JNEPHROL 0000; 00(00): 000-000

DOI: 10.5301/jn.5000129

In vivo assessment of bacteriotherapy on acetaminophen-induced uremic rats

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Abstract

Objectives: **Acetaminophen is a commonly used antipyretic agent which, at high doses, causes renal tubular damage and uremia. Bacteriotherapy affords a promising approach to mitigating uremic intoxication by ingestion of live microbes able to catabolize uremic solutes in the gut. The present study evaluates the nonpathogenic soil-borne urease-positive bacterium Sporosarcina pasteurii (Sp) as a potential urea-targeted component for such an "enteric dialysis" formulation.**

Methods: **Twenty-four albino male rats were randomly divided into 4 groups: The control group (group NC) received distilled water intraperitoneally for 7 days. The positive control group (group U) received 500 mg/kg acetaminophen intraperitoneally for 7 days. The tested group (group UP) was administered Sp at a dosage of 10^9 cells/day for 5 weeks, after receiving 500 mg/kg per day of acetaminophen intraperitoneally for 7 days. Vehicle control (group VC) received only Sp at a dosage of 10^9 cells/day for 5 weeks without acetaminophen treatment. Blood, kidney, liver and stool samples were collected after scarification, for biochemical (urea, creatinine, malondialdehyde, superoxide dismutase, catalase, glutamate oxaloacetate transaminase [GOT] and glutamate pyruvate transaminase [GPT] of blood, kidney and liver) tests. Limited fecal analysis was performed.**

Results: **Blood urea nitrogen (urea, creatinine) and toxicity indicators (GOT, GPT) were increased, and antioxidant enzymes were decreased in group U. Blood urea nitrogen and toxicity indicators were reduced, and antioxidant enzymes were increased significantly in the group UP ($p<0.05$) compared with group U. The number of Sp was increased in Sp-treated groups compared with groups NC and U.**

Conclusions: **The study demonstrated that the bacteria tested reduced blood urea nitrogen levels significantly.**

Key words: *Acetaminophen, Enteric dialysis, Sporosarcina pasteurii, Uremia*

Introduction

Currently chronic kidney disease (CKD) appears to be a foremost problem across the world, and it is ranked fourth among the key diseases in the United States, affecting over 20 million people and growing at 8% yearly (1). Worldwide, the number of patients with CKD is rising, and it is now being recognized as a major public health problem that may reach epidemic levels over the next decade. Uremia is a potentially lethal syndrome of kidney disease demanding instant treatment. The most often used treatment options for uremia include kidney transplantation and dialysis, which are very expensive and not free from side effects. In the United States the cost of treating patients with renal replacement therapy and renal injury will be US $28 billion by the year 2010, and in India 90% patients suffering from kidney disease are not able to afford the cost of uremia management (2). At present, worldwide statistical data on the incidence and prevalence of kidney disease, the resulting mortality and the high cost of treatment demonstrate the requirement for an effective alternative.

The use of analgesics such as acetaminophen regularly over long durations of time can cause analgesic nephropathy, another cause of kidney disease. Acetaminophen overdose may result in potentially fatal hepatic and renal necrosis in humans and experimental animals (2). In the early stage of acetaminophen toxicity, formation of the reactive intermediate *N*-acetyl-p-benzoquinone imine (NAPQI) through cytochrome P450 occurs. At therapeutic doses, NAPQI is removed by conjugation with glutathione sulfhydryl (GSH). High doses of acetaminophen when in-