BRITISH JOURNAL OF HOSPITAL MEDICINE

ARTICLE

Analysis of the Efficacy and Safety of Benzbromarone Combined with Sodium Bicarbonate Tablets in the Treatment of Hyperuricemia

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Abstract

Aims/Background Hyperuricemia is a metabolic disorder characterized by elevated levels of uric acid in the blood. If left untreated, hyperuricemia can progress to gout, which manifests as acute arthritic attacks, and may also lead to uric acid nephrolithiasis and other renal conditions. This widespread condition poses significant risks to human health and quality of life. This study retrospectively evaluated the effectiveness and safety of using benzbromarone in combination with sodium bicarbonate tablets for the treatment of gout associated with hyperuricemia.

Methods The study reviewed the electronic medical records (EMR) of 150 patients with gout and hyperuricemia who were admitted to our hospital between May 2018 and December 2023. These patients were divided into two groups: a control group and a research group. The control group received oral sodium bicarbonate tablets, while the research group was treated with oral benzbromarone tablets in addition to sodium bicarbonate tablets. The study compared the treatment outcomes and adverse reactions between the two groups, as well as assessed changes in blood-related indicators, the number of tophi, pain levels, and quality of life before and after treatment.

Results The research group demonstrated a higher total effective rate compared to the control group ($p < 0.05$). Post-treatment, the research group exhibited significantly lower levels of serum uric acid (UA), serum creatinine (Scr), and urea ($p < 0.05$). Additionally, this group had fewer tophi and lower visual analog scale (VAS) scores compared to the control group ($p < 0.05$). Quality of life scores were also significantly higher in the research group ($p < 0.05$). No statistically significant difference was found in the incidence of adverse drug reactions between the two groups ($p > 0.05$).

Conclusion The combination of benzbromarone and sodium bicarbonate tablets is highly effective in treating gout associated with hyperuricemia. This treatment not only reduces uric acid levels and the number of tophi but also enhances renal function, alleviates pain, and improves the overall quality of life for patients.

Key words: benzbromarone; sodium bicarbonate tablets; hyperuricemia; gout

Submitted: 24 July 2024 Revised: 9 September 2024 Accepted: 11 September 2024

How to cite this article:
Zhu W, Huang K, Zhang X, Deng B. Analysis of the Efficacy and Safety of Benzbromarone Combined with Sodium Bicarbonate Tablets in the Treatment of Hyperuricemia. Br J Hosp Med. 2024. https://doi.org/10.12968/hmed.2024.0453

Introduction

Uric acid (UA), the primary metabolite of purines in the body, can increase the likelihood of gout attacks when serum levels are elevated, a condition known as hyperuricemia (Su et al, 2020). Gout is an inflammatory joint condition resulting from the accumulation of monosodium urate crystals in the joints and/or soft tissues (Eun et al, 2022). In 2017, approximately 7.44 million new cases of gout

were reported globally, with a consistent rise in incidence and prevalence observed over the past 25 years (1992–2017) (Mattiuzzi and Lippi, 2020). Gout and hyperuricemia are associated with an increased risk of developing metabolic syndrome, chronic kidney disease, and cardiovascular diseases (Hansildaar et al, 2021).

Uric acid-lowering therapy is essential for effectively managing hyperuricemia and gout. This can be achieved through lifestyle modifications, including avoiding alcohol, limiting high-purine foods, increasing physical activity, and managing weight (Yu et al, 2023). For patients with poorly controlled gout outside of acute attacks, medication is necessary to alleviate clinical symptoms (Vargas-Santos and Neogi, 2017). Sodium bicarbonate tablets, a commonly used uric acid-lowering drug, help convert uric acid into a more soluble form by raising urine pH, thus facilitating its excretion. However, sodium bicarbonate does not directly lower blood uric acid levels and its role in treating gout is more supportive. To effectively lower uric acid levels, additional treatments are typically required (Xue et al, 2021).

Benzbromarone works by inhibiting the reabsorption of uric acid in the renal tubules, thereby enhancing its excretion from the body. This mechanism effectively reduces blood uric acid levels, making benzbromarone a valuable therapeutic agent for managing hyperuricemia and gout (Azevedo et al, 2019). Despite the potential benefits, there are limited reports on the clinical application of combining sodium bicarbonate tablets with benzbromarone. This study explored this combination as a potentially innovative approach.

