

Analysis of usage of diuretics in medical intensive care unit of SIMS-Shimoga a tertiary care hospital

H. Vedavathi, Shreenivas P. Revankar*

Department of Pharmacology,
Shimoga Institute of Medical
Sciences, Shimoga, Karnataka,
India

Received: 04 August 2015

Revised: 01 September 2015

Accepted: 02 September 2015

***Correspondence to:**

Dr. Shreenivas P. Revankar,
Email: sprevankar@yahoo.com

Copyright: © the author(s),
publisher and licensee Medip
Academy. This is an open-
access article distributed under
the terms of the Creative
Commons Attribution Non-
Commercial License, which
permits unrestricted non-
commercial use, distribution,
and reproduction in any
medium, provided the original
work is properly cited.

ABSTRACT

Background: Patients are admitted in the intensive care unit (ICU) with a history of various acute and chronic clinical conditions associated with organ failures. Compared to the patients admitted in the general wards the mortality and morbidity are high in ICU patients. The patients in ICU are subjected to multiple drugs; diuretic agents are liberally and deliberately used in this setup despite the lack of evidence supporting their benefits.

Methods: The main aim of the study was to know the extent of use of diuretics in the ICU set up, to categorize the use of diuretics in different clinical conditions and different classes of diuretics used. The study also tried to determine adverse events and outcome in critically ill patients. The study was a retrospective cross-sectional of 3 months duration conducted in all patients admitted in the medical ICU of the tertiary care center. The study mainly concentrated on the usage of diuretics and related aspects.

Results: Loop diuretics (54.81%) composed the major class, thiazides (30.84%). Potassium sparing diuretics (7%) and osmotic diuretics (7%) and carbonic anhydrase inhibitors (1%) were the other class of diuretics. The classes of drugs used in ICU along with diuretics were antibiotics (30%), analgesics (9.5%), anti-inflammatory (6.36%), and drugs acting on blood (10.18%) of total drugs used in ICU. Antacids/laxatives (7.3%) and antiemetic (4.8%), the rest of drugs (15%) of drugs used in ICU.

Conclusion: In almost 95% of cases, the combination of other drugs along with diuretics was considered to be rational.

Keywords: Intensive care unit, Diuretics, Rational, Retrospective, Polypharmacy

INTRODUCTION

The intensive care unit (ICU) is a designated area of a hospital facility that is dedicated to the care of patients who are seriously ill. An ICU, also known as an intensive therapy unit or intensive treatment unit or critical care unit, is a special department of a hospital or health care facility that provides intensive care medicine. In 1854, Florence Nightingale left for a Crimean War, where triage, used to separate seriously wounded soldiers from the less-seriously wounded. In 1950, anesthesiologist Peter Safar established the concept of "advanced support of life," keeping patients sedated and ventilated in an intensive care environment. In the 1960s, the importance of cardiac arrhythmias as a source of morbidity and mortality in myocardial infarctions (heart attacks) was recognized. This led to the routine use of cardiac monitoring in ICUs, especially after heart attacks.^{1,2}

ICU cater to patients with severe and life-threatening illnesses and injuries, which require constant, close monitoring and support from specialist equipment and medications in order to ensure normal bodily functions. Common conditions that are treated within ICUs include acute respiratory distress syndrome, trauma, multiple organ failure, and sepsis. Acute liver failure respiratory failure multiple organ dysfunction syndrome, polytrauma coma complications, critical illness polyneuropathy or myopathy critical ventilator-associated pneumonia, etc., are some of the routinely admitted cases in medical ICU.¹ In the modern world, due to advances in the medical sciences separate ICU for medical ICU pediatric ICU, neonatal ICU, psychiatry, trauma ICU, surgical, and post-anesthesia care unit are available. Drugs commonly used in ICU are analgesics, antibiotics antithrombotic, diuretics, inotropes, intravenous (IV) fluids, neuromuscular-blocking drugs; recombinant activated protein C, sedatives, stress ulcer prevention drugs, and vasopressors.^{2,3}

