A prospective, observational study on identification and measurement of Usage pattern of High-risk medication in High- Intensive Care Unit (HICU)

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ABSTRACT: Background: High-alert medications can also be defined as those medications which causes the highest risk of injury when misused, either due to a slim therapeutic window or to previous serious adverse events which was reported. These medications are not always the medications that most frequently lead to adverse events, but when not used as intended, these medications have the most serious consequences. The primary objective of the study is to identify and to measure the usage pattern of HAMs prescription and also to measure the combination therapy of HAMs in different age groups.

Method: The data collected from HICU. Patient case sheet with at least one high risk medications is analyzed and data has been collected based on inclusion criteria. Usage pattern of high-risk medication in different age groups is identified. Storing and labelling of HAMs in HICU is observed.

Result: A total of 65 prescription were analyzed in which males 41(63%) and females 24(37%) which shows the males were dominating over female patients. After analyzing the 65 prescriptions total of 140 HAMs were obtained, in that insulin 29(21%) was found to be highest scale followed by heparin 24(17%) and bisoprolol 23(16%). Considering the different age groups of patients, old adults/geriatrics (60-99 years) were the highest in numbers (54%) and followed by young adults (20-39 years) age groups. Combination therapy of Midazolam and Fentanyl is observed commonly. Almost 10% of patients were organ impairment in which renal impairment patients were maximum in numbers. Six DDI and two ADRs was also analyzed. Around 63% of patients are prescribe with LASA drugs.

Conclusion: In the study, the most frequently used HAM was found to be insulin29(21%) followed by heparin 24(17%) and Bisoprolol 23(16%). Males’ patients are predominating over females where males 41(63%) and females 24(37%). Diabetes mellitus, hypertension and bed ridden patients in the HICU are the reason for prescribing HAMs in this study. Six DDI and two ADRs also identified.

Keyword: High alert medications (HAMs), ISMP (Institute for safe medicines practices), ADRs (adverse drug reactions), MEs (medication errors), DDI (drug-drug interactions)

INTRODUCTION:
High risk medications have narrow therapeutic range and high risk of causing significant patient harm due to unintentional administration or dosing error. High-alert medications pose the highest risk of injury when misused due to a slim therapeutic window or previous adverse events, causing severe consequences when not used properly. ICUs are vital for drug usage studies due to severe illness, chronic ailments, and extensive use. Inaccuracy in medication usage occurs at all stages, including look-alike, sound-alike (LASA) errors, resulting in incorrect prescriptions and administration. Around 27% of hospital prescribing errors result from inaccurate medication histories, with older patients and multiple medications are more susceptible. Incorrect drug selection can lead to errors in patient care, including drug-drug interactions, invalid indication, inappropriate dose, multiple drugs for the same condition and longer therapy duration. Medication safety is defined as freedom from preventable harm with medication use (ISMP Canada, 2007). Medication safety issues can impact health outcomes, length of stay in a healthcare facility, readmission rates, and overall costs to healthcare system. The first step in improving medication safety is to identify medication errors and develop strategies respectively to improve the quality of health care provided.

The Medication Error Reporting System (MERS) has identified high alert medications as high-risk ones that could cause harmful incidents. These medications require special safeguards to reduce errors and ensure patient safety. The top five high alert medications are insulin, opiates, narcotics, injectable potassium chloride, intravenous anticoagulants, and sodium chloride solutions above 0.9%. Special precautions and error prevention strategies will be implemented to prevent harm with identified high alert medications in healthcare facilities.