Methods

Study Subjects

We conducted a retrospective review of electronic medical records for patients at our hospital from May 2018 to December 2023, identified 150 individuals diagnosed with gout and hyperuricemia using propensity score matching (PSM) method. Sample size calculations, using a two-tailed test with a Type I error of 0.05 and a power of 0.8, indicated that 132 subjects were needed based on an incidence of 70% in the control group, 90% in the research group, and an estimated 10% attrition rate. The study included 150 patients who were divided into two groups: the research group and the control group, with 75 patients in each group (Fig. 1).

Inclusion criteria were as follows: clinically diagnosed gout with hyperuricemia; no history of gout attacks in the past two weeks; no use of salicylates or corticosteroids in the past month; and informed consent obtained from patients and their families after they were fully informed about the study. Exclusion criteria included secondary hyperuricemia; history of gastrointestinal surgery or severe gastrointestinal disease; severe hepatic or kidney dysfunction; allergies to the study medications; pregnancy or breastfeeding; and mental illness or cognitive impairment.

This study followed the Declaration of Helsinki and received approval from the Zhongda Hospital Southeast University's ethics committee (No.2019-265). Informed consent was obtained from the patients and their families after they were fully informed about the study.

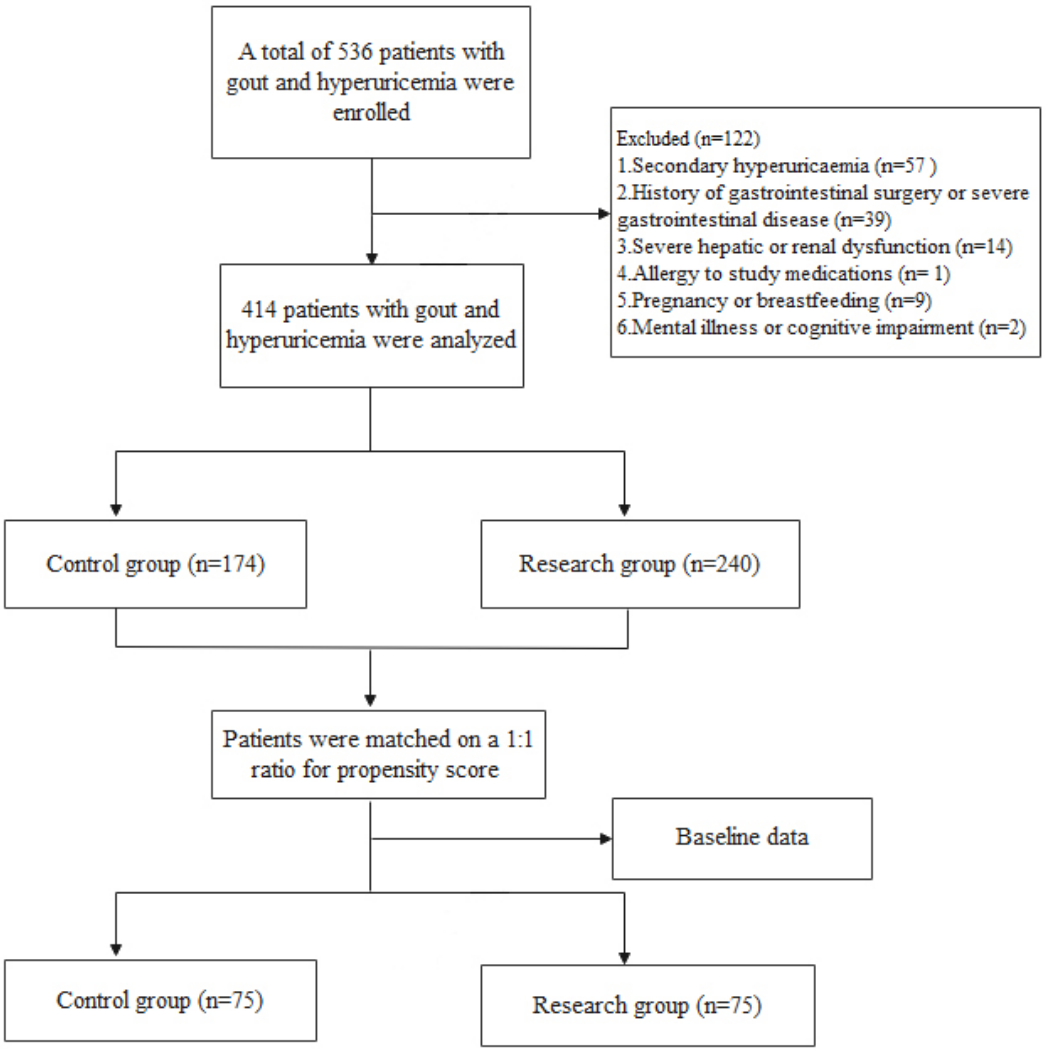

Fig. 1. Propensity score matching (PSM) flowchart.

Treatment

Both groups received basic treatment, which included health education, lipid-lowering therapy, blood pressure management, and dietary guidance. The control group was prescribed oral sodium bicarbonate tablets (National Drug Approval No. H42021752, YuanDa Pharmaceutical Co., Ltd., Wuhan, China) at a dose of 0.3 g, three times daily, with instructions to consume 1.5–2.0 liters of water daily. The research group received an additional oral dose of benzbromarone tablets (National Drug Approval No. J20180056, Hermann, Feucht, Germany) at a dose of 50 mg once daily, in addition to the sodium bicarbonate regimen followed by the control group. Both groups underwent treatment for 8 consecutive weeks.

Observation Indicators

Treatment effects were assessed and graded based on the 2019 national guidelines for gout diagnosis and treatment from China (Chinese Society of Endocrinology, 2020). The grading criteria were as follows: a significant effect was defined as the disappearance of gout-related symptoms, normalization of uric acid levels, or a

