Tropical Journal of Pharmaceutical Research September 2023; 22 (9): 1999-2008
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v22i9.31

Original Research Article

Meta-analysis of the effect of losartan relative to other angiotensin receptor antagonists on serum uric acid level

Jinjie Zhou[1], Yongwei Zhang[2], Lin Cheng[3]*

[1]Department of Cardiovascular Internal Medicine, Huangpu Branch, Shanghai Ninth People´s Hospital, 200011, [2]CCU, TEDA International Cardiovascular Hospital, Tianjin 300457, [3]Bei Tai Ping Zhuang outpatient Department, Central Medical Branche of PLA General Hospital, Beijing, China

For correspondence:* ***Email:* *summer791008@126.com*

Sent for review: 16 May 2023 *Revised accepted: 28 August 2023*

Abstract

Purpose: *To systematically analyze the disparity in uric acid reduction between losartan and other angiotensin receptor antagonists.*
Methods: *A computer-based search was conducted in databases including EMBASE, PubMed, Wanfang, CNKI, Ovid MEDLINE, and Web of Science to identify original literature comparing the impact of losartan with other angiotensin receptor antagonists on blood uric acid levels. Utilizing the Cochrane Collaboration bias risk tool, a quality assessment of the included randomized controlled studies was conducted.*
Results: *A total of 12 publications were obtained, consisting of 6 randomized controlled studies and 6 cohort studies. Five of the twelve publications assessed the impact of losartan compared to valsartan on blood uric acid levels. The heterogeneity analysis yielded I^2 = 98 % ($p < 0.01$), indicating substantial variability among the studies. Findings indicated that losartan was more effective than valsartan in reducing blood uric acid levels (SMD = -3.26, 95 % CI (-5.01 to 1.51), $p < 0.05$). Four publications investigated the impact of losartan versus telmisartan on blood uric acid levels. The results revealed that losartan had a greater effect in reducing blood uric acid levels compared to telmisartan (SMD = -1.77, 95 % CI (-3.411 to -0.13), $p < 0.05$).*
Conclusion: *Among the angiotensin receptor antagonists used as antihypertensive drugs, losartan stands out for its significant ability to reduce uric acid levels. This finding provides a strong evidence-base for making clinical medication decisions.*

Keywords: *Losartan, ValsartanAngiotensin receptor antagonists, Blood uric acid, Meta-analysis*

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, Web of Science, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

Cardiovascular disease is globally recognized as the leading cause of mortality and disability, making it a critical health concern. Elevated levels of uric acid are recognized as a significant contributor to cardiovascular disease, directly associated with an increase in blood pressure [1,2]. Hypertension is a prevalent chronic clinical condition that contributes significantly to the risk of both cardiovascular and cerebrovascular diseases. When patients experience prolonged hypertension, it can lead to symptoms such as palpitations, vomiting, dizziness, and in severe

cases, convulsions and confusion [3,4]. Without prompt and effective blood pressure control, prolonged hypertension can lead to harm to essential organs such as the heart, brain, and kidneys, thereby endangering the well-being, safety, and survival of patients [5]. Hypertension and elevated levels of uric acid have a close relationship with the occurrence of cardiovascular disease. According to the available data, a 59.5 μmol/L elevation in the blood uric acid levels is linked to a 25% higher probability of developing combined hypertension [6]. Hypertension can contribute to a disorder in uric acid excretion, causing it to accumulate in the kidneys and trigger inflammatory reactions. This, in turn, can further increase blood pressure, creating a vicious cycle. Consequently, it is crucial to integrate effective strategies aimed at lowering both blood pressure and uric acid levels into the therapeutic approach when managing patients who have been diagnosed with hypertension and elevated uric acid levels. These interventions have a critical impact on enhancing clinical symptoms and liver function indicators in such patients [7,8].

Currently, drug treatment is commonly used as the primary approach in the clinical management of hypertension combined with high uric acid levels. A well-known antihypertensive medication called losartan is often prescribed for this purpose. Losartan effectively reduces uric acid levels by inhibiting renin, thus counteracting its effects. Additionally, losartan inhibits vasoconstriction and contributes to lowering blood pressure [9,10]. Indeed, losartan can facilitate the swift reabsorption of uric acid within the kidney tubules through its inhibition of urate transporter expression. Additionally, it possesses the ability to alkalize uric acid through the secretory function of the renal tubules. These mechanisms contribute to the effective control of blood uric acid levels [11].