Various risk factors associated with high-risk medications include different administration routes, incorrect infusion rates, drug preparation, dilution, and calculations can cause confusion between IM, IV, intrathecal, and epidural preparations. Misinterpretation
of medication orders, incorrect abbreviation usage, and product availability such as LASA drugs can also lead to overdose. Ambiguous labeling, including unclear concentration and volume information, can lead to look-alike, sound-alike (LASA) errors. The FDA and ISMP have published lists of LASA errors, and pick-lists with similar drug names can increase the risk of drug selection errors.\(^8\)

Certain strategies must be adopted in order to avoid errors with Look Alike Sound Alike (LASA) Medications which includes: Procurement, Storage, Prescribing, Dispensing, Administration, Monitoring, Information, Patient Education and Evaluation. The ISMP predicts that name and labeling confusion contributes to up to 50% of medication errors. A nurse accidentally received daunorubicin instead of prescribed idarubicin due to a color difference. To avoid medication errors, use Tall Man lettering to differentiate sound-alike medications and use additional warning labels for look-alike medicines. Examples includes metFORMIN and metoPROLOL.\(^9\)

In 2006, the Institute of Medicine reported 380,000-450,000 preventable adverse drug events (ADEs) in hospitals due to medication errors, primarily in prescribing, dispensing, and administering stages.\(^6\) Similarly, a study of 280 nurses found that they had insufficient understanding of high alert medication (HAMs) and ICU training. A 93% response rate showed that nurses with a master's degree, those in the ICU ward, lead nurses, and male nurses were the most knowledgeable. However, inconsistencies between doctors and nurses and no clear standard operating procedure for HAMs were common difficulties reported.\(^11\)

In summary, high-alert medications pose the highest risk of injury when misused due to a slim therapeutic window or previous adverse events, causing severe consequences when not used properly. ICUs are vital for drug usage studies due to severe illness, chronic ailments, and extensive use. This study aimed at identification and measurement of usage pattern of high-risk medication in different age groups. It also analyzed the frequency of the high-risk medications prescribed among patients and measured the combination high alert medication (HAMS) prescription.

Medication errors (MEs) are preventable; however, they can result in patient harm and in increased expenses in the healthcare system in terms of hospitalization, prolonged hospitalization and even death [1–8]. In a review from 2007, adverse reactions (ARs) were found to occur in 6.1% of all hospitalizations. Of these, 46% were preventable, that is MEs [6]. MEs are considered ARs that are preventable in contrary to non-preventable ARs that develop despite correct use of drugs. Screening interventions are designed to identify disease and thereby enable earlier intervention and management in an attempt to reduce mortality and morbidity [9]. The idea of creating a screening tool, an algorithm or a clinical decision rule to capture patients with ARs in general is not new [10–15]. Different approaches have been used to develop tools to assist risk assessment or to capture ARs. A review from 2012 evaluated electronic AR detection using electronic triggers [12]. The authors found a wide variety of detection rules, with a large variation in sensitivity (40–94%) and specificity (1.4–89.8%), making it difficult to draw conclusions of the overall efficacy of electronic detection. Medication errors (MEs) are preventable; however, they can result in patient harm and in increased expenses in the healthcare system in terms of hospitalization, prolonged hospitalization and even death [1–8]. In a review from 2007, adverse reactions (ARs) were found to occur in 6.1% of all hospitalizations. Of these, 46% were preventable, that is MEs [6]. MEs are considered ARs that are preventable in contrary to non-preventable ARs that develop despite correct use of drugs. Screening interventions are designed to identify disease and thereby enable earlier intervention and management in an attempt to reduce mortality and morbidity [9]. The idea of creating a screening tool, an algorithm or a clinical decision rule to capture patients with ARs in general is not new [10–15].

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**METHODS:**

**Study design:**
The present study was conducted in a tertiary care hospital using prospective, observational, study design. The inclusion criteria included: HICU patients – the patients admitted in the HICU who has at least one high risk medication in their prescription, patients of either sex and patients above the age of 18years. The exclusion criteria from the study involved: Patients who do not have high alert medication on their treatment chart and pediatrics patients.

**Methodology:**
This study collected data on daily hospital HICU visits and high alert medication usage in a prospective observational study. Data was collected from patients’ case sheets and followed up during their stay. Demographic details, drug prescriptions, doses, and frequency were recorded. Data was collected from patient case sheets, medical charts, laboratory data, physician notes and ISMP list of HAMs. The formulary’s high-risk medications correspond with ISMP-classified HAMs, and various age groups were identified to determine distribution.

