Lactulose efficacy in reduction of nitrogen products, blood potassium and fluid overload in patients with end-stage renal failure

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Abstract

Chronic kidney disease (CKD) is a major public health problem that often goes unrecognized until late-stage disease. Patients with chronic kidney disease face with uremic toxins and hyperkalemia. Also fluid overload in CKD patients is associated with rapid decline in kidney function. Lactulose is a hyper osmotic agent and as a prebiotic plays an important role in regulating serum urea and potassium levels and have some effects on fluid overload. The aim of this study was to evaluate effect of lactulose on serum levels of biochemical products in patients with CKD. In this interventional study 17 patients with end stage of CKD (76.47 % men; mean age 65.88 ± 13.4) were evaluated. All patients received lactulose, 10 ml, 3 times per day for 3 months. Blood samples from all participants were collected before and at the end of intervention to examine changes in biochemical parameters, including potassium, urea, creatinine and uric acid. Lactulose significantly decreased urea levels (p=0.001), blood potassium (0.001) and fluid overload(with due attention to patient’s weight p=0.001) in patients with end-stage renal failure. The decrease in serum creatinin anduric acidwere not significant. Lactulose administration in CKD patients could decrease levels of various deleterious elements especially urea and blood potassium, and its daily use can be recommended in these patients.

Keywords: Lactulose, Chronic kidney disease, Blood urea, Creatinine, Fluid overload
INTRODUCTION

Chronic kidney disease (CKD) is a major public health problem that often goes unrecognized until late-stage disease (Weiner, 2007). In patients with chronic kidney disease, potentially toxic compounds are accumulated in the body, called uremic toxins; all efforts are due to reduce these products (Vanholder et al. 2001). Hyperkalemia is a potential threat to patient safety in CKD and its occurrence increases the odds of mortality (Einhorn et al. 2009). Lactulose is hyper osmotic agent increases stool water contents, softens stool, promotes peristalsis and reduces blood ammonia concentration (Weber, 1997) and also could promote fecal excretion of water, sodium, potassium, ammonium, urea, and protons (Vogt & Frey, 1997). Lactulose, as a prebiotic, plays an important role in regulating nitrogen unwanted products and biochemical parameters in healthy individuals, but there is little information about these effects on patients with kidney failure. In this study, we aimed to evaluate Lactulose efficacy in reduction of nitrogen products, blood potassium and fluid overload in patients with end-stage renal failure.

MATERIALS AND METHODS

In this prospective before-after intervention study, 17 patients with end stage renal disease (ESRD) were evaluated. Patients older than 45 years were included in the study. The exclusion criteria were a history of gastrointestinal or metabolic disease. Participants were advised to maintain their usual diet during the study period. Those who could not keep up with the study protocol or tolerate study medications were excluded. The Ethics Committee of Islamic Azad University of Pharmaceutical Sciences approved the study, and all patients gave informed consent. The study was conducted over an 12-week period. The participants received 10 ml of lactulose syrup, 3 times a day. The doses administered were chosen based on therapeutic recommendations for CKD patients in a way that they would not suffer from negative effects or discomfort. Before and at the end of the study, blood samples were collected. Concentrations of nitrogen waste products were measured before and after lactulose treatment, including urea, creatinine and uric acid. Blood potassium and fluid overload were also evaluated. Statistical analyses were performed using the SPSS software (Statistical Package for the Social Sciences), version 18.0; Continuous variables were expressed as mean ± standard deviation. Differences in the means before and after treatment were evaluated by the repeated measure ANOVA test. A P value less than 0.05, was considered significant.

RESULTS

17 CKD patients including 76.47 % men and 23.53 % women with the mean age of 65.88 were evaluated.

Table 1: Mean Changes in Levels of Blood Nitrogen Products after Treatment with Lactulose in Patients with Chronic Kidney Disease

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before Treatment</th>
<th>After Treatment</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine, mg/dl</td>
<td>9.26±3.47</td>
<td>7.47±3.41</td>
<td>0.07</td>
</tr>
<tr>
<td>Urea, mg/dl</td>
<td>118.02±24.57</td>
<td>105.39±39.41</td>
<td>0.001</td>
</tr>
<tr>
<td>Uric acid, mg/dl</td>
<td>6.05±1.17</td>
<td>5.44±1.57</td>
<td>0.7</td>
</tr>
</tbody>
</table>

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Table 2: Mean change in Level of Blood potassium After Treatment With Lactulose in Patients With Chronic Kidney Disease

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before Treatment</th>
<th>After Treatment</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Potassium</td>
<td>5.51±0.78</td>
<td>4.29±0.49</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Table 3: Mean change in Patient’s weight After Treatment With Lactulose in Patients With Chronic Kidney Disease

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before Treatment</th>
<th>After Treatment</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s weight</td>
<td>75.54±6.30</td>
<td>74.69±6.20</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Mean Changes in Levels of Blood Nitrogen Products after Treatment with Lactulose in Patients with Chronic Kidney Disease are shown in Table 1. Urea level was significantly reduced after the treatment with lactulose. Although there was a decrease in creatinine and uric acid levels, the difference was not significant (Table 1).

Mean change in Level of Blood potassium is shown in Table 2. Potassium was also significantly lower after the treatment with lactulose (Table 2). And according to Table 3 the Fluid overload was significantly reduced after 3 month.

DISCUSSION

Most CKD symptoms or uremia are caused by protein intolerance; symptoms arise because the patient is unable to excrete metabolic products of dietary protein and the ions contained in protein-rich foods. Consequently, CKD patients accumulate salt, phosphates, uric acid and many nitrogen-containing metabolic products, and secondary problems of metabolic acidosis, bone disease and insulin resistance become prominent (Mandayam & Mitch, 2006). Hyperkalemia commonly limits optimizing treatment to slow stage 3 or higher chronic kidney disease (CKD) progression. The risk of hyperkalemia is linked to dietary potassium intake, level of kidney function, concomitant diseases that may affect potassium balance such as diabetes, and use of medications that influence potassium excretion (Lazich & Bakris, 2014). Lactulose is a non-absorbable disaccharide and plays an important role in regulating nitrogen unwanted products. Evidence suggests that metabolism by the enteric flora is necessary for its mechanism of action. When the intestinal flora metabolizes lactulose, bacterial incorporation of nitrogen increases, as does the bacterial mass. The presence of a carbohydrate and the acidic environment caused by the production of organic acids also act to reduce the breakdown of other nitrogen-containing compounds to ammonia and other potential cerebral toxins. The administration of lactulose to humans causes an increase in fecal nitrogen. Lactulose administration causes a reduction in the urea production rate consistent with a reduced entry of ammonia into portal blood (Weber, 1996). Although lactulose adherence is relatively poor in large part due to gastrointestinal adverse effects such as: abdominal pain, bloating, and flatus (Watanabe et al. 1997; Prasad et al. 2007; Dhiman et al. 2000; Meng et al. 2015). It is well tolerated in CKD patients (Cockram et al. 1998).

In this study we evaluated this possibility in patients with advanced CKD and observed a significant reduction in urea and potassium...
level after 3 months of treatment with oral lactulose. As 1 month before and during the study period, all patients were on routine medical management with the same quantity and quality; these reductions could be attributed to lactulose administration. Urea reduction is possibly due to increased fecal excretion of nitrogen products and reduced urinary excretion (De Preter et al. 2006). It is shown that lactulose causes a reduction in urea production in patients with hepatic encephalopathy (Weber, 1996) and increases nitrogen excretion into the fecal fractions in cirrhotic patients (Clausen & Mortensen, 1997).

A study by Tayebi Khosroshahi et al. (2014) showed that using lactulose could reduce nitrogen products including urea and creatinine. However, in our study, we found no significant reduction in creatinine level after treatment with lactulose but we found a significant reduction in blood urea nitrogen. Like our findings, Yang and colleagues, De Preter et al. (2006) observed urea lowering effects of lactulose. Mathialahan & Sandle (2003) reported a significant reduction in potassium level after treatment with lactulose.

Limitation of our study is having no control group, short period of study and number of patients. As another limitation, we could not control patients’ food and lifestyle during the study, which could affect the blood urea nitrogen levels. The longer treatment with lactulose would show better results.

CONCLUSION

Lactulose administration in CKD patients along with other treatments has beneficial effects of reduction of some nitrogen products. In addition, there is a positive effect on blood potassium and fluid overload, the use of lactulose in CKD patients can be suggested in order to receive better therapeutic results. More studies are needed to confirm these findings.

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References


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