However, numerous studies have demonstrated that various angiotensin receptor antagonists effectively reduce uric acid reuptake by inhibiting urate transporter expression, thus inducing uric acid excretion [12]. Although numerous studies have supported the notion that losartan may be more effective than other angiotensin receptor antagonists in reducing uric acid levels, the available evidence is still not sufficiently robust to definitively establish this perspective. The goal of this research is to examine recent research papers that assess the impact of losartan, in comparison to other angiotensin receptor antagonists, on the levels of uric acid in the bloodstream. By systematically examining the differences between losartan and other medications, the study aims to provide clinical references for treating patients with hypertension and elevated uric acid levels.

METHODS

Inclusion criteria

Randomized controlled or cohort studies conducted in Chinese or English, adhering to the diagnostic criteria outlined in the WHO/International Hypertension Consortium (ISH) guidelines (diastolic blood pressure ≥ 90 mmHg and systolic blood pressure ≥ 140 mmHg), patients with serum uric acid levels ≥ 420 μmol/L in men or ≥ 360 μmol/L in women, complete baseline data and relevant information on blood uric acid levels or changes before and after treatment, intervention with losartan in the experimental group while the control group used other angiotensin receptor antagonists, informed consent obtained from patients or their family members, and availability of complete and accurate clinical data.

The publications were excluded based on the following criteria: duplication or overlap in patient populations, inclusion of basic or overview literature, inaccessibility of full-text due to design issues, unpublished grey literature, inclusion of abstracts, case reports, meta-analyses, or pathology reports, lack of clarity regarding interventions, absence of data or values, incomplete or inaccurate clinical data, and literature focusing on the intolerance of study subjects to trial-related drugs.

Screening strategy of publications

A computerized search of original literature published in databases such as EMBASE, PubMed, CNKI, Wanfang, Ovid MEDLINE, and Web of Science was conducted to investigate the impact of losartan compared to other angiotensin receptor antagonists on blood uric acid levels. The search strategy combined subject-specific terms with free-text keywords. During the timeframe ranging from the database's inception until March 2023, data retrieval occurred. The Chinese search terms were Losartan, angiotensin receptor antagonist, blood uric acid, and losartan. The English search terms were Losartan, angiotensin receptor antagonist, blood uric acid, and losartan.

Data extraction and quality evaluation

Two researchers were selected for unified training, screened independently according to unified and standardized evaluation methods,

and further checked the screening results. Retrieved publications were screened through Endnote X9, and incomplete and repeatedly published literatures were excluded. Then, titles and abstracts of literatures were read. The process involved removing irrelevant literature and then conducting a thorough evaluation of the full text to establish if the publications fulfilled the inclusion criteria and were subsequently included. Should the two reviewers have differing opinions, the participation of a third researcher will be sought to facilitate the discussion and determine the inclusion of the publications. The data extraction included the following information: the titles of the included literatures, the researcher, the year of publication, the total sample size, the type of research, the intervention measures, and the dosage of drugs for the basic characteristics of the literatures. Additionally, it encompassed the baseline data of the research subjects, such as age, sex, and blood uric acid level.

Utilizing the Cochrane Collaboration bias risk tool, two researchers independently assessed the quality of the included randomized controlled studies. The evaluation contents were as follows: First, both the generation and allocation concealment of random sequences were assessed as low-risk, indicating high-quality publications. Second, the generation of the random sequence was considered low-risk, but other items were assessed as having some risk, resulting in medium-quality publications. Third, any publications that did not conform to the criteria set in the first or second point were regarded as low-quality. Assessment of the quality of the included cohort studies was carried out using the Newcastle Ottawa Scale (NOS). The evaluation criteria were as follows: The literature was divided into three categories based on the assigned scores: low-quality (1 - 3 points), medium-quality (4 - 6 points), and high-quality (7 - 9 points). If two researchers identify subjective selection bias during the screening process, it should be dealt with through discussion or, if required, evaluated by a third researcher to establish a consensus.

Statistical analysis

RevMan 5.4 software was utilized for processing the meta-analysis. The effect index for count data was set as the Standardized Mean Difference (SMD), while for measurement data, the Mean or Standard Deviation (SD) was used as the effect index. Additionally, a forest plot was utilized to graphically represent the corresponding 95% confidence interval (CI). The evaluation of heterogeneity among the studies involved the application of the I^2 statistic. In cases where the p-value surpassed 0.1 and I^2 fell below 50%, it suggested minimal statistical heterogeneity among the included studies, facilitating the utilization of the fixed effect model. A situation where $p < 0.1$ and $I^2 > 50$ % implied that the included studies demonstrated statistical heterogeneity, thereby prompting the choice of the random effect model. The reasons for heterogeneity were analyzed. actors potentially contributing to heterogeneity underwent subgroup analysis and sensitivity analysis, leading to the exclusion of publications with higher sensitivity. Additionally, a funnel plot was generated to visualize potential publication bias.