RESULTS:

Age and Gender distribution analysis on usage of High-risk medication:

A total of 65 prescriptions with high-risk medications were analyzed during the study period, out of which 63% were males and 37% were females. Age is one of the major factors in taking medicines especially while administration of high-risk medications. A total of 65 patients of age groups from 13 an above are analyzed in the study period where the age groups of old adults/geriatrics (>60-99) were the highest in numbers (54%) and followed by the young adults (20-39) which is (25%), middle-aged adults (18%) and teenagers (03%). (FIGURE 01)

![Age distribution of male and female patients](image)

**FIGURE 01:** Schematic representation of distribution of HRMs in different age group and gender.

As the figure states, the age groups of old adults/geriatrics (>60-99) were the highest in number to receive HRMs.

Prevalence of High-Risk Medications prescriptions in HICU:

A total of 141 number of high-risk medications were identified in 65 cases at HICU. Out of which insulin (21%) was the most frequently prescribed high-risk medication. According to comparison studies of HAMs prescription dose with the hospital formulary (HICU) recommended dose, prescription dose of Potassium chloride, magnesium chloride, midazolam, fentanyl and morphine were having dose variations from the recommended dose of the HICU. Except those drugs others are prescribed as recommended dose. (FIGURE 02)
FIGURE 02: Schematic representation of frequency of HRMs prescribed in HICU
Out of 141 medications prescribed in HICU, insulin (21%) was found to be the most frequently prescribed high-risk medication.

Distribution of combination therapy of HAMs prescribed in HICU:
Various combination therapy of high alert medications was identified during the study period. Out of total number of patients in the study, 4 patients were found to have combination therapy of high-risk medication. In which Midazolam + fentanyl (50%) was in the lead followed by 50% Dextrose + Insulin (25%) and Morphine + Midazolam (25%). (TABLE 01)

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>COMBINATION THERAPY</th>
<th>NO. OF PATIENTS</th>
<th>PERCENTAGE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50% DEXTROSE + INSULIN</td>
<td>1</td>
<td>25%</td>
</tr>
<tr>
<td>2</td>
<td>MIDAZOLAM + FENTANYL</td>
<td>2</td>
<td>50%</td>
</tr>
<tr>
<td>3</td>
<td>MORPHINE + MIDAZOLAM</td>
<td>1</td>
<td>25%</td>
</tr>
</tbody>
</table>

TABLE 01: Distribution of combination therapy of HAMs in HICU.
Out of various combination of high-alert medications, Midazolam + fentanyl (50%) was in the lead for highest usage.

Distribution of patients based on system impairment:
A total of 10 patients were identified with renal and hepatic impairment where very close monitoring of patients is needed during the time of prescribing high alert medications. Out of 65 cases altogether 10 (15%) cases were organ impairment in which renal impairment (80%) was highest in number and hepatic impairment (20%). (FIGURE 03)
FIGURE 03: Schematic representation of renal and hepatic impairment patients receiving high-risk medications

Patients with impairment where very close monitoring of patients is necessary during the time of prescribing high alert medications.

Out of 8 patients with renal impairment, 3 patients were prescribed with potassium chloride which causes development of hyperkalemia and renal failure. Two patients were prescribed with magnesium sulphate which can cause revere renal impairment. Remaining 3 patients were prescribed with other high-risk medications which does not cause renal impairment. Among two patients with hepatic impairment, one patient was prescribed with heparin which can lead to hepatic impairment if dose adjustment is not corrected.

Distribution of patients based on Adverse drug reactions:
During the study period two adverse drug’s reaction have been observed which was caused by the high-risk medications prescribed to the patients at HICU. Altogether 2(3%) patients were found to have adverse drug reactions caused by high-risk medications. Atropine induced psychosis was settled by discontinuing atropine. Similarly, heparin DAPT induced epistaxis was managed by discontinuation of heparin. (TABLE 02)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Total no. of patients</th>
<th>Patient with ADRs</th>
<th>Type of ADRs</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atropine</td>
<td>1</td>
<td>1</td>
<td>Atropine induced psychosis</td>
<td>Discontinued atropine</td>
</tr>
<tr>
<td>Heparin</td>
<td>24</td>
<td>1</td>
<td>Heparin DAPT induced epistaxis</td>
<td>Discontinued heparin</td>
</tr>
</tbody>
</table>

TABLE 03: Distribution of patients based on ADRs
Altogether 2(3%) patients were found to have adverse drug reactions caused by high-risk medications.