Diuretics also called natriuretic are drugs which cause a net loss of sodium (Na⁺) and water in urine. The majority of diuretics have action on kidneys, i.e., nephrons the functional unit of the kidney. Diuretics can be classified based on efficacy, chemical structure, site, and mechanism of action.⁴ It can be summarized as shown in the Table 1.^{5,6}

METHODS

The study was a retrospective, cross-sectional study conducted for a period of 3 months. The study was carried out in all patients admitted in the medical ICU during the period irrespective of their clinical diagnosis. The study was mainly carried out based on the detailed analysis of the case records of the patients. The patients were divided into two groups those who were on diuretics at least once during their stay in ICU and patients who were not on any diuretics during

their stay in ICU. The patients were subcategorized based on the systems involved and clinical diagnosis. The following parameters were taken into consideration and analyzed: number of days of stay in the hospital ICU, the number of days and dose of diuretics used, and the class of diuretic used. The other drugs used along with the diuretics and an average number of drugs used. Possible investigations carried out and their relevance with the use of diuretics. Mortality and morbidity rate associated with the patients in ICU.

RESULTS

A total of 69 patients were admitted out of which 55 (80%) recovered, mortality was 20%. The cause of high mortality was patients had come with an advanced stage of disease and were aged. The mean age of patients admitted in ICU was 53.6 years. The recovery was better in renal related (100%)

Table 1: The various class of diuretics and their mechanism of action.

Efficacy	Class (site of action)	Mechanism of action	Examples
High	Loop diuretics (thick ascending loop of henle)	Inhibit Na/K/2Cl cotransport	Fruseamide, bumetanide, torsemide, azosemide, ethacrynic acid
Moderate	Thiazides (distal convoluted tubule)	Inhibit Na/Cl cotransport	Chlorthiazide, hydrochlorthiazide, bendroflumethizide, benzethizide, polythizide, clopamide
	Thiazides related (distal convoluted tubule)	Inhibit Na/Cl co transport	Chlorthalidone, metalazone, xipamide, indapamide, quinethazone
Low	Potassium sparing (collecting tubule)	Minerelocorticoid receptor antagonist, inhibitor of renal epithelial Na ⁺ channels	Spirolactone, canrenone, eplerenone Triamterene amiloride
	Carbonic anhydrase inhibitors (proximal convoluted tubule)	Inhibits carbonic anhydrase enzyme	Acetazolamide, dichlorphenamide, methazolamide, dorzolamide, brinzolamide
	Osmotic diuretics (descending loop of henle/proximal convoluted tubule)	Osmotic action increases	Mannitol, glycerine, isosorbide

Apart from this, there are other newer agents like vasopressin antagonists like conivaptam tolvaptam, lixivaptam. Adenosine A1 receptor antagonists like rolphylline

Table 2: The categorization of the patients admitted in the hospital MICU.

System involved	Clinical condition	Distribution		Outcome
		Total	Male/female	
Cardiovascular	MI, CCF, HTN	18	10/8	12
Respiratory	Pulmonary edema, asthma, COPD	12	07/05	10
Gastro-hepatic	Ascitis	10	08/02	09
Renal	ARF, CRF, post-dialysis	15	10/05	15
CNS	Stroke, head injury	03	01/02	02
Multiorgan failure	Multifactorial	05	02/03	00
Septicemia	Various infectious cases	03	02/01	00
Miscellaneous	Others	03	03/01	02
Total		69	43/27	50

MICU: Medical intensive care unit, MI: Myocardial infarction, CCF: Congestive cardiac failure, HTN: Hypertension, COPD: Chronic obstructive pulmonary disease, ARF: Acute renal failure, CRF: Chronic renal failure, CNS: Central nervous system

Table 3: The diuretic indicated and used.