reduction of more than 30% compared to pre-treatment levels; an effective outcome was characterized by significant improvement in gout-related symptoms, with uric acid levels reduced by 10–30% compared to pre-treatment levels; and ineffective was defined as when neither of the above criteria was met. The total effective rate = significant effective number + effective number/total number.

Blood samples (5 mL) were collected from patients before and after treatment. These samples were centrifuged for 15 minutes to separate the serum, which was then analyzed using an automatic biochemical analyzer (Labomed Inc FACA401, Fisher Scientific, Waltham, MA, USA) to measure UA, serum creatinine (Scr), and urea levels. The number of tophi was evaluated using ultrasound (Logic E9, GE HealthCare Technologies Inc., Wauwatosa, WI, USA), and joint pain was assessed with the visual analog scale (VAS) (Qu et al, 2024), ranging from 0 to 10, where lower scores indicated reduced pain levels.

Patients were followed up regularly, and any adverse reactions during treatment were recorded, including gastrointestinal issues (nausea, vomiting, diarrhea), rashes, fever, and liver function abnormalities (alanine transaminase, aspartate aminotransferase, total bilirubin). Quality of life was measured both prior to and four weeks after treatment using the SF-36 scale (Chandratre et al, 2013), which covers general health (GH), role-physical (RP), mental health (MH), and social functioning (SF), with scores ranging from 1 to 5, where higher scores indicated an improved quality of life. All measurements were performed by experienced doctors.

Statistical Analysis

Data analysis and visualization were conducted using GraphPad Prism 6 software (GraphPad Software, Inc., San Diego, CA, USA). PSM method was used to balance the baseline data, generated by multivariate logistic regression model. The medication taken was the dependent variable, and the baseline information (age, BMI, diseases course, gender, smoking history, alcohol history, hypertension, and diabetes) were the independent variables. The research and control groups were matched in a 1:1 ratio (no caliper values) and the matching method was single nearest neighbour with no replacement. For categorical data, the chi-square test was employed when the theoretical frequency (T) was ≥ 5 and the sample size (N) was ≥ 40. When $1 \leq T < 5$ and $N \geq 40$, the continuity-corrected chi-square test was used. Fisher's exact test was applied when $T < 1$ and $N < 40$. For quantitative data, the Shapiro-Wilk test was used to assess the normal distribution of continuous variables. Normally distributed continuous variables were expressed as mean $\pm$ standard deviation (SD). To compare continuous data between groups, independent *t*-tests and Mann–Whitney U-test were performed, while paired *t*-tests were used to evaluate changes within the same group before and after treatment. Statistical significance was defined as a p-value < 0.05.