Drug-drug interaction with HAMS prescription:
Drug-drug interactions with HAMS prescription was found during the study where Heparin was highly interacted drugs with other prescribed drugs. (TABLE 04)

<table>
<thead>
<tr>
<th>HAMS drug</th>
<th>No. of patients</th>
<th>Interacting drug</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium sulphate</td>
<td>1</td>
<td>Doxycycline</td>
<td>Decreases the levels of doxycycline by inhibition of GI absorption</td>
</tr>
<tr>
<td>Heparin</td>
<td>1</td>
<td>Azithromycin</td>
<td>Increases effect of heparin by decreasing metabolism</td>
</tr>
<tr>
<td>Heparin</td>
<td>1</td>
<td>Aspirin</td>
<td>Both increase anticoagulation</td>
</tr>
<tr>
<td>Heparin</td>
<td>1</td>
<td>Potassium chloride</td>
<td>Both increases potassium level</td>
</tr>
</tbody>
</table>
Among the various High-risk medications prescribed, Heparin was found to be highly interacting drug.

Various look alike-sound alike (LASA) drugs were found which was prescribed in the prescriptions. LASA drugs of the hospital (HICU) is compared with the LASA drugs prescribed in the prescription. Altogether 4 LASA drugs were found during the study time which confused in the handling of the medicines. Above mentioned LASA drugs are HAMs drugs listed in the HICU and prescribed to 41(63%) individual patients. (TABLE 05)

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**TABLE 04: Drug-drug interactions with HAMs.**

Among the various High-risk medications prescribed, Heparin was found to be highly interacting drug.

**TABLE 05: LASA drugs distributions among the HRM drugs:**

Various look alike-sound alike (LASA) drugs were found which was prescribed in the prescriptions. LASA drugs of the hospital (HICU) is compared with the LASA drugs prescribed in the prescription. Altogether 4 LASA drugs were found during the study time which confused in the handling of the medicines. Above mentioned LASA drugs are HAMs drugs listed in the HICU and prescribed to 41(63%) individual patients. (TABLE 05)

**TABLE 05:**

<table>
<thead>
<tr>
<th>DRUGS</th>
<th>No. of patients</th>
<th>LOOK ALIKE</th>
<th>SOUND ALIKE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enoxaparin 40mg</td>
<td>4</td>
<td>Enoxaparin 60mg</td>
<td>Enoxaparin 60mg</td>
<td>Color/size/label/name</td>
</tr>
<tr>
<td>Noradrenaline 4mg</td>
<td>5</td>
<td>Diazepam 5mg</td>
<td>-</td>
<td>color</td>
</tr>
<tr>
<td>Human Actrapid 40iu/ml</td>
<td>29</td>
<td>Human mixtard 40iu/ml</td>
<td>Human mixtard 40iu/ml</td>
<td>Size/color/name/dosage</td>
</tr>
<tr>
<td>Dextrose 50%</td>
<td>3</td>
<td>-</td>
<td>Dextrose 25%</td>
<td>Name/dosage</td>
</tr>
</tbody>
</table>

**DISCUSSION:**

A study analyzing 65 HICU prescriptions found that males (63%) were more likely to receive hospitalizations than females (37%). This may be due to risk factors like smoking, alcoholism, and road traffic accidents. Old adult/geriatric patients (54%) are the most admitted to the HICU with at least a minimum number of high-alert medications (HAMs). This high number of prescriptions leads to drug-drug interactions, ADRs, and medication errors, causing health problems. The study analyzed 65 patients aged 13-65, with older patients being more prevalent. Safe handling and management of HAMs are crucial for patient safety and care. A study identified 140 high-risk medications prescribed in 65 HICU cases, with insulin being the most frequently prescribed. This is due to increased cases of diabetes mellitus and hypertension, as well as invasive procedures and critical conditions. Anesthetics like fentanyl, midazolam, morphine, and pethidine were found.

