VOLUME - 13, ISSUE - 05, MAY - 2024 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

General Medicine

A PROSPECTIVE STUDY ON ASSESSMENT OF METABOLIC DERANGEMENTS FOLLOWING ADMINISTRATION OF LOOP DIURETICS IN A TERTIARY CARE HOSPITAL

P. Suji	Doctor of Pharmacy (PHARM.D), Annamalai university, Chidambaram.
R. Ramsundar	Doctor of Pharmacy (PHARM.D), Annamalai university,Chidambaram.
Dr. Ananthi K S	Post Graduate, Department of General medicine, Government Cuddalore Medical College and Hospital.
Dr. Saritha K Narayanan*	M.D., Associate Professor, Department of General medicine,Government Cuddalore Medical College and Hospital. *Corresponding Author
Dr. B. Jayanthi	M. Pharm., P.h.D, Post Graduate, Department of General medicine, Government Cuddalore Medical College and Hospital.

ABSTRACT The kidney's function is to produce an ultrafiltrate of plasma, which can subsequently be altered to produce urine by selectively absorbing and secreting it in accordance with the patient's physiological requirements. Loop Diuretics interferes with these mechanisms and boost urine production and reduce volume overload. The specific utilization of furosemide therapy remains variable with limited high-quality data to guide best practices. Diuretics can cause hypokalemia and change in renal parameters, however this research suggests that they can be used safely in short term under careful observation. We aimed to study metabolic derangements following administration of Loop Diuretics in the Department of General Medicine. **Methods:** This is a prospective study of patients who received Loop Diuretics (furosemide) at the Department of General Medicine, Government Cuddalore Medical College and Hospital (GCMCH). We focused on assessing metabolic derangements during short term hospitalization of the patient receiving furosemide. We have recorded RFT, serum electrolytes and blood pressure at the time of admission and compared with post loop diuretic (furosemide) administration. **Result:** A total of 106 patients were analysed, based on normal Renal Function Test and normal potassium levels on presentation. 100% of the patient showed no RFT Changes and majority of the patients showed no significant electrolyte changes during short term hospitalization. **Conclusion:** To conclude, there are no significant metabolic derangements following administration of Loop Diuretics with normal renal function on presentation during short term hospitalization.

KEYWORDS : Creatinine, Furosemide, Loop Diuretics, Renal Function Test, Serum Electrolytes, Urea.

1. INTRODUCTION

The kidneys are paired bean-shaped organ located retroperitoneally between the transverse process of T12-L3 vertebrae on either side of vertebral column. The Renal Medulla is an area found in the inner part of each kidney. Renal pyramids are the structural elements that make up each medulla. Renal pyramids consist of blood vessels and elongated portions of tube like structure that collect filtrate. The medulla region is darker in color than the outer surrounding area called the Renal cortex. The Renal pelvis collects the urine and passes it to the ureter.

Kidney function can be assessed through measuring the values of serum urea and serum creatinine. BUN is a nitrogen-containing substance that is produced in the liver as a byproduct of the urea cycle and protein metabolism.

Serum urea levels increases in conditions where renal clearance decreases (in acute and chronic renal failure/impairment). Compared to urea, serum creatinine provides more accurate assessment of renal function.

Creatinine is continuously produced by the body, which is a byproduct of creatine phosphate in muscle. There is a difference in creatinine levels between men and women, with lower creatinine values in children and those with decreased muscle bulk. The Diet also alters creatinine values. As GFR increases in pregnancy, lower creatinine values are found in pregnancy and so the obstetric patients are excluded from the study. Serum creatinine is also called later marker of renal impairment. Renal function might be decreased by 50% before a rise in serum creatinine.

When kidney function declines, the ability of the kidneys to filter blood is efficiently reduced. Some kidney function loss is normal with age, and people can even function normally with one kidney. Patients with CKD experience a progressive loss in function that is initially asymptomatic. As the disease progresses patient may present with volume overload, hyperkalemia, metabolic acidosis, hypertension, anemia. No direct correlation between the serum levels of blood urea nitrogen, creatine or GFR and the development of these symptoms.

Furosemide is a common loop diuretic[4]. They are powerful drugs capable of increasing sodium excretion and urine output even when renal function is markedly impaired[13]. Furosemide directly blocks ion transport by binding to the translocation pocket on the extracellular surface of sodium-potassium-chloride symporters. These drugs inhibit sodium-potassium-chloride symporter at the apical surface of thick ascending limb cells along the loop of Henle (NKCC2, gene *SLC12A1*). This transporter reabsorbs (directly and indirectly) up to 25% of filtered salt; its blockade is responsible for most natriuretic effects of loop diuretics. By blocking the sodium-chloride cotransport system, furosemide prevents the proximal and distal tubules as well as the thick ascending loop of Henle from reabsorbing sodium and chloride. This causes an excessive excretion of water in addition to sodium, chloride, magnesium, and calcium. Torsemide also produces noticeable improvement in the NYHA functional class[19]. In this study only furosemide (loop diuretics) was taken into consideration because it is more frequently prescribed in the hospital.