RESULTS

Screening process of literature

Databases such as CNKI, Pumbed, Wanfang, Ovid MEDLINE, EMBASE, and Web of Science were searched through the computer. A total of 171 publications were initially obtained out of which 85 publications with duplicate and overlapping data sets were excluded, and after reading the titles and abstracts, 99 publications without obvious correlation with this study were excluded, and 72 publications were obtained.

After reading the full text, 28 publications of basic or review type were excluded. Other publications that were excluded include, 3 publications of which the full text could not be obtained due to design problems, 7 publications of which the intervention measures were not clear, 11 publications of which were abstracts, case reports, meta-analyses, and pathology reports, 6 publications of which the clinical data were incomplete or inaccurate, 7 publications of which the research subjects were intolerant to trial related drugs. Finally, 12 publications were obtained [12-23]. The screening process for publications is shown in Figure 1.

Basic characteristics and quality evaluation of the included publications

In total, 12 publications were included in this study, mainly published from 1999 to 2020, including 6 randomized controlled studies and 6 cohort studies. The main attributes of the publications included in the study are outlined in Table 1. According to the criteria set for evaluating publications, it was found that 5 out of the 6 randomized controlled studies were low-quality, while 1 study met the requirements to be considered high-quality. The quality evaluation results of the included publications, displayed in Table 2 and Table 3, revealed that among the 6

cohort studies, 5 were high-quality publications, whereas 1 publication was rated as medium quality.

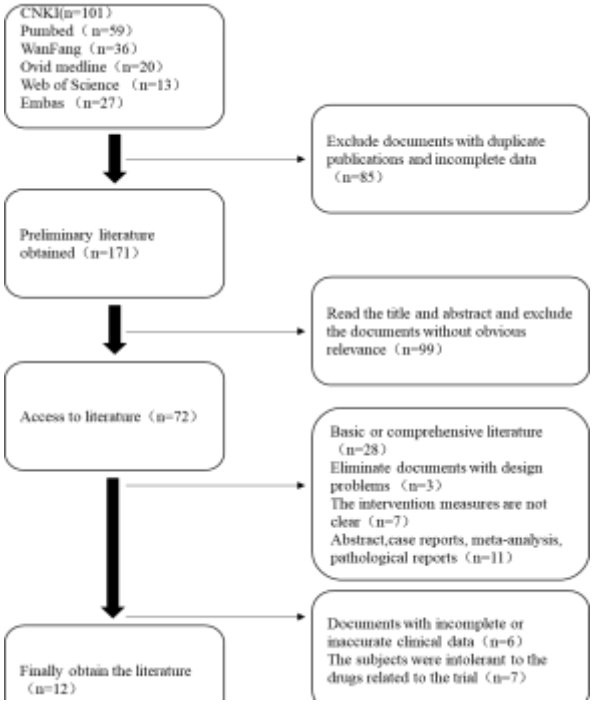

Figure 1: Flow chart of publications screening

Meta-analysis

Losartan versus valsartan

Five literature sources explored the influence of losartan in comparison to valsartan on blood uric acid levels. Notably, these studies exhibited considerable heterogeneity, with an I^2 value of 98 % and a statistically significant *p*-value of less than 0.01. The analysis incorporated a random-effects model to account for variability. Results of Forest plot showed that losartan was better than valsartan in reducing serum uric acid (SMD = -3.26, 95 % CI (-5.01 to 1.51), $p < 0.05$) (Figure 2).

Losartan versus telmisartan

A total of four literature reports were included in the analysis to investigate the impact of losartan versus telmisartan on blood uric acid levels. The findings revealed considerable heterogeneity, with an I2 value of 96 % and a *p*-value less than 0.01. The analysis incorporated a random-effects model to account for variability. Results of forest plot showed that losartan was better than telmisartan in reducing serum uric acid (SMD = -1.77, 95 % CI (- 3.411 to -0.13), $p < 0.05$). (Figure 3).

Losartan versus other angiotensin receptor antagonists

In comparison to other angiotensin receptor antagonists, losartan's effect on blood uric acid levels has been examined in 6 different publications. Great heterogeneity was observed among the literatures (I^2 = 98 %, $p < 0.01$). The analysis incorporated a random-effects model to account for variability. The results of Forest showed that losartan was superior to other angiotensin receptor antagonists in reducing serum uric acid, including eplesartan, irbesartan candesartan cilexetil, olmesartan (SMD = -1.26, 95 % CI (-2.94 to 0.42), $p < 0.05$) (Figure 4).

Evaluation of publication bias

Funnel plots were generated for the six publications that compared the impact of other angiotensin receptor antagonists on blood uric acid levels. The results revealed asymmetry in both the left and right sides of the funnel plot. The study identified the presence of publication bias, potentially attributed to several factors, including the small sample size, low quality of the included publications, and other variables. Refer to Figure 5 for further details.

DISCUSSION

The coexistence of hypertension and hyperuricemia significantly raises the risk of cardiovascular events occurring. Therefore, in the process of clinical treatment, it is necessary to control patients' hypertension symptoms and lower their blood uric acid levels. This approach facilitates the timely elimination of purine metabolic by-products and ultimately enhances patients' prognosis [24,25]. Losartan, as an angiotensin receptor antagonist, exhibits optimal antihypertensive effects. It functions by inhibiting the renin-angiotensin system, thereby reducing aldosterone secretion and vasoconstriction. This mechanism leads to a decrease in peripheral vascular dilation and vascular resistance, ultimately resulting in antihypertensive effects [26,27]. Furthermore, losartan also contributes to uric acid reduction. Its primary mode of action involves inhibiting the transport of urate by urate-transport proteins, leading to a decrease in the accumulation of uric acid in the proximal convoluted tubules. This process alkalizes uric acid in the urine, ultimately leading to reduced uric acid levels [28]. A large number of research reports have shown that losartan is superior to other angiotensin receptor antagonists in reducing uric acid [21,23].

Table 1: Basic characteristics of the included literature

Included publications	Cases (test group/ control group)	Interventions		Study period: weeks (W) and month (m)	Blood uric acid level (μMol/L)			
		Test group	control group		*Before treatment in the experimental group*	*After treatment in the experimental group*	*Control group before treatment*	*After treatment in the control group*
Puig 1999 [12]	30/30	Losartan	Ipsartan	4W	392.50±22.80	-13.30±7.20	417.40±41.69	15.20±8.00
Würzner 2001 [13]	13/13	Losartan	Irbesartan	8W	538.00±26.00	491.00±20.00	552.00±25.00	544.00±30.00
Hamada 2010 [14]	64/65	Losartan	Telmisartan	2m	512.70±88.40	512.70±123.80	486.20±97.20	574.60±106.08
Hamada 2010 [14]	64/65	Losartan	Candesartan Cilexetil	2m	512.70±88.40	512.70±123.80	486.20±97.20	530.40±106.08
Nishida 2013 [15]	214/266	Losartan	Valsartan	12m	457.90±95.40	445.50±49.50	468.50±110.50	485.30±107.00
Nishida 2013 [15]	214/185	Losartan	Telmisartan	12m	457.90±95.40	445.50±49.50	472.00±95.50	483.50±95.50
Nishida 2013 [15]	214/458	Losartan	Candesartan Cilexetil	12m	457.90±95.40	445.50±49.50	489.70±106.00	502.10±106.00
Nishida 2013 [15]	214/192	Losartan	Olmesartan	12m	457.90±95.40	445.50±49.50	476.50±106.00	493.30±106.60
Zhou Jian 2017 [16]	43/43	Losartan	Valsartan	2m	481.60±46.80	297.60±23.30	478.10±52.40	431.90±37.50
Wu Lihua 2017 [17]	40/40	Losartan	Valsartan	4W	471.12±59.73	321.12±45.73	469.97±44.87	455.17±65.07
Gao Yan 2017 [18]	53/53	Losartan	Telmisartan	-	485.20±33.70	347.10±36.20	486.10±34.60	420.40±33.70
Wang Yang 2017 [19]	34/34	Losartan	Valsartan	8W	478.59±50.64	320.65±21.76	479.98±50.71	460.48±47.64
Zou Wen 2019 [20]	40/40	Losartan	Valsartan	-	496.13±12.34	430.12±10.45	495.21±12.34	495.13±12.12
Lin Qifen 2019 [21]	25/25	Losartan	Telmisartan	8W	483.57±42.34	301.39±31.25	482.78±41.69	450.18±38.94
Qiu Hong 2020 [22]	30/30	Losartan	Ipsartan	-	481.32±40.12	440.51±37.52	395.67±32.11	356.13±31.32
Tian Wenliang 2020 [23]	30/30	Losartan	Irbesartan	12W	504.50±53.60	335.20±13.30	496.60±52.10	490.90±48.70

Table 2: Quality evaluation of included randomized controlled studies

Included studies	Random method	Allocation concealment	Patients and implementation person blindness	Outcome evaluation person blindness	Of the outcome data integrity	Selective reporting of findings	Other sources of bias
Puig 1999 [12]	High risk	unknown	Low risk	Low risk	unknown	Low risk	Low risk
Würzner 2001 [13]	unknown	unknown	High risk	Low risk	Low risk	Low risk	Low risk
Hamada 2010 [14]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Zhou Jian 2017 [16]	High risk	unknown	High risk	High risk	unknown	Low risk	Low risk
Wu Lihua 2017 [17]	unknown	unknown	Low risk	Low risk	Low risk	Low risk	Low risk
Lin Qifen 2019 [21]	unknown	High risk	Low risk	Low risk	Low risk	Low risk	Low risk

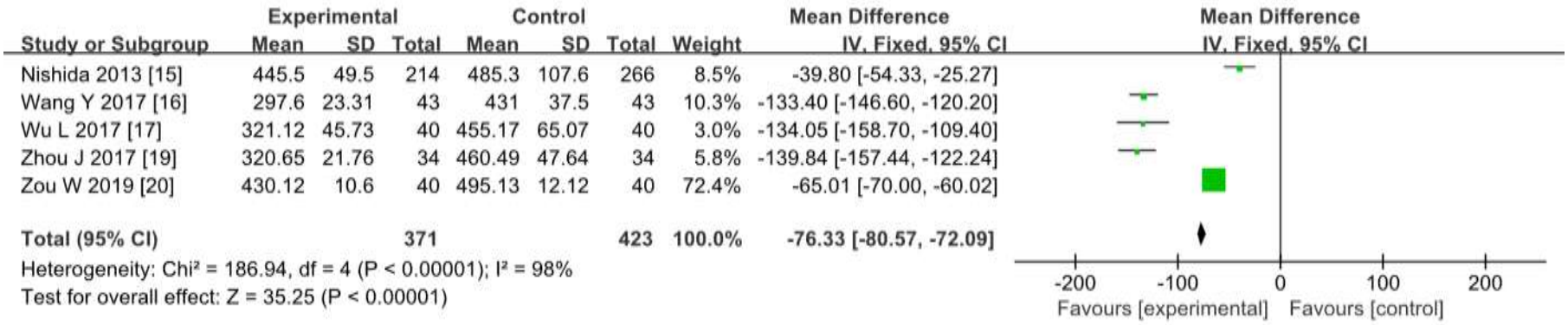

Figure 2: Effect of losartan compared with valsartan on serum uric acid level

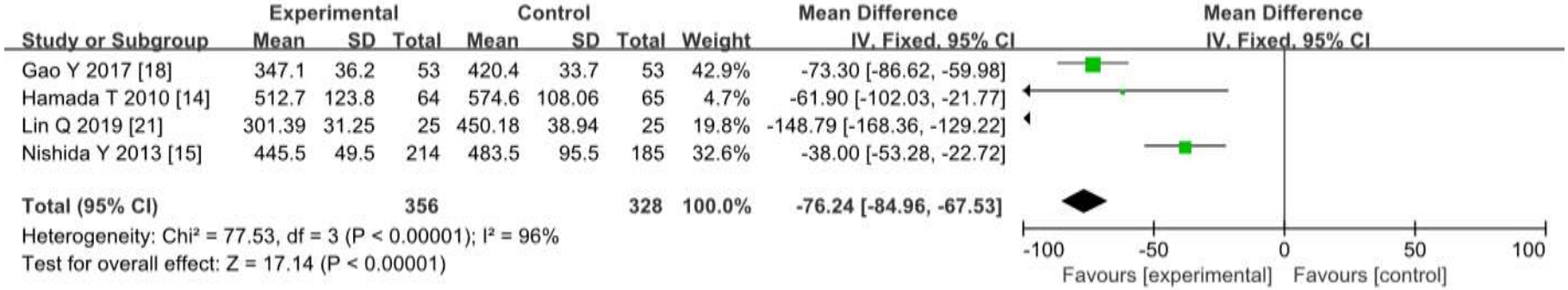

Figure 3: Effect of losartan on serum uric acid level in comparison to telmisartan

