FRACTIONAL EXCRETION OF UREA IN SEVERELY DEHYDRATED ELDERLY WITH DEMENTIA

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ABSTRACT

Fractional excretion of urea (FEurea) 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 FEurea higher than young people under the same conditions. That faced us with the fact that there is no information about FEurea 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 FEurea.

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

RESUMEN

La excreción fraccional de urea (EFurea) 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 un paciente 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.

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

INTRODUCTION

Fractional excretion of urea (FEurea) 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 inappropriate...
Fractional Excretion of Urea

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 \(\text{FE}_{\text{urea}}\) (60%) than healthy young adults under similar conditions (\(\text{FE}_{\text{urea}}\): 50%)\(^3,4\). There is no information about \(\text{FE}_{\text{urea}}\) values during abnormal renal perfusion states in the elderly.

We present two cases that illustrate that \(\text{FE}_{\text{urea}}\) 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 \(\text{FE}_{\text{urea}}\) (20%) (Table 1).

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

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, orthotatic 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 (ampicilline + sulbactam) and water was added to his tube-feeds. He was discharged after six days of admission (Table 2).

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

Table 2: Laboratories of Case 2

Discussion

Urea is almost exclusively synthesized in the liver and excreted 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, reabsorption, secretion and excretion, resulting finally in a \(\text{FE}_{\text{urea}}\) of 50% \(^5\). Urea reabsorption 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 reabsorption of sodium. The alteration of all the above mentioned proximal factors can increase the \(\text{FE}_{\text{urea}}\) value, as is the case when an osmotic diuretic is used\(^6,7\). Moreover, there is urea reabsorption in the papilary collecting tubules because vasopressin hormone stimulates the local urea channels (UT1). The proximal and distal tubular urea handling shows the tight relationship between urea and water reabsorption along the nephrons\(^5\).

During renal hypoperfusion urea reabsorption is increased, reaching the \(\text{FE}_{\text{urea}}\) values lower than 35%. On the other hand during situations of water overload (syndrome of inappropriate antidiuretic hormone secretion) \(\text{FE}_{\text{urea}}\) 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 \(\text{FE}_{\text{urea}}\) in healthy elderly respect to those found in young people have been reported\(^3,4\). However, the \(\text{FE}_{\text{urea}}\) in the elderly people during renal hypoperfusion states is not yet described. In the present report it could be appreciated that the values of \(\text{FE}_{\text{urea}}\) 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 \(\text{FE}_{\text{urea}}\) as a young patient. It appears that the aged kidney would be able to reach low \(\text{FE}_{\text{urea}}\) 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 \(\text{FE}_{\text{urea}}\) (\(\text{FE}_{\text{urea}}\): 20%), but then when she was normotensive but still dehydrated, she showed a high \(\text{FE}_{\text{urea}}\): 40-65%.

Classical urinary indices such as fractional 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 reabsorption.7,8

Following mechanism is speculated to explain the high FEurea seen in the elderly, a high FEurea could be secondary to an elevated urea secretion or a reduced urea reabsorption. Since recent renal physiologic studies demonstrated that the proximal tubular function is preserved in healthy old people, it is unlikely that urea secretion and proximal urea reabsorption would explain this phenomenon. Conversely, it was documented that the function of the distal nephron is reduced in the elderly, a reduced urea reabsorption in the papillary collecting tubules could explain the elevated FEurea. Other factors that could explain an elevated FEurea 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 FEurea 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 reabsorption9, and water metabolism studied in severe dementia showed a trend towards water retention and than its loss10.

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.

REFERENCES

Comment of the reviewer Prof. Marta Sofia López Rodriguez.
Assistant Professor in Anesthesiology of Higher Institute of Medical Science. Cira García Reyes Clinic. Havana City. Cuba

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 FEurea 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 FEurea. 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 FEurea 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 FEurea 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 Malvinder S. Parmar, MD, FRCP, FACP
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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 FEurea could be a useful index to evaluate and manage ARF in these situations. As comment, FEurea to a great extent relates inversely to the proximal reabsorption 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. FEurea is affected by body composition in elderly patients with high variability, so nutritional and hydration state should be established in this population. Finally, Musso et al. describe an very interesting management in elder patients with ARF, using FE urea as reference index.