2. MATERIALS AND METHODS

This is the prospective study performed in the Department of General Medicine, Government Cuddalore Medical College and Hospital, Tamilnadu, India. This study was conducted

after Institutional Review Board and Ethics Committee clearance. The primary objective of the study was to assess the metabolic derangements following administration of Loop Diuretics. A total of 106 patients were included in the study based on inclusion and exclusion criteria.

Inclusion Criteria:

Patients with age group greater than 18 years and Patients receiving furosemide with normal RFT on presentation were included in the study.

Exclusion Criceria:

Known case of CKD or acute renal failure, Patient with abnormal potassium values at the time of admission, Obstetric patients, patients with Septic shock, hepatic encephalopathy and out patients were excluded.

3. OBSERVATION AND RESULTS

Gender Wise Distribution

Table 1: Gender wise distribution among patients receiving loop diuretics

S. NO	GENDER	NUMBER OF PATIENTS (n= 106)	PERCENTAGE (%)
1	Male	55	52
2	Female	51	48

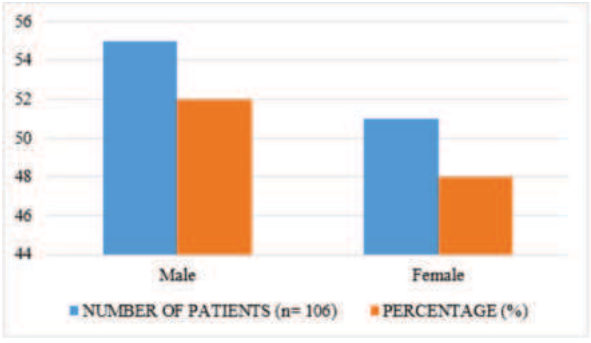

Figure 1: Gender wise distribution among patients receiving loop diuretics

From the above observation, out of 106 samples, male 55 (52%) received more furosemide than the female 51 (48%)

Age Wise Distribution

Table 2: Age wise distribution of patients receiving loop diuretics

S. NO	AGE GROUP	NUMBER OF PATIENTS (n=106)	PERCENTAGE (%)
1	18-40	4	3.8%
2	40-60	42	39.6%
3	>60	60	56.6%

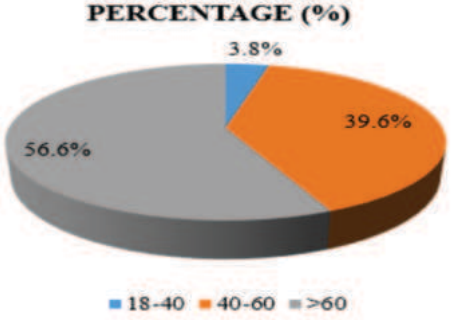

Figure 2: Age wise distribution of patients receiving loop diuretics

This study revealed that, the use of loop diuretics was more prevalent in the age group greater than 60 years (56.6%) followed by patients between age group of 40 – 60 years (39.6%) and patients between age group of 18 – 40 years (3.8%).

Dose Wise Distribution

Table 3: Dose wise distribution of patients receiving loop diuretics

S. NO	DOSE OF FUROSEMIDE	NUMBER OF PATIENTS (n= 106)	PERCENTAGE (%)
1	20mg	53	50%
2	40mg	45	42.5%
3	60mg	4	3.8%
4	80mg	4	3.8%

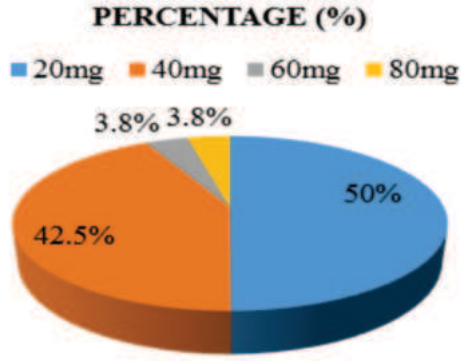

Figure 3: Dose wise distribution of patients receiving loop diuretics

This study revealed that, maximum number of patients received 20mg(50%) and 40 mg(42%) of furosemide and few number of patients only received 60 mg(4%) and 80 mg(4%) .

