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Study on Prescribing Pattern of High Alert Medications in the Medical Intensive Care Unit

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Abstract: *The Institute of Safe Medication Practices (ISMP), the Institute for Healthcare Improvement (IHI), and the Joint Commission (JC) are some of the organizations providing the guidelines concerning the use of high alert medications. According to ISMP, high alert medications are responsible for most of the adverse drug events in the intensive care units. High alert medications are characterized with a narrow therapeutic window, causing blood concentration-dependent critical therapeutic failures or adverse drug events. The top five High Alert Medications that cause adverse events include anticoagulants, sedatives, insulin, opioids, and injectable potassium chloride concentrate. The aim of the present study was to understand the prescribing pattern of High Alert Medications in the Medical Intensive Care Unit as a prospective observational study. The mean age group of the study population was 59.22±49.91 years and a majority (36%) was in late adulthood (51-65 years) stage. The duration of hospitalization varied between 3.50±2.28 days and 33.37±30.33 days. A total of 1227 drugs were prescribed, of which, 223 (18.77%) were High Alert Medications. Injection noradrenalin, fentanyl, midazolam, dopamine, and fosphenytoin sodium were found to be the most frequently prescribed High Alert Medications. Their dilution methods, a rate of infusion, stability, the rate of administration and admixture compatibility were also studied.*

Key words*: High alert medications, high risk medications, adverse drug events, injections, intensive care unit.*

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I. Introduction

Adverse drug events in the Intensive Care Units appear to be caused by a relatively small number of medications, designated as High Alert Medications by the Institute of Safe Medication Practices (ISMP)[1]. These groups of medications include twenty-two categories and twelve specific medications. Most of them are characterized by a narrow therapeutic window, causing blood concentration-dependent critical therapeutic failures or adverse drug events.

High alert medications are the group of medications characterized by the narrow therapeutic window, often causing adverse drug events in the Intensive Care Units. Adrenergic agonists, adrenergic antagonists, anesthetic agents, antiarrhythmics, antithrombotic agents including anticoagulants, Factor Xa inhibitors, direct thrombin inhibitors, thrombolytics and glycoprotein IIb/IIIa inhibitors, cardioplegic solutions, chemotherapeutic agents, dextrose- hypertonic, dialysis solutions for peritoneal and hemodialysis, epidural or intrathecal medications, oral hypoglycemic agents, insulin, inotropic medications, subcutaneous and IV liposomal forms of drugs (e.g., liposomal amphotericin B) and conventional counterparts (e.g., amphotericin B desoxycholate), moderate sedation agents such as dexmedetomidine, midazolam, narcotics/opioids, neuromuscular blocking agents, parenteral nutrition preparations, radiocontrast agents, hypertonic sodium chloride for injection (> 0.9%) are the important categories of High Alert Medications specified by the Institute of Safe Medication Practices (ISMP). EPINEPHrine, subcutaneous epoprostenol, IV insulin (U-500), magnesium sulfate injection, methotrexate oral, opium tincture for non-oncologic use, oxytocin, nitroprusside sodium for injection, potassium chloride for injection, concentrate potassium phosphates injection, promethazine, and vasopressin are the specific medications of High Alert List as per ISMP [2]. The Institute for Healthcare Improvement (IHI) and the Joint Commission (JC) also provides guidelines on using High Alert Medications[3,4]. Though the number of drug categories and specific medications identified as High Alert Medications varies with these agencies, all relevant organizations identify five specific High Alert Medication of classes - anticoagulants, sedatives, insulin, opioids and injectable potassium chloride concentrate as the top five High Alert Medications[5]. Studies are needed to identify the frequently used High Alert Medication in our study site.

II. Objectives and Methodology

To study the prescribing pattern of High Alert Medications in the Medical Intensive Care Unit and to prepare MICU specific High Alert Medication List.

Study design: A prospective observational study.

Study location: The Medical Intensive Care Unit (MICU) of a multispecialty tertiary care private corporate hospital.

Study duration: September 2016 – March 2017.

Sample size: 100 patients.

Inclusion criteria: Patients admitted to the MICU and receiving at least one High Alert Medication along with other medications were included.

Exclusion criteria: Patients admitted to the MICU but not receiving High Alert Medications were excluded from the study.

Method: The study protocol was approved by the Institutional Ethical Committee. Clinical and demographic details of the patients such as age, gender, date of admission, date of discharge, major diagnosis, and co-morbid conditions were recorded in customized data entry forms. Details of High Alert Medications and other medications prescribed, their strength and dosing schedule were also noted down during daily ward rounds. The most commonly prescribed High Alert Medications and their therapeutic classes were identified. Results were expressed as the number of drugs per prescription and mean number of High Alert Medications per prescription. A list of High Alert Medications commonly used in the Medical Intensive Care Unit was then prepared.

III. Results

The prescriptions of one hundred patients admitted to the Medical Intensive Care Unit were reviewed for the use of High Alert Medications. The mean age group of the study population was 59.22±49.91 years and the majority (36%) was in the late adulthood (51-65 years). Sixty-five percentages of them were male patients. Their duration of hospitalization varied between 3.50±2.28 days and 33.37±30.33 days. The mean number of drugs prescribed to the study population ranged from 16.16±12.49 to 42.33±21.33. The demographic details of the study subjects are shown in table 1. Diabetes Mellitus (15.59%), systemic hypertension (13.76%), respiratory disorders (11.01%), renal failure (7.33%), head injury (7.33%) and stroke (6.88%) were a major diagnosis of the study population. A total of 1227 drugs were prescribed which included anti-infective agents (16.95%) followed by anti-ulcer drugs (14.9%), anti-asthmatics (12.6%), anti-emetics (6.76%) and anti-hypertensive drugs (4.56%). Details are summarized Table 2.

Of the 1227 drugs prescribed to the study population, 223 (18.77%) were High Alert Medications. Various High Alert Medications prescribed are presented in table 3. Injection noradrenaline (18.8%), injection fentanyl (13.9%), injection midazolam (11.2%), injection dopamine (8.5%) and injection fosphenytoin sodium (6.7%) were found to be the most frequently prescribed High Alert Medications.

Table no 1: Demographic data (n = 100)

s. no	Age group	No of patients (%)	Mean age (yrs) ± sd	Gender	Duration of hospitalization	No of drugs prescribed
1	Childhood (1-12)	0	59.22±49.91	Male 65	0	0
2	Adolescent (13-18)	0			0	0
3	Early adulthood (19-35)	19			5.34±1.89	16.35±9.47
4	Adulthood (36-50)	12			5.53±1.24	17.81±8.85
5	Late adulthood (51-65)	36			3.50±2.28	16.16±12.49
6	Young adulthood (66-74)	17			4.19±1.93	17.34±9.55
7	Old adulthood (75-84)	14			6.36±1.09	17.44±10.20
8	Old age (85-95)	2		Female 35	33.37±30.33	42.33±21.33

Table no 2: Categories of drugs prescribed (n= 1227)

Drugs	No. of patients	No. of drugs	Percentage
Anti-infective	63	208	16.95
Anti-ulcer	10	173	14.9
Anti-asthmatic	10	148	12.6
Anti-emetic	36	83	6.76
Anti-hypotensive	37	73	5.95
Nutritional supplements	05	68	5.54
Analgesic	20	61	4.97
Anti-coagulant and anti-platelet	22	58	4.73
Anti-hypertensive	46	56	4.96
Anti-epileptic	22	46	3.75
Anti-hyperlipidemic	20	42	3.42
Insulin and OHA	16	35	2.85
Anxiolytics and sedatives	26	30	2.44
Anti-inflammatory	10	27	2.20
Anti- Alzheimers disease	15	24	1.96
Anti-arrhythmic	09	23	1.87
Anti-anginal	16	20	1.63
Liver protective	04	14	1.14
Laxative	03	10	0.81
Antitubercular	02	7	0.75
Eye lubricants	02	6	0.49
Anti-cholinergic	02	6	0.49
Antidotes	03	5	0.41
Anti-cancer	02	4	0.33

Table no 3: Categories of High Alert Medications prescribed in the MICU (n =223)