Clinical condition	Diuretic indicated for use	Diuretic used	Inference
Edema			
Hepatic	High ceiling loop	Furosemide	Rational
Renal	High ceiling loop	Furosemide	Rational
Cardiac	High ceiling loop, thiazide	Furosemide, chlorthiazide	Rational
Pulmonary	High ceiling loop	Furosemide	Rational
HTN	High ceiling loop, thiazides	Furosemide, chlorthiazide	Rational Rational
Ascitis	Potassium sparing, high ceiling loop, thiazides	Spironolactone, chlorthiazide, furosemide	Rational
Congestive heart failure	Potassium sparing	Spironolactone	Rational
With blood transfusion	High ceiling loop	Furosemide	Rational
Counteract K ⁺ loss with thiazides diuretics	Potassium sparing	Spironolactone	Rational
Increased intracranial tension	Osmotic	Mannitol	Rational
Hypercalcemia	High ceiling loop, thiazides	No cases admitted	-----
Miscellaneous		Furosemide	Rational

HTN: Hypertension

followed by gastro-hepatic (90%). In cardiovascular and respiratory related conditions, the recovery rate was 80% and 83%, respectively. Septicemia had poor recovery rate at 33% and was worst in case of multi organ failure cases.

The use of diuretics in patients was based on the standard protocol of treatment and on laboratory investigations. The various class of diuretics and different clinical conditions in which they were used is highlighted in the table. They were basically used in cardiovascular, renal and gastro hepatic conditions. In the majority of the cases, the use of diuretics was considered to be rational.

Table 4 represents the various class of diuretics used; it was found that loop diuretics (54.81%) composed the major class followed by thiazides (30.84%). Potassium sparing diuretics (7%) and osmotic diuretics (7%) and carbonic anhydrase inhibitors (1%) were the other class of diuretics used, the newer class of diuretics was not used in this set up, and some patients received combination of two or more class of diuretics. Loop diuretics were used in edema related to hepatic, renal, pulmonary, and cardiac causes and in hypertension (HTN). Potassium sparing diuretics were first choice drugs in ascites and congestive cardiac failure (CCF) and to counter K⁺ loss. Mannitol was found beneficial in conditions associated with increased intracranial tension.

Table 5 represents various classes of drugs used along with diuretics. Antibiotics were the highly prescribed drugs in the ICU, almost every patient admitted in the ICU had received one or the other group of antibiotics as prophylaxis or as curative. The majority of the patient admitted in ICU had a history of diabetes mellitus, HTN or both and were on antidiabetic, antihypertensive, and other related drugs.

Table 4: The various class of diuretics used.

Class of diuretics	Used in number of cases	Total number of doses	Percentage
Loop diuretics	39	815	54.6
Thiazide	12	434	28.4
Potassium sparing	05	104	7.00
Osmotic	05	104	7.00
Carbonic anhydrase	01	15	1.00
Others	00	20	2.00
Total	62	1492	

Table 5: The other class of drugs used along with diuretics.

Class of drug	Total no of doses	Percentage
Antibiotics	6696	30.20
Antihypertensives	1230	5.40
Antidiabetic	2640	11.6
Analgesics	2160	9.54
Anti-inflammatory	1440	6.36
Drugs on blood	2304	10.18
Antacids or laxatives	1656	7.31
Antiemetic	1104	4.87
Miscellaneous	3394	15.00
Total	22624	

The classes of drugs used in ICU along with diuretics were analgesics (9.5%), anti-inflammatory (6.36%), and drugs acting on blood (10.18%) of total drugs used in ICU.

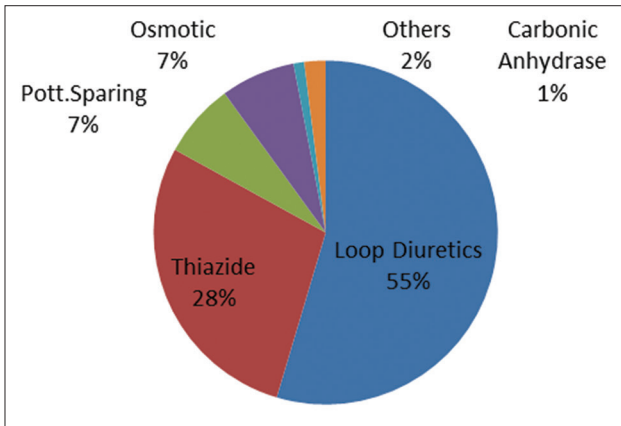


Figure 1: The various class of diuretics used.