Distribution Based On Rft

Table 4: Distribution based on RFT of patients receiving loop diuretics

CREATININE LEVEL	UREA LEVEL	NO. OF PATIENTS (n=106)	PERCENTAGE
0.6 mg/dl	<15 mg/dl	0	0
0.6-1.3 mg/dl	15-45 mg/dl	106	100%
>1.3 mg/dl	>45 mg/dl	0	0

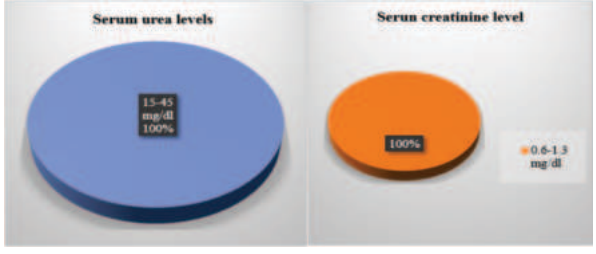

Figure 4: Distribution based on urea and creatinine levels

From the above observation, the patients receiving loop diuretics have not shown any deviations in urea and creatinine level post furosemide administration.

Distribution Based On Blood Pressure

Table 5: Blood pressure level of patients receiving loop diuretics

BLOOD PRESSURE	NO. OF PATIENTS	PERCENTAGE
INCREASED (>10% increased BP from baseline)	0	0%
DECREASED (>10% decreased BP from baseline)	47	44%
NO CHANGES (±10% from the baseline)	60	56%

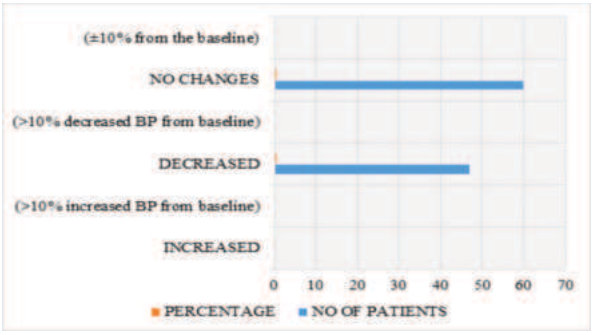

Figure 5: BP level of patients receiving loop diuretics

This study revealed that the maximum number of patients receiving loop diuretics have shown no changes in blood pressure (56%) followed by decrease in blood pressure (44%).

Distribution Based On Potassium

Table 6: Potassium level of patients receiving loop diuretics

POTASSIUM LEVEL	NO OF PATIENTS	PERCENTAGE
INCREASED	0	0%
DECREASED	3	2.80%
NO CHANGES	103	97.20%

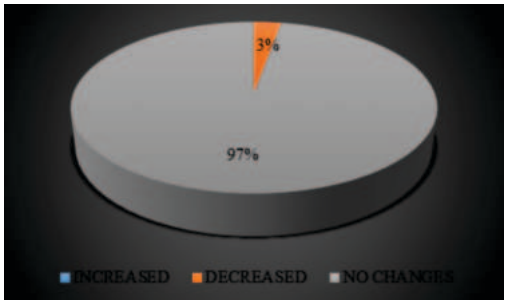

Figure 6: Potassium level of patients receiving loop diuretics

This study reveals, that the maximum number of patients receiving loop diuretics have shown no changes in potassium level (97.20.%) and few number of patients show decrease (2.8%) in potassium level.

4. DISCUSSION

In this study we focused on assessing metabolic derangements during short term hospitalization of the patient receiving loop diuretics. We have noted RFT, serum electrolytes and blood pressure at the time of admission and compared with post loop diuretic (furosemide) administration.

In this study a total of 106 cases were included based on Inclusion and Exclusion criteria. Gender wise distribution of patients receiving loop diuretics shows that male 55 (52%) received more furosemide than the female 51 (48%) which is similar to study conducted by Tyler P. Rasmussen, Noah N. Williford, Christopher DeZorzi, Aziz Hammoud, Brenden J. Boyle,Yunshu Zhou, Patrick Ten Eyck, and Milena A. Gebska[1] stated female received significantly lower doses of furosemide as compared to men at the time of symptom recognition and during entire hospitalization.

From the study, the use of loop diuretics was more prevalent in the age group greater than 60 years (56.6%) that can be compared with study conducted by Carla Rodriguez- Cillero Didier Menu, Philippe Athis, Sophie Perrin, Mélanie Dipanda, Sanaa Asgassou, Hélène Guepet, Emmanuel Mazen, Patrick Manckoundia , Alain Putot stated that age was associated with a linear increase in furosemide use and a decrease in recommended heart failure therapeutic prescriptions[22].

