Post-print: Benzbromarone Combined with Sodium Bicarbonate in the Treatment of Hyperuricemia Complicated by Essential Hypertension

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Abstract

Objective To investigate the clinical efficacy of benzbromarone combined with sodium bicarbonate in the treatment of hyperuricemia complicated with essential hypertension. Methods A total of 126 patients with hyperuricemia and essential hypertension were enrolled and randomly divided into groups A, B, and C using the random number table method, with 42 cases in each group. Group A received benzbromarone alone, group B received sodium bicarbonate alone, and group C received benzbromarone combined with sodium bicarbonate. Changes in serum creatinine, serum uric acid (UA), 24-hour urinary UA, blood urea nitrogen, triglycerides, and 24-hour mean systolic and diastolic blood pressure were compared among the three groups before and after treatment. Results After 5 weeks of treatment, serum UA, 24-hour systolic and diastolic blood pressure in all three groups were significantly reduced compared with baseline ($P<0.05$), while urinary UA was significantly increased ($P<0.05$). Furthermore, serum UA, 24-hour mean systolic and diastolic blood pressure in group C were lower than those in groups A and B ($P<0.05$), and urinary UA was higher than that in groups A and B ($P<0.05$). All these differences were statistically significant. Conclusion Benzbromarone combined with sodium bicarbonate in the treatment of hyperuricemia complicated with essential hypertension can effectively reduce serum UA, 24-hour mean systolic and diastolic blood pressure, increase urinary UA excretion, and demonstrates significant clinical efficacy, warranting promotion and application.

Full Text

Preamble

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Benzbromarone Combined with Sodium Bicarbonate in the Treatment of Hyperuricemia Complicated with Primary Hypertension

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Abstract

Objective: To investigate the clinical efficacy of benzbromarone combined with sodium bicarbonate in the treatment of hyperuricemia complicated with primary hypertension.

Methods: A total of 126 patients with hyperuricemia and primary hypertension were enrolled and randomly divided into three groups (A, B, and C) of 42 patients each using a random number table method. Group A received benzbromarone alone, group B received sodium bicarbonate alone, and group C received combination therapy with both drugs. Changes in serum creatinine, serum uric acid (UA), 24-hour urinary UA, blood urea nitrogen, triglycerides, and 24-hour mean systolic and diastolic blood pressure were compared before and after treatment.

Results: After 5 weeks of treatment, serum UA, 24-hour mean systolic and diastolic blood pressure were significantly lower than baseline in all three groups ($P<0.05$), while urinary UA was significantly higher ($P<0.05$). Furthermore, group C exhibited lower serum UA, 24-hour mean systolic and diastolic blood pressure compared to groups A and B ($P<0.05$), and higher urinary UA ($P<0.05$). All differences were statistically significant.

Conclusion: Benzbromarone combined with sodium bicarbonate effectively reduces serum UA, 24-hour mean systolic and diastolic blood pressure, and increases urinary UA excretion in patients with hyperuricemia complicated by primary hypertension. This combination therapy demonstrates significant clinical efficacy and warrants broader clinical application.

Keywords: benzbromarone; sodium bicarbonate; hyperuricemia; primary hypertension

Introduction

With improvements in living standards and changes in dietary patterns and lifestyle, the incidence of hyperuricemia (HUA) has increased significantly, seriously affecting public health and quality of life. Multiple studies have demonstrated that HUA is closely associated with cardiovascular diseases including primary hypertension, coronary heart disease, and heart failure, and that reducing serum UA levels can decrease the risk of cardiovascular events such as primary hypertension [1-4]. Benzbromarone is a commonly used urate-lowering agent in clinical practice [5], while sodium bicarbonate can assist in uric acid

reduction by alkalinizing urine [6-7]. Although numerous studies have reported on benzbromarone combined with other drugs for urate reduction [8-10], systematic research on its combination with sodium bicarbonate is lacking, and no studies have investigated this combination for treating HUA complicated with primary hypertension. Therefore, it is essential to fully recognize the role of HUA in the development, progression, and prognosis of primary hypertension. This study examined blood pressure, serum UA, and urinary UA levels in patients with HUA and primary hypertension to investigate and compare the clinical effectiveness of benzbromarone and sodium bicarbonate combination therapy for HUA with primary hypertension.

Methods

1.1 General Patient Data

A total of 126 hospitalized patients with primary hypertension and HUA were randomly selected from February 2014 to February 2016. Inclusion criteria: diagnosis of hypertension met the standards of the 2010 Chinese Guidelines for the Management of Hypertension, and diagnosis of HUA met the criteria of the Expert Consensus on the Diagnosis and Treatment of Asymptomatic Hyperuricemia with Cardiovascular Disease. Exclusion criteria: severe cardiac, hepatic, or renal insufficiency; secondary hypertension; thyroid disease; diabetes mellitus; severe anemia; and alcohol abuse. All patients and their families provided informed consent for participation in this study.