Kidney function is crucial for regulating fluids, electrolyte balance, and drug excretion. Kidney failure can result from disease, injury, or drug intoxication. Uremia reduces glomerular filtration, leading to a longer drug elimination half-life. Liver dysfunction affects drug clearance and plasma protein binding, affecting distribution and elimination processes. Portal-systemic shunting in advanced liver cirrhosis decreases pre-systemic elimination, increasing drug absorption. Renal and hepatic impairments increase the risk of prescribing high-alert medications. Dose adjustment and monitoring laboratory parameters can reduce patient risk.

Opioids are commonly used as analgesics during major accidents and surgeries, but their use can cause adverse effects like constipation, respiratory depression, and cardiovascular events. In HAMs prescriptions, 66% of patients use combination therapy, with midazolam and fentanyl being common. Patients with allergies to other medications, such as penicillin, cefixime, paracetamol/amiodipine, and cetirizine, also experience adverse effects.

Data from comparison studies shows dose variations in high alert medications like potassium chloride, magnesium chloride, midazolam, morphine, and fentanyl. These variations may be due to dosage adjustments for safety and better patient care. Hospitals will create a separate hospital formulary and follow international guidelines for handling and use of drugs. Special considerations are applied to highly toxic or narrow therapeutic range drugs, as errors or mishandling can cause severe consequences and contribute to patient risks.

Drug-drug interactions (DDIs) are common causes of adverse drug reactions (ADRs) in the elderly due to poly-therapy. These interactions increase the complexity of therapeutic management and increase the risk of clinically relevant drug interactions, leading to the development of ADRs. Poly-therapy may also determine the “prescribing cascade,” where patients are at risk of developing further ADRs. Heparin is a common drug that interacts with other drugs. DDI can be categorized into pharmacokinetic (absorption,
distribution, metabolism, excretion) and pharmacodynamic (direct effect at receptor function, interference with biological control processes, and additive pharmacological effect).

Adverse drug events (ADEs) are common due to the widespread use of prescription and nonprescription medications. Polypharmacy is the strongest risk factor, with elderly patients being particularly vulnerable. Pharmacists play a crucial system-level role in planning and leading medication safety programs and improvement initiatives, including developing risk-specific protocols, evaluating high-risk processes, evaluating medication error data, implementing new technologies, and fostering robust error reporting processes. Adverse events in diabetes are mainly caused by inappropriate abbreviation, poor knowledge, performance lapses, safety system failures, and poor communication. To prevent errors, it is crucial to recognize correct concepts of insulin dosage, dosage expression, and use a dedicated syringe.

LASA drugs require rechecking color, size, name, and dosage before prescribing, dispensing, and administering. Risk reduction strategies include double check, special labeling, clinical pharmacist review, non-verbal order, proper storage, and ISMP guidelines.

CONCLUSION:
High Alert Medications are frequently associated with harm, the complications arise from the mishandling of HAMs can cause serious life-threatening problems and when they are misused the risk of serious injury or death is high. In the study, the most frequently used HAM was found to be insulin 29(21%) followed by heparin 24(17%) and Bisoprolol 23(16%). Old adults/geriatrics patients are more in numbers as compared to patients below >60 years of age in the HICU. Males’ patients are predominating over females where males 41(63%) and females 24(37%). Diabetes mellitus, hypertension and bed ridden patients in the HICU are the reason for prescribing HAMs in this study.

In the study around 15% of patients out of 65 are with renal Impairment hepatic impairment. This reveals that critical conditions patients are associated with any of the health complications. Various HAMs prescription dose was compared with hospital formulary recommended (HICU) dose and found to dose variations in some of the drugs like potassium chloride, morphine, fentanyl, magnesium chloride and midazolam. Except those other drugs was prescribed as recommended dose. Drug-drug interactions was observed and analyzed wherein Heparin was common and bisoprolol. Altogether 63% of patients were prescribed with LASA drugs where HUMAN ACTRAPID 40iu/ml and HUMAN MIXTARD 40iu/ml was common due to its size, color, name and dosage.

REFERENCES: