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Original Research Article

Fractional excretion of urea and fractional excretion of sodium in differentiation of the acute kidney injury in eastern state of Jharkhand, Ranchi, India

Authors
Dr Jitendra Kumar Naik (M.D. General Medicine)[1], Dr Arun Kumar Mahato[2], Dr Rajendra Kumar Jha[3]
[1]Assistant Professor, Lakhiram Agrawal Memorial Govt. Medical College, Raigarh, CG, India
[2,3]Professor & HoD, Dept. of General Medicine, RIMS, Ranchi
Corresponding Author
Dr Jitendra Kumar Naik (M.D. General Medicine)
Assistant Professor, Lakhiram Agrawal Memorial Govt. Medical College, Raigarh, CG, India

Abstract
Background: *Acute kidney injury is the sudden impairment of kidney function, resulting in the retention of urea and other nitrogenous waste products normally cleared by the kidney. Main objective of the present study is to compare the fractional excretion of urea (FEUrea) and fractional excretion of sodium (FENa) in differential diagnosis of Acute Kidney Injury.*
Research Design: *Clinical observation and experimental design were done for the purpose of present study.*
Method: *We are selected in participants for the present study, these consecutive randomly admitted patients in the department of medicine in Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India.*
Sample: *Total 75 Patients were selected in the present study.*
Result: *Finding of the present study fractional excretion of sodium (FENa) ROC curve (0.957), standard error (0.039), 95% of confidence interval (0.835 to 0.995) and the level of significant in p-value (0.5) is 0.0001; fractional excretion of urea (FEUrea) ROC curve is 0.976, standard error (0.028), 95% of confidence interval (0.865 to 0.995) and the level of significant in p value (0.5) is 0.0001.*
Conclusion: *Finding of the result concluded that the FEUrea showed higher sensitivity and specificity in differentiating prerenal from intrinsic AKI in patients irrespective of diuretic exposure.*
Keywords: *Fraction Excretion of Sodium, Fraction Excretion of Urea, Acute Kidney Injury.*

Introduction

Acute kidney injury is the sudden impairment of kidney function, resulting in the retention of urea and other nitrogenous waste products normally cleared by the kidney (Harrisons principle of internal medicine18th ed.). Acute Kidney Injury (AKI) complicates 5-7% of acute care hospital admission and up to 30% of admission to the intensive care unit. In severe cases mortality remains as high as 50% particularly in those admitted to the ICU. The causes of AKI other than urinary tract obstruction are usually divided into 2

categories prerenal and intrinsic causes of AKI. Although pathological studies are lacking, the leading cause of persistent AKI in critically ill patients is believed to be acute tubular necrosis. It is usually assumed that it is a spectrum that leads from prerenal AKI to intrinsic AKI. Many publications advocate use of urine indices to differentiate. However diuretic therapy or sepsis may affect these indices. Since urea reabsorption takes place mainly at proximal convoluted tubule and is unaffected by use of diuretics and so fractional excretion of urea may be more reliable than fractional excretion of sodium. However, distinguishing prerenal AKI from intrinsic AKI is needed because it helps to choose treatment for critically ill patients.

The term AKI has largely replaced acute renal failure (ARF), reflecting the recognition that smaller decrements in kidney function that do not result in overt organ failure are of substantial clinical relevance and are associated with increased morbidity and mortality. AKI (acute kidney injury) is common and it is associated with high morbidity and mortality. The loss of kidney function that defines AKI is most easily detected by measurement of the serum creatinine, which is used to estimate the glomerular filtration rate (GFR).

Prior lack of consensus in the quantitative definition of AKI, in particular, has hindered clinical research since it confounds comparisons between studies. Some definition employed in clinical studies have been extremely complex, with graded increments in serum creatinine for different baseline serum creatinine Values (Mehta, et al 2003; Hou, et al 1983).

Objective

The main objective of current study is to compare the fractional excretion of urea (FEUrea) and fractional excretion of sodium (FENa) in differential diagnosis of Acute Kidney Injury.

Research design

Clinical observation and experimental design were done for the purpose of present study.

Method-

Sources of data

We are selected in participants for the present study, these consecutive randomly admitted patients in the department of medicine in Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India.