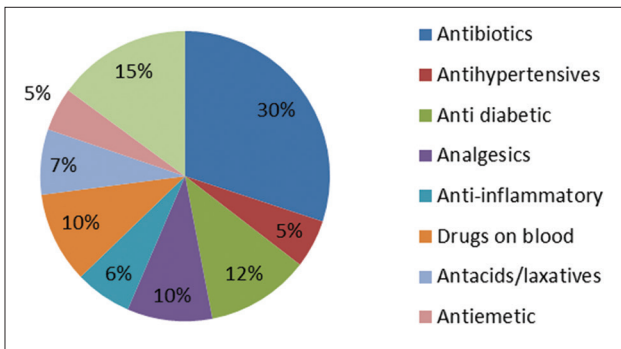


Figure 2: The various class of drugs used along with diuretics.

Antacids/laxatives (7.3%) and antiemetic (4.8%) were prescribed to patients. Apart from these, the rest of drugs constituted 15% of drugs used in ICU. In almost 95% of cases, the combination of other drugs along with diuretics was considered to be rational.

DISCUSSION

Furosemide (lasix) was the most common used drug in the set up. In acute left ventricular failure and acute pulmonary edema it produced alarming effect. In some patients not responding to furosemide IV bumetanide was tried. In CCF patients furosemide, 20-60 mg once daily morning dose was used had better effect.⁷ Higher doses of furosemide in the range of 100-200 mg every 6 hourly benefitted the patient. In a few cases of acute renal failure (ARF) and chronic renal failure (CRF) also furosemide was better used, in ARF loop diuretics convert oliguric ARF to non oliguric ARF, if flushes out the intratubular casts. In CRF also furosemide was the diuretic of choice as it is known to reduce edema due to CRF. In a few cases, furosemide was combined with other diuretics as in the case of HTN and case of severe resistant edema. Furosemide was used for forced diuresis in case of barbiturate poisoning. Here it acts by rapid excretion of acidic drug by diuretic effect as well as alkalization of urine.⁸ In the majority of cases, loop diuretics mainly furosemide was the commonly used diuretic. The usual dose

was 20-80 mg once a day, but in some cases of nephrotic syndrome higher doses were tried.

Thiazide diuretics were the second choice diuretic in our set up. Hydrochlorothiazide was the most common used thiazide diuretic, the others such as chlorthalidone and xipamide, were occasionally used. They were more often used in mild to moderate cases of edema.⁹ In few cases of uncontrolled HTN also the thiazide diuretic was used along with other antihypertensive drugs. In resistant cases of edema, they were used along with loop diuretics. There were no admitted cases of diabetes insipidus or hypercalcemia in ICU. However, it has been found that thiazide diuretics are effective in nephrogenic diabetes insipidus as they decrease positive free water clearance.¹⁰

Potassium sparing diuretics were the third most common used classes of diuretics. Spironolactone was the available drug. Spironolactone was commonly used in cardiac patients mainly to contract K⁺ loss due to thiazides and loop diuretics. It was the drug of choice in ascites patients due to cirrhosis of the liver and nephrotic edema.¹¹ Spironolactone was used along with thiazide diuretics the rationale in its use was. It breaks the resistance to thiazide diuretics and restabilizes its response.¹²

Mannitol and glycerol were the available osmotic diuretics in the set up. Mannitol was barely used. In patients with head injury,^{13,14} strokes or conditions which were associated with raised intracranial tension. Other than these they were not used in routine conditions. The other cases were mannitol can be used dialysis induced HTN (dialysis equilibrium syndrome),¹² Glaucoma, etc., we did not encounter these clinical cases in our ICU, its use in ARF was not entertained. It was found that the other class of diuretics namely carbonic anhydrase inhibitors (acetazolamide), triamterene and amiloride (inhibitors of renal epithelial Na⁺ channel) were of less value in our ICU set up. They were rarely used. In the majority of the cases, the combination of diuretics with other drugs was rational. As we know that multiple drug therapy is commonly practiced in ICU set up. It is very difficult to maintain rationality of drug combinations as one drug may counteract the adverse action of the other.