Patients were randomly assigned using a digital table method to three groups: benzbromarone treatment group (A), sodium bicarbonate treatment group (B), and combination therapy group (C). Baseline comparisons showed no statistically significant differences among the three groups in age, gender, systolic blood pressure, diastolic blood pressure, body mass index (BMI), triglycerides, serum creatinine, serum UA, urinary UA, or blood urea nitrogen .

1.2 Treatment Protocol

Group A received benzbromarone alone (50 mg once daily), group B received sodium bicarbonate alone (0.5 g three times daily), and group C received combination therapy with both agents at the same dosages. All patients were instructed to follow a low-fat, low-purine diet.

1.3 Observation Parameters

During hospitalization, seated blood pressure was measured three times daily and averaged. Systolic blood pressure, diastolic blood pressure, height, and BMI were recorded. Changes in serum creatinine, serum UA, urinary UA, blood urea nitrogen, and triglycerides were observed and compared before and after treatment.

1.4 Statistical Analysis

Data were analyzed using GraphPad Prism 5.01 software. Measurement data are expressed as mean ± standard deviation and compared using t-tests. Enumeration data are expressed as percentages and compared using chi-square tests. Comparisons between any two of the three groups (A, B, and C) were performed using one-way ANOVA with LSD method. $P<0.05$ was considered statistically significant.

Results

2.1 Comparison of Blood Pressure and Other Biochemical Indicators

Compared with baseline, 24-hour mean systolic and diastolic blood pressure decreased significantly in all three groups after treatment ($P<0.05$). No statistically significant differences were observed in triglycerides, blood urea nitrogen, or serum creatinine after treatment ($P>0.05$) .

2.2 Comparison of Serum UA and Urinary UA Before and After Treatment

Serum UA levels were significantly lower after treatment in all three groups compared with baseline ($P<0.05$). Post-treatment serum UA in group C was significantly lower than in groups A and B ($P<0.05$). Twenty-four-hour urinary UA was significantly higher after treatment in all three groups ($P<0.05$), with group C showing higher levels than groups A and B ($P<0.05$) .

Discussion

With national economic development and changes in dietary structure and lifestyle, the incidence of HUA has been increasing annually [11]. Recent studies have shown that hypertension, hyperlipidemia, and obesity are often accompanied by HUA. Viazzi et al. [2] demonstrated that HUA in children is an independent risk factor for cardiovascular events including primary hypertension. Epidemiological studies in adults have similarly shown that HUA is a risk factor for hypertension, and that serum UA levels can predict the development and prognosis of hypertension [12-13], with each 60 mol/L increase in serum UA associated with a 25% increased risk of hypertension [2-3]. Although the mechanism by which HUA causes hypertension remains incompletely understood, research indicates that serum UA can stimulate renin secretion, activate the renin-angiotensin system, inhibit nitric oxide synthase, cause renal vasoconstriction, and induce arterial smooth muscle cell proliferation, thereby leading to hypertension [14-15].

Benzbromarone is a commonly used urate-lowering drug that reduces serum UA by inhibiting active reabsorption of UA in the kidneys and promoting its excretion [5]. Sodium bicarbonate can alkalinize urine in hyperuricemic patients, maintain normal pH, dissolve uric acid, and promote UA excretion [7,16].

Numerous studies [8-10] have found that benzbromarone combined with other drugs can exert synergistic effects to maximally reduce serum UA and increase urinary UA excretion. Our study similarly found that benzbromarone alone, sodium bicarbonate alone, and combination therapy all significantly reduced serum UA and increased urinary UA excretion in hyperuricemic patients. However, the combination therapy group demonstrated significantly superior clinical effects in reducing serum UA and increasing urinary UA excretion compared to either monotherapy group ($P<0.05$), suggesting a synergistic effect between benzbromarone and sodium bicarbonate.

Multiple studies have shown that reducing serum UA levels helps control blood pressure and improve renal function [17-19]. Our results demonstrate that both the benzbromarone group and the combination therapy group significantly reduced 24-hour mean systolic and diastolic blood pressure in hyperuricemic patients ($P<0.05$). Research indicates that HUA is closely related to hypertension, and that UA reduction can effectively control blood pressure [3]. Therefore, the blood pressure-lowering effect of benzbromarone in HUA patients is likely related to its reduction of serum UA levels. The sodium bicarbonate group also reduced serum UA levels but did not lower blood pressure, consistent with the findings of Chen et al. [6]. This suggests that while sodium bicarbonate reduces serum UA, it may also cause excessive sodium load, affecting cardiac function and leading to elevated blood pressure, thereby offsetting the blood pressure-lowering contribution of UA reduction.

In summary, benzbromarone combined with sodium bicarbonate effectively reduces serum UA, 24-hour mean systolic and diastolic blood pressure, and increases urinary UA excretion in patients with HUA complicated by primary hypertension. This combination therapy demonstrates significant clinical efficacy and warrants broader clinical application.

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Note: Figure translations are in progress. See original paper for figures.