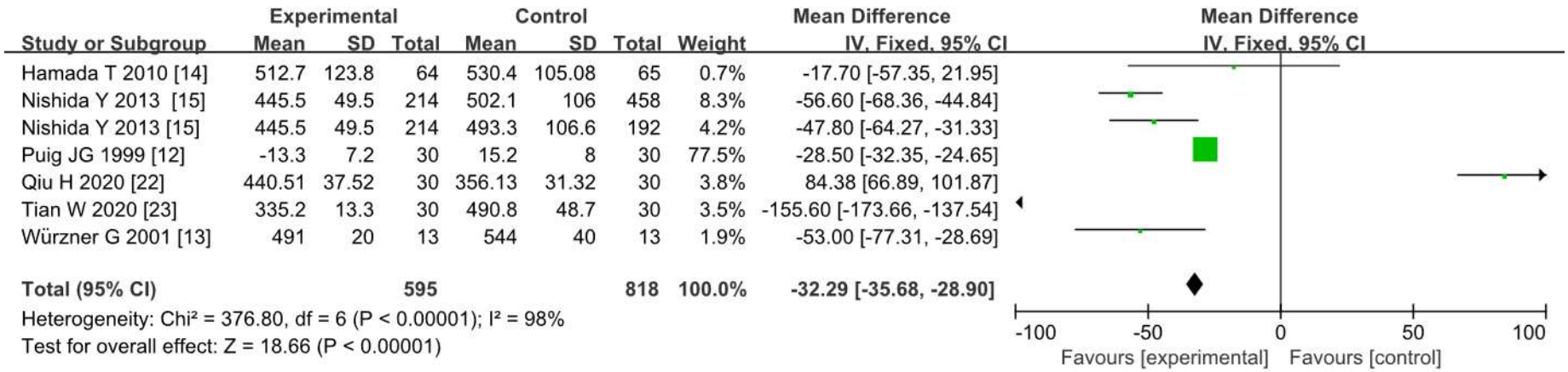

Figure 4: Impact of losartan on blood uric acid level compared with other angiotensin receptor antagonists

Table 3: Quality evaluation of included cohort studies

Included literature	Selectivity	Expose	Comparability	NOS score
Nishida 2013 [15]	4	2	1	7
Gao Yan 2017 [18]	2	2	1	4
Wang Yang 2017 [19]	3	2	3	8
Zou Wen 2019 [20]	3	2	2	7
Qiu Hong 2020 [22]	2	2	3	7
Tian Wenliang 2020 [23]	4	2	2	8

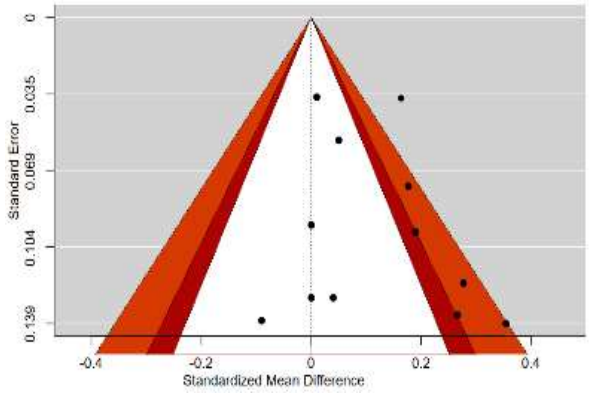

Figure 5: Funnel plot analysis of publication bias

However, there is currently a paucity of systematic analyses in this area. Therefore, this research had the purpose of systematically analyzing the differences between losartan and other angiotensin receptor antagonists in reducing blood uric acid levels. To accomplish this objective, the study meticulously extracted recent original publications that specifically explored the effects of losartan in comparison to alternative angiotensin receptor antagonists on the concentrations of uric acid in the blood. The aim of this research is to yield valuable references for the clinical handling of patients diagnosed with hypertension and coexisting hyperuricemia and to propose novel strategies for improved management of such patients.