Table 1. Baseline characteristics of the two groups before PSM.

Group	Control group (n = 174)	Research group (n = 240)	χ^2/t	p value
Age (years), mean ± SD	49.67 ± 12.26	50.96 ± 13.58	1.010	0.313
BMI (kg/m^2), mean ± SD	23.18 ± 2.93	22.75 ± 3.12	1.434	0.151
Disease course (months), mean ± SD	8.16 ± 3.79	7.34 ± 3.42	2.263	0.024
Gender, n (%)			0.160	0.690
Female	14 (2.29)	22 (9.16)		
Male	160 (97.71)	218 (90.84)		
Smoking history, n (%)			4.034	0.045
Yes	71 (40.8)	75 (31.25)		
No	103 (59.2)	165 (68.75)		
Alcohol history, n (%)			4.835	0.028
Yes	78 (44.83)	82 (34.17)		
No	96 (55.17)	158 (65.83)		
Hypertension, n (%)			0.150	0.698
Yes	57 (32.76)	83 (34.58)		
No	117 (67.24)	157 (65.42)		
Diabetes, n (%)			3.962	0.047
Yes	51 (29.31)	93 (38.75)		
No	123 (70.68)	147 (61.25)		

Note: BMI, body mass index; SD, standard deviation.

Results

Comparison of Baseline Characteristics before and after PSM

The baseline data of the two groups before PSM are shown in Table 1, and there were significant differences in disease course, smoking history, alcoholism history, and diabetes between the two groups ($p < 0.05$). Detailed data are shown in Table 1.

The baseline characteristics, including age, body mass index (BMI), duration of illness, gender, smoking habits, alcohol use, history of hypertension, and history of diabetes, did not differ significantly between the two groups after PSM ($p > 0.05$). Detailed information is provided in Table 2.

Evaluation of Clinical Effectiveness

Table 3 shows detailed data on the clinical effectiveness of the two groups of patients after PSM. The research group exhibited a significantly higher overall effectiveness rate compared to the control group ($p < 0.05$).

Analysis of Uric Acid and Renal Function Markers

The baseline levels of UA, Scr, and urea were similar between the two groups ($p > 0.05$). Following treatment, both groups experienced a significant reduction in UA, Scr, and urea levels. However, the reduction was more pronounced in the research group compared to the control group ($p < 0.05$). Detailed results are presented in Fig. 2.

Table 2. Baseline characteristics of the two groups after PSM.

Group	Control group (n = 75)	Research group (n = 75)	χ^2/t	p value
Age (years), mean ± SD	49.45 ± 12.84	50.37 ± 12.41	0.446	0.656
BMI (kg/m^2), mean ± SD	23.12 ± 2.54	22.87 ± 2.51	0.605	0.545
Disease course (months), mean ± SD	8.08 ± 3.41	7.56 ± 3.11	0.976	0.330
Gender, n (%)			0.315	0.575
Female	6 (8.00)	8 (10.67)		
Male	69 (92.00)	67 (89.33)		
Smoking history, n (%)			1.884	0.170
Yes	30 (40.00)	22 (29.33)		
No	45 (60.00)	53 (70.67)		
Alcohol history, n (%)			0.990	0.320
Yes	34 (45.33)	28 (37.33)		
No	41 (54.67)	47 (62.67)		
Hypertension, n (%)			0.263	0.608
Yes	28 (37.33)	25 (33.33)		
No	47 (62.67)	50 (66.67)		
Diabetes, n (%)			0.839	0.360
Yes	18 (24.00)	23 (30.67)		
No	57 (76.00)	52 (69.33)		

Note: BMI, body mass index; SD, standard deviation.

Table 3. Evaluation of clinical effectiveness.