S.No.	Category	Name of drug	No.	Percentage
1.	Adrenergic agonist IV	Noradrenaline	42	18.83
2.	Opioids IV	Injection fentanyl	31	13.90
		Injection tramadol	5	2.24
		Injection morphine	4	1.79
	Opioids - Transdermal	Opioid analgesic patch	1	0.44
3.	Moderate sedation agents IV	Midazolam	25	11.21
		Lorazepam	1	0.44
4.	Inotropic medications IV	Dopamine	19	8.52
		Dobutamine	10	4.48
5.	AntiConvulsants	Fosphenytoin	18	8.70
6.	Antithrombotic agents: Anticoagulants	Injection heparin sodium	15	6.72
		Injection low molecular weight heparin	5	2.24
		Injection enoxaparin	5	2.24
		Tablet warfarin	1	0.44
7.	Insulin, subcutaneous and IV	Insulin regular	13	5.82
		Insulin isophane/ regular-subcutaneous	4	1.79
		Insulin lispro	1	0.44
		Human insulin-subcutaneous	1	0.44
		Insulin isophane -subcutaneous	1	0.44
8.	Anesthetic agents IV	Atropine	6	2.69
		Lidocaine	1	0.44
9.	Other specific medications	Injection vasopressin	9	4.03
10.	Chemotherapeutic agents, oral	Tablet azathioprine	1	0.44
		Tablet imatinib mesylate	1	0.44
11.	Parentral nutrition preparations	Calcium gluconate	2	0.89
		Sodium bicarbonate 9.5 %	1	0.44

IV. Discussion

Noradrenaline is reported to oxidize during the infusion with saline alone whereas dextrose reduces the oxidation. It is stable in 5% dextrose in water in a pH range of 3.6 to 6.0. Hence, noradrenaline may be mixed with dextrose and saline. Norepinephrine injections have a pH of 3.0 to 4.5. Since oxidation is accelerated at pH > 5.5-6, it should not be mixed with bicarbonate, alkaline buffered antibiotics or barbiturates[6]. Above 6.0, considerable loss of potency may occur. Thus, use of norepinephrine in admixtures with pH above 6 is not recommended. Injection fentanyl was administered as admixtures either with midazolam or with midazolam and atracurium. These admixtures were found to be compatible with each other. Apart from the above admixtures, injection midazolam when administered as an admixture of fentanyl and morphine was also found to be compatible. Midazolam has been associated with respiratory depression and respiratory arrest, especially when used for sedation in noncritical care settings[7,8]. Settings using these medications shall follow continuous monitoring of respiratory and cardiac function. The initial dose and all subsequent doses should always be titrated slowly.

Serious, life-threatening, or fatal respiratory depression may occur with the use of fentanyl. During the initiation of therapy or following a dose increase, it is essential to monitor for respiratory depression**.** Moreover, use with CYP3A4 inhibitors or inducers may change fentanyl plasma levels resulting in a fatal overdose. It is also reported that the concomitant use of opioids with benzodiazepines or other CNS depressants, including alcohol, may lead to deep sedation, respiratory depression, coma, and death**.**

Injection dopamine was diluted with 250 ml or 500 ml of 5% dextrose in water or normal saline and administered by IV infusion. Fosphenytoin was diluted with D5W or NS to a final concentration of 1.5 to 25 mg phenytoin sodium equivalents (PE) /Ml[9]. The infusion rate was not more than 150 mg phenytoin sodium equivalents (PE)/min to avoid serious cardiovascular events. Fosphenytoin sodium USP 75 mg is equivalent to phenytoin sodium 50 mg [10]. Careful cardiac monitoring is needed during and after administering IV fosphenytoin sodium. Although the risk of cardiovascular toxicity increases with infusion rates above the recommended infusion rate, these events have also been reported at or below the recommended infusion rate. In such cases, reduction in the rate of administration or discontinuation of dosing may be needed.[11,12]

Prescriptions of injection lorazepam, an intermediate-acting benzodiazepine, were also noted during the study. Sterile water for injection, normal saline or D5W was used for diluting this medication immediately prior to use. The rate of injection was found to be less than 2 mg per minute.

V. Conclusion

One thousand two hundred and twenty-seven drugs were prescribed in the study population in the Medical Intensive Care unit during the study period, of which, 223 (18.77%) were High Alert Medications. The most frequently prescribed High Alert Medication categories were adrenergic agonists IV, Opioids IV, moderate sedation agents IV, inotropic medications and anticonvulsants and the top five specific medications were noradrenaline, fentanyl, midazolam, dopamine,and injection fosphenytoin sodium. The study also resulted in the preparation of a MICU specific High Alert Medication List which can serve as a useful tool for monitoring adverse drug events.

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