The research sample for this study consisted of 12 publications, evenly split between 6 randomized controlled trials and 6 cohort studies. The results of this study showed that losartan was better than other angiotensin receptor antagonists in reducing uric acid. One possible explanation for this could be that losartan exhibits a stronger inhibitory effect on the expression of urate transport proteins compared to other angiotensin receptor antagonists. Consequently, this mechanism leads to a reduction in uric acid levels [29]. According to Borghi [30] and other experts, it has been established through expert consensus that losartan is the sole angiotensin receptor antagonist that exhibits a noticeable effect in reducing uric acid levels. Consequently, the findings of this study align closely with previous research reports and expert consensus. In 2015, a meta-analysis conducted by several scholars demonstrated that losartan's ability in reducing uric acid levels was significantly superior to that of other angiotensin receptor antagonists. However, it is worth noting that the aforementioned study only encompassed 7 publications examining the uric acid-lowering effect of losartan in comparison to other angiotensin receptor antagonists. As a result, the present study carries more weight and credibility.

Despite achieving some insightful findings, this study still has several limitations. Firstly, the study did not provide an explanation for factors such as medication combinations and renal function, which may influence uric acid levels. This lack of information introduces uncertainty regarding the actual effectiveness of uric acid reduction after treatment. Secondly, the meta-analysis highlighted the suboptimal quality of the literature included in the study. The majority of the studies did not provide comprehensive information on randomization and allocation concealment methods, contributing to the heterogeneity observed in the results. Moreover, the limited number of literature sources within the past five years implies a lack of comprehensive coverage on the research topic, potentially affecting the comprehensiveness of the meta-analysis. Lastly, it is crucial to approach the results of this study with caution due to the potential presence of selection bias, emphasizing the need for further research to confirm these findings.

CONCLUSION

Among the angiotensin receptor antagonists, losartan demonstrates the potential to reduce uric acid levels, offering an evidence-based foundation for making informed clinical medication decisions and guiding medical practice. To enhance the credibility of the findings, it is imperative to include more high-quality publications in future studies, considering the limitations posed by the small sample size and the quality of the included literature.

DECLARATIONS

Acknowledgements

None provided.

Funding

None provided.

Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. The study was conceptualized, designed, and the manuscript was initially drafted by Jinjie Zhou and Lin Cheng. The experimental data was collected, analyzed, and interpreted by Jinjie Zhou and Yongwei Zhang. Revisions for important intellectual content were done by Yongwei Zhang and Lin Cheng. All authors, including Jinjie Zhou, reviewed and approved the final manuscript for publication.

REFERENCES

1. *Katsiki N, Kouvari M, Panagiotakos DB, Borghi C, Chrysohoou C, Mikhailidis DP, Pitsavos C. The association between serum uric acid levels and 10 year cardiovascular disease incidence: results from the Attica prospective study. Rev Cardiovasc Med 2021; 22: 991-1001.*
2. *Chilunga FP, Henneman P, Requena-Méndez A, Meeks K, Beune E, Mannens MMAM, Agyemang C. Hyperuricaemia and its association with 10-year risk of cardiovascular disease among migrant and non-migrant African populations: The Rhodam study. Trop Med Int Health 2020; 25: 496-505.*
3. *Husain MJ, Datta BK, Kostova D, Joseph KT, Asma S, Richter P, Jaffe MG, Kishore SP. Access to cardiovascular disease and hypertension medicines in developing countries: an analysis of essential medicine lists, price, availability, and affordability. J Am Heart Assoc 2020; 9: e015302.*
4. *Wang Y, Wang Y, Du H. Effect of combined use of home blood pressure monitoring and nifedipine on blood pressure compliance and quality of life of patients with essential hypertension. Trop J Pharm Res 2022; 21: 2009-2016.*
5. *Dorobantu M, Tautu OF, Dimulescu D, Sinescu C, Gusbeth-Tatomir P, Arsenescu-Georgescu C, Mitu F, Lighezan D, Pop C, Babes K, et al. Perspectives on hypertension's prevalence, treatment and control in a high cardiovascular risk East European country: data from the Sephar III survey. J Hypertens 2018; 36: 690-700.*
6. *Hou L, Zhang M, Han W, Tang Y, Xue F, Liang S, Zhang B, Wang W, Asaiti K, Wang Y, et al. Influence of salt intake on association of blood uric acid with hypertension and related cardiovascular risk. PLoS One 2016; 11: e0150451.*
7. *Zhao P, Shi W, Shi Y, Xiong Y, Ding C, Song X, Qiu G, Li J, Zhou W, Yu C, et al. Positive association between weight adjusted wait index and hyperuricemia in patients with hypertension: the China H-type Hypertension Registry study. Front Endocrinol (Lausanne) 2022; 13: 1007557.*
8. *Salman M, Shehzadi N, Khan MT, Islam M, Amjad S, Afzal O, Mansoor S, Qamar S, Peerzada S, Khan AH, et al. Erectile dysfunction: prevalence, risk factors and involvement of antihypertensive drugs intervention. Trop J Pharm Res 2016; 15: 869-876.*
9. *Matsumura K, Arima H, Tominaga M, Ohtsubo T, Sasaguri T, Fujii K, Fukuhara M, Uezono K, Morinaga Y, Ohta Y, et al. Comfort investigators Effect of losartan on serum uric acid in hypertension treated with a diabetic: the comfort study. Clin Exp Hypertens 2015; 37: 192-196.*
10. *Fan L, Guo Y, Wu Q, Hu T, Chen X, Guo J, Liu Y, Lu Y, Lin M. Mechanism of xuezhuo Huayu Yiqi Tongluo formula in the treatment of uric acid nephropathy based on network pharmacology, molecular docking, and in vivo experiments. Evid Based Complement Alternat Med 2023; 2023: 6931644.*
11. *Mouri Y, Natsumeda M, Okubo N, Sato T, Saito T, Shibuya K, Yamada S, On J, Tsukamoto Y, Okada M, et al. Successful treatment of acute uric acid nephropathy*