In the present study, out of 106 patients, 53 (50%) patients were receiving 20mg frusemide, 45 (42.5%) patients were receiving 40mg frusemide, 4 (3.8%) patients were receiving 60mg and 4 (3.8%) patients were receiving 80mg had no changes in renal parameter that can be compared with study conducted by Ruchit.A.Shah, Vijayakumar Subban, Anitha Lakshmanan reveals administration of 100mg\24hr furosemide shows no worsening of renal function and electrolyte levels15.

Loop diuretics (furosemide) is majorly prescribed in patients with Coronary Artery Disease[2] to reduce congestion but without Renal alterations which can be compared with the study that evaluated diuretic strategies in acute decompensated heart failure conducted by Ruchit.A.Shah, , Vijayakumar Subban b, Anitha Lakshmanan showed no difference in renal function and electrolyte levels15.

Patients with normal renal function did not exhibit any variation in urea level following the administration of furosemide in the current investigation. To date, the association of furosemide with renal function has only been mentioned in a small number of research studies.

In the present study, the patients receiving loop diuretics have not shown any deviations in creatinine level with normal RFT on presentation which is compared to the study conducted by Olcay Dilken, Aysegul Kapucu, Bülent Ergin that showed no significant alterations of urine output percentage and furosemide does not improve creatinine clearance but in contrast it further increased plasma creatinine in AKI patients[5].

In the present study,56% patients showed no changes in blood pressure, 44% showed decrease in blood pressure which is similar to the study conducted by Michael Davidov, M.D., Niko's Kakaviatos, M.D., and Frank A. Finnerty, JR., M.D which demonstrated that the doses of furosemide more than 120mg consistently decreases arterial pressure[17]. This can also be compared with the meta-analysis by Tao Han Lee,George Kuo ,Chih-Hsiang Chang,Yen Ta Huang,Chieh Li Yen,Cheng-Chia Lee,Pei Chun Fan,Jia-Jin Chen that stated besides preventing the sodium retention and extra cellular fluid volume expansion associated with standard antihypertensive agents, larger dose of furosemide exerted an additional antihypertensive effect[11].

In the present study, maximum number of patients receiving loop diuretics had no significant changes in serum potassium levels which is similar to the study conducted in Italy in 2000 by Giuseppe Zuccala, ClaudioPedone, AlbertoCocchi, MarcoPahor, Luciana, Carosella, Pierugo Carbonin, Roberto Bernabei reveals repeated analyses in patients on loop diuretics the hypokalemic effect of these agents was heavily dependent upon advancing age. Indeed, diuretic treatment was associated with potassium loss only in patients aged 75 and older[23].

Our data suggest that furosemide dosing during hospitalization does not have large clinical impact on renal function, with statistically significant association. This suggests that additional research towards examining diuretic renal effects or using loop diuretics as the primary method of controlling volume overload is needed, as our study provides additional evidence that furosemide is being effective loop diuretics in short term hospital stay of the patients without altering normal renal function. Our data do not address the renal effects of long-term loop diuretic exposure.

5. CONCLUSION

- Renal parameters remain unchanged after furosemide administration in short term hospital stay of the patients with no renal dysfunction at the time of admission.
- Frusemide is primarily prescribed in patients with

Coronary Artery Disease to reduce congestion, in combination with spironolactone to reduce elevated blood pressure, in Acute pulmonary edema to reduce volume overload and prescribed less frequently in the patients with other comorbidities. Diuretic therapy (furosemide) is also given in liver cirrhosis and CKD patients.

- In patients with normal renal function, had no discernible difference on serum electrolytes levels before and after administration of loop diuretics.
- Overall, there are no significant metabolic derangements following administration of furosemide in short term hospitalization.