Group	Markedly effective, n (%)	Effective, n (%)	Ineffective, n (%)	Total effective rate, n (%)
Control group (n = 75)	10 (13.33)	46 (61.33)	19 (25.33)	56 (74.67)
Research group (n = 75)	39 (52.00)	30 (40.00)	6 (8.00)	69 (92.00)
χ^2	–	–	–	8.112
p value	–	–	–	0.004

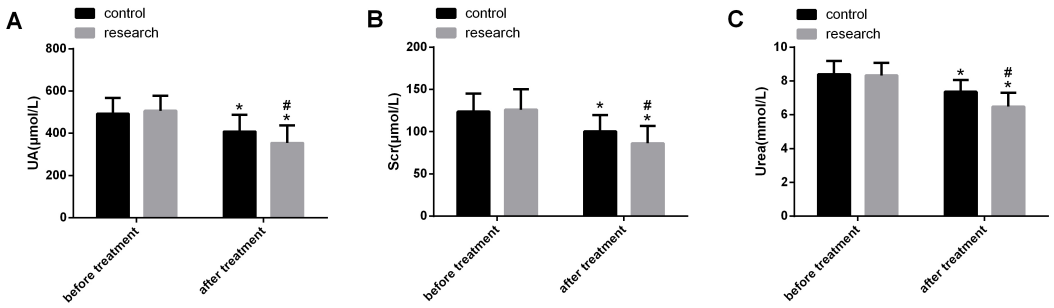

Fig. 2. Analysis of uric acid and renal function markers. (A) UA levels in both groups before and after treatment. (B) Scr levels in both groups before and after treatment. (C) Urea levels in both groups before and after treatment. Note: *$p < 0.05$ compared to the same group before treatment; $^{\#}p < 0.05$ compared to the control group at the same time. UA, uric acid; Scr, serum creatinine.

Table 4. Analysis of adverse reactions.

Group	Gastrointestinal reactions, n (%)	Rash, n (%)	Fever, n (%)	Abnormal liver function, n (%)	Total incidence, n (%)
Control group (n = 75)	6 (8.00)	1 (1.33)	2 (1.33)	0 (0.00)	9 (10.67)
Research group (n = 75)	9 (12.00)	3 (4.00)	2 (2.67)	2 (2.67)	16 (21.33)
χ^2	0.667	0.257	0.257	–	2.352
p value	0.414	0.612	0.612	0.497	0.125

Note: Fisher's exact test was used for the analysis of abnormal liver function.

Comparison of Tophi Count and Pain Scores

Prior to treatment, there were no significant differences in the tophi count and VAS scores between the two groups ($p > 0.05$). Following treatment, both groups experienced significant decreases in tophi count and VAS scores, with the research group showing a more pronounced reduction compared to the control group ($p < 0.05$). Refer to Fig. 3 for details.

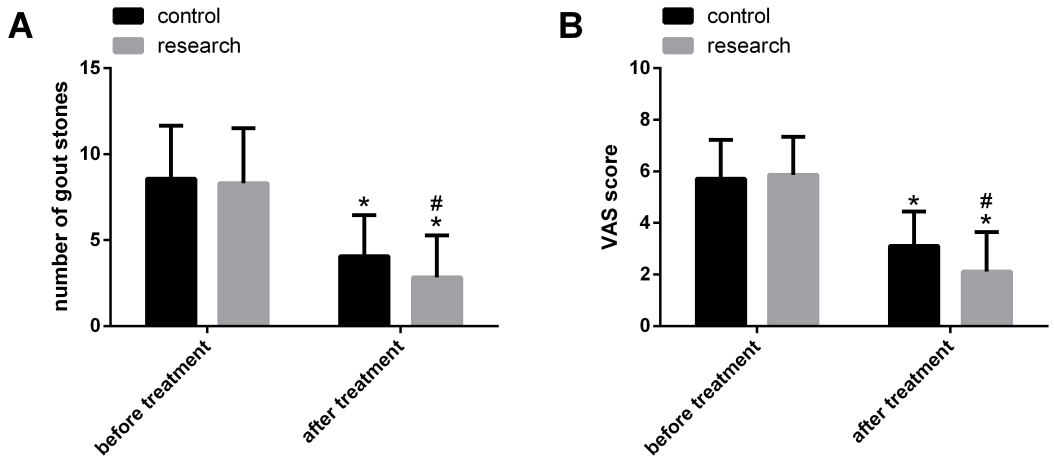

Fig. 3. Comparison of tophi count and pain scores. (A) Comparison of tophi count before and after treatment in both groups. (B) Comparison of VAS scores before and after treatment in both groups. Note: $^{*}p < 0.05$ compared to the same group before treatment; $^{\#}p < 0.05$ compared to the control group at the same time point. VAS, visual analog scale.

Analysis of Adverse Reactions

The most common adverse reactions in both groups were related to the gastrointestinal system. Statistical analysis indicated no significant difference in the frequency of these adverse reactions between the two groups ($p > 0.05$). Refer to Table 4 for details.

Evaluation of Quality-of-Life Improvements

Before treatment, the SF-36 quality of life scores for GH, RP, MH, and SF dimensions showed no significant differences between the two groups ($p > 0.05$). Post-treatment, both groups exhibited significant improvements in these dimen-

sions, with the research group achieving notably higher scores than the control group ($p < 0.05$). Detailed results are illustrated in Fig. 4.

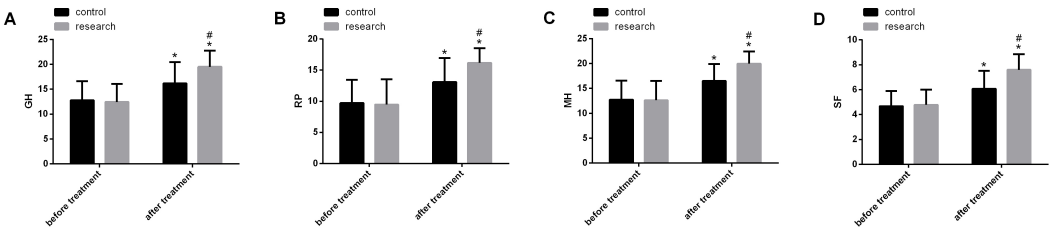

Fig. 4. Evaluation of quality-of-life improvements. (A) GH scores for both groups, pre- and post-treatment. (B) RP scores for both groups, pre- and post-treatment. (C) MH scores for both groups, pre- and post-treatment. (D) SF scores for both groups, pre- and post-treatment. Note: $^{*}p < 0.05$ when compared to pre-treatment within the same group; $^{\#}p < 0.05$ when compared to the control group at the same time point. GH, general health; RP, role-physical; MH, mental health; SF, social functioning.

Discussion

As living standards improve and dietary patterns shift in China, there has been an increasing prevalence of gout. This trend is attributed to the long-term consumption of diets high in fat, sugar, protein, and purines, as well as prolonged smoking and alcohol consumption (Zhu et al, 2022). These dietary and lifestyle habits lead to elevated levels of uric acid in the blood, a primary factor in the development of gout. Furthermore, the rising prevalence of obesity and metabolic syndrome exacerbates the risk of developing this condition (Cai et al, 2024). Gout is characterized by joint redness, swelling, restricted movement, and tenderness; if left untreated, it can lead to complications such as kidney damage and joint destruction, significantly impairing the patient's quality of life (Zhang et al, 2023; Zhou et al, 2020). Currently, there is no specific curative treatment for gout; existing strategies focus on managing acute attacks and providing effective long-term maintenance (Qaseem et al, 2017). Anti-inflammatory medications, including non-steroidal anti-inflammatory drugs (NSAIDs), and urate-lowering agents, such as xanthine oxidase inhibitors, are commonly used in the clinical management of gout (Liu et al, 2023). These medications are essential for controlling acute inflammation and reducing uric acid levels in the blood, both of which are key factors in gout pathogenesis. NSAIDs alleviate pain and inflammation during acute attacks, while urate-lowering therapies are crucial for long-term management to prevent recurrence and complications associated with chronic hyperuricemia. However, the clinical efficacy of these medications is often limited by adverse reactions and relapse upon discontinuation, resulting in suboptimal patient satisfaction (Shi et al, 2023).