Sample exclusion

Sample selection process we are excluded in some circumstances and illnesses such as patients below age group of 14 years, known case of chronic kidney disease, contrast nephropathy, rhabdomyolysis, acute glomerulonephritis, patient not giving consent, receiving osmotic diuretics eg. Mannitol, end stage of kidney disease receiving renal replacement therapy, obstructive nephropathy, renal transplantation and diabetic nephropathy.

Sample inclusion criteria and sample selection procedure

Total 75 Patients were selected in the present study. The criteria follow below e.g. decreased urine output (urine output < 0.5ml/kg/h) and the raised blood urea and serum creatinine.

Sample were fulfilling above criteria included and divided in two group- Prerenal AKI and Intrinsic AKI. These group were again divided in two sub-group depending upon whether they had received diuretics or not. Sub-group of division were based on history, physical examination, investigation, response to intravenous fluid reversibility of function, recovery of renal functions test, need for renal replacement therapy and staged according to recent KDIGO criteria, then fractional excretion of sodium and fractional excretion of urea were calculated in each patient.

Statistical analyses

Data were treated in the purpose of study, the logistic regression, ROC curve and descriptive analyses were done by the help of SPSS 16.

Result and Discussion

Acute kidney injury is the abrupt loss of kidney function, resulting in the retention of urea and other nitrogenous waste products and abnormalities in regulation of extracellular fluid volume and electrolytes. Because pre-renal acute kidney injury and acute tubular necrosis (intrinsic AKI) both may need intravenous fluid administration but the risk of volume overload is more in case of later, so as a careful differentiation of AKI is helpful in deciding treatment strategy of patients.

Fractional excretion of sodium (FENa) and fractional excretion of urea (FEUrea) are useful in such situation to differentiate between prerenal and intrinsic causes of AKI. We studied the over a period of one year. In our study total 75 patients with acute kidney injury were included considering inclusion and exclusion criteria. They were divided in prerenal and intrinsic AKI and were again subdivided on the basis of diuretic exposure and data were analyzed.

Table 1 shows the patients with no diuretic exposure (gold std-type of AKI) type of AKI 1=intrinsic, 0=pre-renal ROC curve (for fractional excretion of sodium)

Variable	Fractional excretion of sodium
Classification variable	type of AKI
Select	Exposure Diu. =0
Positive group	
type of AKI	= 1
Sample size	15
Negative group	
type of AKI	= 0
Sample size	23

Disease prevalence (%)	Unknown

Area under the ROC curve	0.957
Standard error	0.039
95% Confidence interval	0.835 to 0.994
Significance level P (Area=0.5)	0.0001

Table 2 shows the Patients with diuretic exposure (gold std-type of AKI) type of AKI 1=intrinsic, 0=pre-renal

ROC curve (for fractionation excretion of urea)

Variable	fractional excretion of urea
Classification variable	type of AKI
Select	Exposure of Diuretic =1
Positive group	
type of AKI	= 1
Sample size	16
Negative group	
type of AKI	= 0
Sample size	21

Disease prevalence (%)	Unknown

Area under the ROC curve	0.976
Standard error	0.028
95% Confidence interval	0.863 to 0.995
Significance level P (Area=0.5)	0.0001

Table 3 shows the Patients with diuretic exposure (gold std-type of AKI) type of AKI 1=intrinsic, 0=pre-renal ROC curve (for fractionation excretion of urea)

Criterion	**Sensitivity**	**95% CI**	**Specificity**	**95% CI**	**+LR**	**-LR**
>=10.75	100.00	79.2 - 100.0	0.00	0.0 - 16.3	1.00	
>27.86	100.00	79.2 - 100.0	76.19	52.8 - 91.7	4.20	0.00
>28.27	93.75	69.7 - 99.0	76.19	52.8 - 91.7	3.94	0.08
>33.76 *	93.75	69.7 - 99.0	95.24	76.1 - 99.2	19.69	0.07
>42.29	75.00	47.6 - 92.6	95.24	76.1 - 99.2	15.75	0.26
>43.38	75.00	47.6 - 92.6	100.00	83.7 - 100.0		0.25
>110	0.00	0.0 - 20.8	100.00	83.7 - 100.0		1.00

+LR : Positive likelihood ratio

-LR : Negative likelihood ratio

Finding of the present study fractional excretion of sodium (FENa) ROC curve (0.957), standard error (0.039), 95% of confidence interval (0.835 to 0.995) and the level of significant in p-value (0.5) is 0.0001; fractional excretion of urea (FEUrea) ROC curve is 0.976, standard error (0.028), 95% of confidence interval (0.865 to 0.995) and the level of significant in p value (0.5) is 0.0001.