REFERENCES

1) Kevin Damman, John Kjekshus, et,al. (2015) Loop diuretics, renal function and clinical outcome in patients with heart failure and reduced ejection fraction. https://doi.org/10.1002/ejhf.462.
2) David E. Lanfear, Edward,L.Peterson,KarenWells, et,al. Relationship of Loop Diuretic Dosing and Acute Changes in Renal Function during Hospitalization for Heart Failure. 10.4172/2155-9880.1000164.
3) A. B. Libório, M. L. Barbosa,T. T. Leite,V. B. Sá,(2020) Impact of loop diuretics on critically ill patients with a positive fluid balance.https://doi.org/10.1111/anae.14908
4) Advancing the evidence for diuretic therapy for heart failure: implications of the ADVOR and TRANSFORM-HF trials .Anthony E Peters, Robert J Mentz, Stephen J Greene.*European Heart Journal - Cardiovascular Pharmacotherapy, Volume 9, Issue 4, June 2023, https://doi.org/10.1093/ehjcvp/pvad002.*
5) Olcay Dilken, Aysegul Kapucu,Bülent Ergin, et,al. Furosemide exacerbated the impairment of renal function, oxygenation and medullary damage in a rat model of renal ischemia/reperfusion induced AKI.
6) Blaithin A. McMahon and Lakhmir S. Chawla The furosemide stress test: current use and future potential.
7) Paul N. Yu MD, et,al. Effect of furosemide on hemodynamics and lung water in acute pulmonary edema secondary to myocardial infarction.https://doi.org/10.1016/0002-9149(79)90049-3.
8) Acute Effect of Furosemide on Glomerular Filtration Rate in Diastolic Dysfunction.https://doi.org/10.1080/08860220701641777.
9) Jennifer E. Flythe 1 2, Julia H. Narendra 1, et,al. Efficacy, Safety, and Tolerability of Oral Furosemide Among Patients Receiving Hemodialysis: A Pilot Study. https://doi.org/10.1016/j.ekir.2022.07.003.
10) William J. Mroczek MD, Michael Davidov MD, Frank A. Finnerty Jr. MD, FACC Large dose furosemide therapy for hypertension: Long-term use in 22 patients. https://doi.org/10.1016/0002-9149(74)90615-8.
11) Tao Han LeeID 1, George Kuo1,2 et,al. Diuretic effect of co-administration of furosemide and albumin in comparison to furosemide therapy alone: An updated systematic review and meta-analysis. https://doi.org/10.1371/journal.pone.0260312.
12) L. Dodion, Y. Ambroes & N. Lameire. A comparison of the pharmacokinetics and diuretic effects of two loop diuretics, torasemide and furosemide, in normal volunteers. https://doi.org/10.1007/BF00541463.
13) The place of loop diuretics in the treatment of acute and chronic renal failure D Russo1,B Memoli,V E Andreucci https://pubmed.ncbi.nlm. nih.gov/1295711/.
14) Chien-Te Lee,1,2 Hung-Chun Chen,2 Li-Wen Lai,3 Kim-Chong Yong,3 and Yeong-Hau H. Effects of furosemide on renal calcium handling. https://doi.org/10.1152/ajprenal.00038.2007.
15) RuchitA. Shah b, Vijayakumar Subban b, Anitha Lakshmanan et,al. A prospective, randomized study to evaluate the efficacy of various diuretic strategies in acute decompensated heart failure. https://doi.org/10.1016/j.ihj.2014.03.006.
16) N Makhoul, T Riad, S FriedStrom& F R Zveibil. Furosemide in pulmonary oedema: Continuous versus Intermittent. https://doi.org/10.3109/tcic.8.6.273.276.
17) Michael Davidov, M.D., Nikos Kakaviatos, M.D., and Frank A. Finnerty, JR., M.D. Anti hypertensive Properties of Furosemide. https://doi.org/10.1161/01.CIR.36.1.125
18) Akikazu Nomura MD, Hisakazu Yasuda MD, Masaru Minami MD, et,al. Effect of furosemide in congestive heart failure. https://doi.org/10.1038/clpt.1981.145.
19) Kazuhiko Kido, Mikiko Shimizu, Masayuki Hashiguchi et, al. Comparing torsemide versus furosemide in patients with heart failure: A meta-analysis. https://doi.org/10.1016/j.japh.2019.01.014.
20) Jose L Santos, Patricio Zanardi, Veronica Alo, Marcelo Rodriguez, Federico Magdaleno, Virginia De Langhe, Vanina Dos Santos, Giuliana Murialdo, Andrea Villoldo, Micaela Coria et,al., Journal of Clinical Medicine 2021. Pulmonary edema in COVID-19 treated with furosemide and negative fluid balance (NEGBAL): a different and promising approach.
21) Valerie W Rusch, Linda Artman, Frederick W Cheney. Effect of furosemide on fully established low pressure pulmonary edema.
22) Carla Rodriguez-Cillero, Didier Menu, Philippe d'Athis, Sophie Perrin, Mélanie Dipanda. Potentially inappropriate use of furosemide in a very elderly population: An observational study. 2017. https://doi.org/10.1111/ijcp.12975.
23) Giuseppe Zuccala, Claudio Pedone, Alberto Cocchi, Marco Pahor, Luciana Carosella, Pierugo Carbonin, Roberto Bernabi. Older Age and In-Hospital Development of Hypokalemia From Loop Diuretics: Results From a Multicenter Survey.