phase shows a hypothetical risk level for human error in some tasks; in this discussion, this would be titration of a drug to a patient. When a closed-loop system is implemented for titration, the human risk will decrease (although not to zero), and new risks are introduced. The first is "application error"—the risk that the closed-loop is used on an inappropriate patient it was not designed to manage, resulting in improper management. The second is "system error"—an error in the mechanical or software components of the system that results in improper drug infusion. The net risk after adoption should decrease the total risk to the patient to justify adoption in the first place, and over time the system should be refined and improved to further reduce all 3 risk profiles. The specific risk levels will vary greatly depending on the application and the closed-loop system itself. (Note that other drug-related risks, for example, compounding errors in the pharmacy or risk of allergic reaction in the patient, would remain constant through time in this scenario and are not considered in the graph.)[(44)]

If there is greater precision in dosing there is unlikely to be as many errors related to under dosing and overdosing of medication.[(44)] There may also be less distractions allowing the clinician to focus on clinical decisions. This technology is in its infancy but may well be a routine part of anaesthesia in the future.

CONCLUSION

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