Fractional excretion of sodium (FENa) has been routinely used for differentiating intrinsic from prerenal AKI. However, the values of FENa are usually affected by the commonly used medications as diuretics, dopamine and norepinephrine, and also by some clinical condition such as myoglobinuria, radio contrast induced renal failure and different causes of metabolic acidosis etc. On the country, the fractional excretion of urea (FEUrea) is suggested to be used instead of FENa with better reliability to differentiate between prerenal from intrinsic AKI, as its value are not affected by the aforesaid drugs or medical conditions. In our study we performed a prospective observation in patients with acute kidney injury (AKI) to explore the differentiation between FENa and FeUrea in differentiating intrinsic from prerenal AKI.

In this study we use the KDIGO criteria to classify our patients. We found that our result was in the agreement with study by Kaplan and Kohn(1992) and Carvounis et al (2002). Kaplan and Kohn (1992) studied the retrospectively and concluded FEUrea< 35%to be a sensitive index to renal perfusion, despite the prior administration of furosemide. In our study cutoff was 36.15% which was nearby to 35%.

Carvounis et al (2002) investigated that the patients with prerenal azotemia had a FENa< 1 %, only 48% of patients who were prerenal and on diuretic therapy had a low FENa. By contrast, 89% of this latter group had a FEUN (fractional excretion of urea nitrogen) of 35%. In all the prerenal cases FEUN had the best sensitivity and specificity (90 and 96% respectively), and the negative and positive predictive value (99 and &75%, respectively). Our results were nearly similar with sensitivity and specificity 93.55% and 93.45% for FEUrea in combined group. The PPV (positive predictive value) and NPV (negative predictive value) both were 93.5%. the FEUrea is less effective in patients with infection, as cytokines interfere with the urea transporters in the kidney and colon.

Lim et al (2009) studied the cut off value of T-AKI (transient AKI) was defined as FEUrea<30 according to the ROC curves, sensitivity and specificity of FEUrea were 92% and 87% in non-diuretic group and 96% and 83% in diuretic groups respectively. They concluded that FEUrea is as good as FENa at distinguishing T-AKI from P-AKI in patients administered with diuretics. We found that FEUrea is higher and good sensitivity and specificity. Our results were also in agreement with study by Diskin et al (2010), they concluded that FEUrea is more accurate in patients receiving diuretics. (95 vs 54%, p< 0.0001), yet both tests accurately detected the presence of intrinsic renal disease (FEUrea 85%). The FEUrea performed significantly better (98 to 49%, p<0.0001) in detecting pre-renal azotemia, and that advantage came exclusively in patients taking diuretics (p< 0.0001). Darmon et al (2011) concluded that the FEUrea is little help in distinguishing renal from prerenal AKI in critically ill patients receiving diuretic therapy. FEUrea with the area under the receiver operating characteristics curve being 0.59 (95% confidence interval, 0.49 to 0.70; P = 0.06). sensitivity was 63% and specificity was 54% with a cutoff of 35%. However in the subgroup of patients receiving diuretics, the result were similar, however, they stated that few of their patients received diuretics and poor performance of the urinary indices was therefore related to low statistical power.

But again our finding was also related with Dewitte et al (2012), they whey concluded that FEUrea had better sensitivity (83% Vs 49%) and specificity (75% Vs 71%) for renal differentiated from prerenal AKI specially in diuretic exposed group. But the cutoff value for FEUrea was 40% a

level which was higher than our result. Yassin et al (2013) concluded that FEUrea as more sensitive, specific and less affected by the use of diuretics in differentiating renal from prerenal azotemia in patients with AKI complicating circulatory shock.

Conclusion

Finding of the result concluded that the FEUrea showed higher sensitivity and specificity in differentiating prerenal from intrinsic AKI in patients irrespective of diuretic exposure.

Conflict of interest- authors are declaring that no any conflict of interest.

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