There is a significant relationship between gout and hyperuricemia. Excessively high levels of uric acid can lead to the accumulation of urate crystals in renal tubules or joints. This accumulation can cause inflammation and damage in these areas, resulting in kidney impairment or joint issues such as pain, swelling, and

reduced mobility. Proper management of UA levels is essential to prevent these complications and maintain overall health (Elsaid et al, 2023).

The concentration of UA in the human body is influenced by renal transporters responsible for urate reabsorption. Located on the luminal membrane of the proximal tubule, Urate Transporter 1 (URAT1) facilitates the uptake of urate from the tubular fluid into the cells of the proximal tubule (Hou et al, 2023). Benzbromarone primarily decreases UA levels in the blood by blocking the URAT1 transporter, thus increasing urate excretion and helping to control and treat gout and related symptoms (Chen et al, 2021).

Normally, uric acid is widely distributed in the form of urate and can be filtered through the glomeruli. When the pH is below 5.5, uric acid becomes less soluble and can form uric acid stones (He et al, 2022). Using sodium bicarbonate tablets can alkalize the urine, promoting the dissolution of uric acid in the urine.

The findings of this retrospective study indicate a significantly higher overall treatment efficacy in the research group compared to the control group. Patients in the research group showed notable reductions in UA, Scr, and urea levels, as well as a decrease in the number of tophi and VAS scores following treatment. These results suggest that the combined use of benzbromarone and sodium bicarbonate tablets provides a more effective therapeutic benefit for managing gout and hyperuricemia. This combination therapy appears to offer better outcomes in reducing key clinical markers and alleviating symptoms associated with these conditions.

The effectiveness of this combination therapy is due to the fact that the mechanisms by which benzbromarone and sodium bicarbonate tablets lower uric acid do not interfere with each other. This allows the medications to exert their effects simultaneously, leading to a more effective and rapid reduction in blood uric acid levels. Consequently, this inhibits the formation of urate crystals, prevents significant damage to kidney function and joints, and reduces patient pain.

Moreover, the research group did not exhibit a notable increase in adverse reactions with the combined therapy, suggesting that the dual-drug regimen maintains a favorable safety profile. The data imply that this combination of medications can be administered without increasing the risk of adverse effects, supporting their concurrent use in clinical settings.

Quality of life can reflect the health status of individuals or populations from multiple perspectives and is a key indicator used by scholars globally to measure the therapeutic effects of certain treatments. This study retrospectively analyzed the quality of life among patients in both cohorts. As expected, the research group showed higher scores in the GH, RP, MH, and SF dimensions compared to the control group. These results highlight the substantial efficacy of combining benzbromarone with sodium bicarbonate tablets. Furthermore, this study provides valuable evidence supporting the broader application of these two medications in clinical practice, potentially improving patient outcomes and informing future treatment guidelines.

However, this study has certain limitations due to its retrospective nature. First, it did not investigate the optimal dosage of benzbromarone combined with sodium bicarbonate tablets for treating gout and hyperuricemia. Second, it did not include

long-term follow-up of clinical outcomes in either group, making it impossible to assess potential relapse situations. Addressing these limitations in future research would be beneficial.

Conclusion

In conclusion, the combination of benzbromarone and sodium bicarbonate tablets is effective in treating gout with hyperuricemia. This regimen effectively lowers uric acid levels, improves kidney function, reduces pain, enhances quality of life, and demonstrates a favourable safety profile.

Key Points

- The combination of benzbromarone and sodium bicarbonate tablets demonstrates superior efficacy in treating gout and hyperuricemia.
- This combination therapy effectively reduces the amount of tophi and alleviates patient pain.
- No significant adverse reactions were observed with the treatment of benzbromarone combined with sodium bicarbonate tablets.
- The combination therapy significantly improves patients' quality of life.

Availability of Data and Materials

The data analyzed was available on the request for the corresponding author.

Author Contributions

WHZ and KKH designed the research study and wrote the first draft. XYZ and BZD performed the research. XYZ and BZD analyzed the data. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study followed the Declaration of Helsinki and received approval from the Zhongda Hospital Southeast University's ethics committee (No.2019-265). Informed consent was obtained from the patients and their families after they were fully informed about the study.

Acknowledgement

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

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