Revista Electrónica de Biomedicina
Electronic Journal of Biomedicine

ISSN: 1697-090X

FRACTIONAL EXCRETION OF UREA IN SEVERELY DEHYDRATED ELDERLY WITH DEMENTIA

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Rev Electron Biomed / Electron J Biomed 2005;1:32-35

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ABSTRACT

Fractional excretion of urea (FE_{urea}) is a useful marker to evaluate renal perfusion in people with normal renal function. The value of this marker in a well hydrated person is around 50%, in a low renal perfusion state is lower than 35%, and in an over-hydrated state is higher than 65%.

A recent study reported that well-hydrated healthy old and very old people had FE_{urea} higher than young people under the same conditions. That faced us with the fact that there is no information about FE_{urea} values during abnormal renal perfusion states in the elderly.

We present two dehydrated elderly patients with dementia that provided us with an opportunity to evaluate the FE_{urea}.

Conclusion: We observed that only during severe dehydration an old patient with dementia reached a low FE_{urea} (20%) as a young person. When these patients were dehydrated (hypernatremic) but not hypotensive they showed FE_{urea} higher than a young patient. It seems that new FE_{urea} values are needed in this age group to interpret altered renal perfusion states.

RESUMEN:
La excreción fraccional de urea (EF_{urea}) es un marcador útil en la evaluación del estado de perfusión renal en personas con riñón normofuncionante. El valor de este marcador en un paciente bien hidratado es de alrededor del 50%, en una persona con hipoperfusión renal es menor del 35% y en una persona sobrehidratada es mayor del 65%. Estos valores de referencia provienen de estudios en personas jóvenes.

Un estudio reciente demostró que en personas ancianas (edad entre 65-79 años) y muy ancianas (edad mayor a 79 años) sanas y en buen estado de hidratación, la EF_{urea} fue mayor que la observada en jóvenes sanos normohidratados. Esto nos hizo notar que no existen hasta la fecha valores normales conocidos de EF_{urea} en pacientes gerontes cursando estados de alteración de la perfusión renal.

Presentamos los siguientes casos clínicos por ser una buena oportunidad para apreciar el valor de EF_{urea} alcanzado por personas ancianas dementizadas bajo un estado de severa hipoperfusión renal, a raíz de un cuadro de deshidratación con severa hipernatremia.

Conclusión: De los dos casos analizados sólo uno presentó en sus inicios además de severa deshidratación hipotensión arterial, y fue sólo en ese contexto que logró una EF_{urea} baja (EF_{urea} 20%) como la que hubiera logrado una persona joven. Fuera del estado de hipotensión y aun con signos de deshidratación (hipernatremia) ambos pacientes ancianos y dementizados mostraron valores de EF_{urea} más elevados que los que hubiera logrado un paciente joven. Pareciera que nuevos valores de referencia de EF_{urea} son necesarios para la interpretación de los estados de alteración de la perfusión renal en esta población.

INTRODUCTION

Fractional excretion of urea (FE_{urea}) is a useful marker to evaluate renal perfusion and in adult with normal renal function it is 50%, in a low renal perfusion state (dehydration, cirrhosis, cardiac failure, etc) is lower than 35%, and in an over-hydrated states (syndrome of inappropiate

antidiuretic hormone secretion) is higher than 65% [1,2].

A recent study reported that well-hydrated healthy old and very old people had a higher FE_{urea} (60%) than healthy young adults under similar conditions (FE_{urea}: 50%)[3,4]. There is no information about FE_{urea} values during abnormal renal perfusion states in the elderly.

We present two cases that illustrate that FE_{urea} values in elderly patients with dementia reach to adult levels only during severe dehydration.

Case Report

Case 1: A seventy-three years old female nursing-home patient suffering from severe dementia, immobility syndrome, fecal and urine incontinence, was admitted to our hospital due to a respiratory infection in the context of a recent history of a poor access to water, hypotension, dryness of the tongue and axillae, hypernatremia and acute renal insufficiency. Plasma glucose was in normal range.

She was initially treated with intravenous antibiotics and intravenous normal saline until her blood pressure and renal function improved. We continued to add tap water in her tube feeds to ensure complete rehydration.

She improved and was discharged after six days of admission. We observed that only during severe dehydration she reached a low FE_{urea} (20%) (Table 1).

Days	1	2	3	4	5
Serum Sodium (mmol/l)	173	168	161	156	140
Serum Urea (mg/dl)	174	180	151	107	40
Serum Creatinine (mg/dl)	3.1	2.8	1.5	2.2	1
Fractional Excretion of Urea (%)	20	32	41	65	76
Fractional Excretion Of Sodium (%)	1.1	1	-	-	0.8
Serum Urea / Serum Creatinine	56	64	101	48	40

TABLE 1: Laboratories of Case 1

Case 2: A ninety-seven years old male nursing-home patient suffering from severe dementia and immobility syndrome was admitted to our hospital due to a respiratory infection. He had hypersomnia, a recent history of a poor access to water, dryness of the tongue and axillae, orthortatic drop in blood pressure, hypernatremia and acute renal insufficiency. Plasma glucose was in normal range.

The patient was on no medication and nourished by tube-feeding. He was started on intravenous antibiotics (ampiciline + sulbactam) and water was added to his tube-feeds. He was discharged after six days of admission (Tablr 2).

Days	1	2	3	4	5
Serum Sodium (mmol/l)	157	150	148	145	136
Serum Urea (mg/dl)	85	68	60	55	45
Serum Creatinine (mg/dl)	1.7	1.3	1.2	1	0.8
Fractional Excretion of Urea (%)	44	56	60	--	64
Fractional Excretion of Sodium (%)	1.6	2.2	0.9	0.8	--
Serum Urea / Serum Creatinine	50	52	50	55	56

TABLE 2: Laboratories of Case 2

DISCUSSION

Urea is almost exclusively synthesized in the liver and excreated by the kidney, and this substance constitutes the way by which the organism eliminates the nitrogen that comes from the amino-acids. In the kidney urea undergoes many processes such as filtration, reabsorbtion, secretion and excretion, resulting finally in a FE_{urea} of 50% [5]. Urea reabsorbtion takes place mostly in the proximal tubules as a consequence of passive forces such as the peritubular capillary oncotic pressure and the osmotic pressure generated by the reabsorbtion of sodium. The alteration of all the above mentioned proximal factors can increase the FE_{urea} value, as is the case when an osmotic diuretic is used[5,6]. Moreover, there is urea reabsorbtion in the papilary collecting tabules because vasopressin hormone stimulates the local urea channels (UT1). The proximal and distal tubular urea handling shows the tight relationship between urea and water reabsorbtion along the nephrons[5].

During renal hypoperfusion urea reabsorbtion is increased, reaching the FE_{urea} values lower than 35%. On the other hand during situations of water overload (syndrome of inappropiate antidiuretic hormone secretion) FE_{urea} reaches values higher than 65% [1,2]. This phenomenon appears to be secondary to urea secretion in the distal segment of the proximal tubules[5].

Higher values of FE_{urea} in healthy elderly respect to those found in young people have been reported[3,4]. However, the FE_{urea} in the elderly people during renal hypoperfusive states is not yet described. In the present report it could be appreciated that the values of FE_{urea} reached by severe dehydrated elderly patient with dementia were higher than those that would have been reached by young adults. Only one of the two patients who was severely hypotensive was able to reach a low FE_{urea} as a young patient. It appears that the aged kidney would be able to reach low FE_{urea} values only under an extreme stimulus such as shock secondary to severe dehydration. For instance, when our patient was hypotensive she was able to reach a low FE_{urea} (FE_{urea}:20%), but then when she was normotensive but still dehydrated, she showed a high FE_{urea}: 40-65%.