The basic investigations for monitoring the adverse effects related with diuretics were done in the majority of patients overall the safe use of diuretics was better practiced in ICU set up.

Regarding the adverse event profile of diuretics, it was very difficult to come into conclusions due to multiple drug therapy. In the majority of the cases, the reporting of adverse drug reactions was poor. There is need for framing proper guidelines in detecting adverse events due to diuretics in ICU set up. Furthermore, there is need for proper sensitization of clinicians in this regard. This is a retrospective study has some limitations as it is based on the available records. A prospective study can overcome the

limitations. As the study was retrospective, we had to rely mainly on the available data and past records and we could not follow the patient. Errors due to confounding and bias are more common as in any other retrospective studies.¹⁵ The advantage here was it could be conducted in a smaller scale and required less time to complete, and analysis was better with multiple outcomes. If still larger population was considered for analysis, we could have come out with better and accurate outcomes.

CONCLUSION

ICU is a set up where the condition of the patient is critical and usually on multiple drug therapy. Diuretics are among the commonly used class of drugs for one or the other reasons. Such studies with the usage of drugs will be beneficial in designing standard protocols. Of treatment, drug use, pharmacovigilance and pharmacoeconomic aspects of therapy or drug. Furosemide is commonly used diuretic followed by thiazide, potassium sparing diuretics, and osmotic diuretics.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Safar P, Dekornfeld TJ, Pearson JW, Redding JS. The intensive care unit. A three year experience at Baltimore city hospitals. *Anaesthesia.* 1961;16:275-84.
2. Weil MH, von Planta M, Rackow EC. Critical care medicine: Introduction and historical perspective. In: Shoemaker W, editor. *Textbook of Critical Care Medicine.* Philadelphia: WB Saunders; 1988: 1055-73.
3. European Society of Hypertension-European Society of Cardiology Guidelines Committee. 2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. *J Hypertens.* 2003;21(6):1011-53.
4. Srivastava SK. *A Complete Textbook of Medical Pharmacology.* 1st Edition., Vol. 1. India: Avichal Publishing Company; 2012.
5. Udaykumar P. *Medical Pharmacology.* 3rd Edition. New Delhi: CBS Publishers; 2006: 113-27.
6. Brenner GM, Stevens CW. *Pharmacology.* 3rd Edition. Cheltenham: Elsevier Publishers; 2012: 138-9.
7. Tripathi KD. *Essentials of Medical Pharmacology.* 7th Edition. New Delhi: Jaypee Publications; 2013: 579-93.
8. Venkataram R, Kellum JA. The role of diuretic agents in the management of acute renal failure. *Contrib Nephrol.* 2001;(132):158-70.
9. Ellison DH. The physiologic basis of diuretic synergism: its role in treating diuretic resistance. *Ann Intern Med.* 1991;114(10):886-94.
10. Sica DA, Gehr TW. Diuretic combinations in refractory Oedema states: pharmacokinetic-pharmacodynamic relationships. *Clin Pharmacokinet.* 1996;30(3):229-49.
11. Kellum JA. Use of diuretics in the acute care setting. *Kidney Int Suppl.* 1998;66:S67-70.
12. Anand IS, Kalra GS, Harris P, Poole-Wilson PA, Panzali A, Guili F, et al. Diuretics are essential and sole treatment in chronic heart failure. *Cardiosource.* 1997;18:852-7.
13. Ghajar J, Hariri RJ, Narayan RK, Iacono LA, Firlik K, Patterson RH. Survey of critical care management of comatose, head-injured patients in the United States. *Crit Care Med.* 1995;23(3):560-7.
14. Jeevaratnam DR, Menon DK. Survey of intensive care of severely head injured patients in the United Kingdom. *BMJ.* 1996;312(7036):944-7.
15. Park K. *Parks Text Book of Preventive and Social Medicine.* 23rd Edition. India: Bhanot Publishers; 2015: 342-50.

Cite this article as: Vedavathi H, Revankar SP. Analysis of usage of diuretics in medical intensive care unit of SIMS-Shimoga a tertiary care hospital. *Int J Basic Clin Pharmacol* 2015;4:941-5.