Classical urinary indices such as fraccional excretion of sodium, urinary osmolality, and plasma urea / plasma creatinine ratio are not reliable indices to distinguish between renal hypoperfusion and acute tubular necrosis in the elderly. The reason for this phenomenon is that the renal physiology changes secondary to the senescence process lead old people to tubular frailty, salt wasting and reduced capability to water reabsorbtion[7,8].

Following mechanism is speculated to explain the high FE_{urea} seen in the elderly, a high FE_{urea} could be secondary to an elevated urea secretion or a reduced urea reabsorbtion. Since recent renal physiologic studies demostrated that the proximal tubular function is preserved in healthy old people[4], it is unlikely that urea secretion and proximal urea reabsorbtion would explain this phenomenon. Conversely, it was documented that the function of the distal nephron is reduced in the elderly[4], a reduced urea reabsorbtion in the papilary collecting tubules could explain the elevated FE_{urea}. Other factors that could explain an elevated FE_{urea} are: a high protein diet, an osmotic diuretic, and a water diuresis[5]. Our studied patients were neither on a high protein diet nor received osmotic diuretics. However, water diuresis can result in high FE_{urea} and could be another explanation. This phenomenon appears to be more so related to the ageing process than to severe dementia, as the characteristic medullary hypotonicity of the old people reduced their capability of water reabsorbtion[9], and water metabolism studied in severe dementia showed a trend towards water retention and than its loss[10].

CONCLUSION

It appears that the fractional excretion of urea in dehydrated elderly patients with dementia shows higher values compared to the young adults, except for severe dehydration with hypoperfusion in which the elderly patient could reach values that are seen in young. Further studies are required in order to define the expected fractional excretion of urea values in the elderly population during altered renal perfusion states.

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Musso et al present two elderly patients with dementia who were dependent on others for their water intake and developed severe dehydration with resulting hypernatremia and were able to reach the low FE_{urea} only during severe dehydration, as seen in young individuals with dehydration. They describe the pathophysiologic processes in the ageing kidney and suggest that it is the alterations in the distal tubular function in the elderly kidney that likely is responsible for the high FE_{urea}. However, the distal urea absorption is dependent, not only on the urine flow rates but also on vasopressin activity. Although plasma vasopressin levels are elevated in the elderly but increased vasopressin secretion/unit increase in plasma tonicity reflects a decrease in collecting tubule sensitivity to vasopressin. Authors suggest that water diuresis, related to ageing, can result in high FE_{urea} and could be another explanation but less likely. It is important to note that the patients presented here are unique, in the sense that both have dementia and problems with immobility where the oral intake is dependent on the others and these observations may not be applied to other elderly patients and the current data is limited. I agree that further evaluation of FE_{urea} in elderly patients is required because of the age related changes in renal function, poor muscle mass and possibly associated malnutrition - for effective assessment of the elderly patients with volume depletion.

Comment of the reviewer Prof. Marta Sofía López Rodríguez.
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Fractional excretion of urea (FE_{urea}) has been used to distinguish between the failure prerenal and acute tubular necrosis. Musso and collaborators highlight in the presented cases, the modifications of the FE_{urea} in the elderly with renal hypoperfusion underline that the classic approaches of fractional excretion of sodium, urinary osmolarity, and plasma urea/plasma creatinine ratio lose utility for the diagnosis in these patients for the physiological changes that happen. The high level of FE_{urea} are explained by a reduced urea reabsorption in the papillary collecting tubules but new investigations should be carried out to ratify this discovery..

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Musso et al report, shows two elderly patients with dementia and they developed acute renal failure by water depletion. They shows that FE_{urea} could be a useful index to evaluate and manage ARF in these situations. As comment, FE_{urea} to a great extent relates inversely to the proximal reabsortion water. Thus, this increases when renal perfusion decreases and filtration fraction increases. For this reason the use of indexes that reflect proximal tubular function in ARF are valuable as lithium and acid uric clearance. FE_{urea} is affected by body composition in elderly patients with high variability, so nutritional and hydration state should be established in this population. Finnally, Musso et al. describe an very interesting management in elder patients with ARF, using FE urea as reference index.

Received November 6, 2004.
Published January 7, 2005