with rasburicase in a primary central nervous system lymphoma patient showing a drafting response to methotrexate case report. J Clin Med 2022; 11: 5548.

12. *Puig JG, Mateos F, Buño A, Ortega R, Rodriguez F, Dal-Ré R. Effect of eprosartan and losartan on uric acid metabolism in patients with essential hypertension. J Hypertens 1999; 17: 1033-1039.*
13. *Würzner G, Gerster JC, Chiolero A, Maillard M, Fallab-Stubi CL, Brunner HR, Burnier M. Comparative effects of losartan and irbesartan on serum uric acid in hypersensitive patients with hyperuricaemia and gout. J Hypertens 2001; 19: 1855-1860.*
14. *Hamada T, Mizuta E, Kondo T, Hirai M, Yamada K, Kato M, Shigemasa C, Yamamoto Y, Ninomiya H, Igawa O, et al. Effects of a low dose antihypertensive in combination with losartan, telmisartan, or candesartan on serum urate levels in hypertensive patients. Arzneimittelforschung 2010; 60: 71-75.*
15. *Nishida Y, Takahashi Y, Susa N, Kanou N, Nakayama T, Asai S. Comparative effect of angiotensin II type I receptor blockers on serum uric acid in hypersensitive patients with type 2 diabetes mellitus: a retrospective observational study. Cardiovasc Diabetol 2013; 12: 159.*
16. *Zhou J, Gu J. Comparison of clinical effects of losartan and Valsartan in the treatment of hypertension complicated with hyperuricemia. Electronic J Clin Med Lit 2017; 4: 762.*
17. *Wu L, Jiang Y, Su Hao, Gao L. Effect of losartan on serum uric acid in patients with hypertension complicated with hyperuricemia. Chin J Integrative Med Cardio-/Cervical Dis 2017; 15: 1758-1760.*
18. *Gao Y. Comparative study on the efficiency of losartan and telmisartan in the treatment of hypertension with hyperuricemia electronic. J Clin Med Lit 2017; 4: 350.*
19. *Wang Y. Comparison of clinical effects of losartan and Valsartan in the treatment of hypertension complicated with hyperuricemia. Guide of China Medicine 2017; 15: 131-132.*
20. *Zou W. Clinical value of losartan in the treatment of hypertension complicated with hyperuricemia. J North Pharm 2019; 16: 92-93.*
21. *Lin Q, Yu P, Su D, Fan L, Chen L. Analysis on the difference of clinical effects between losartan and telmisartan in the treatment of hypertension with hyperuricemia. Guizhou Med J 2019; 43: 271-274.*
22. *Qiu H, Yin Y. Corrective effect observation on treatment of mild and moderate hypertension with hyperuricemia with alisartan ester. Home Medicine 2020: 147.*
23. *Tian W. Comparison of clinical effects between losartan and irbesartan in the treatment of senile essential hypertension with hyperuricemia. Jilin Med J 2020; 41: 341-342.*
24. *Zhao P, Shi W, Shi Y, Xiong Y, Ding C, Song X, Qiu G, Li J, Zhou W, Yu C, et al. Positive association between weight adjusted wait index and hyperuricemia in patients with hypertension: the China H-type Hypertension Registry study. Front Endocrinol (Lausanne) 2022; 13: 1007557.*
25. *Lin X, Wang X, Li X, Song L, Meng Z, Yang Q, Zhang W, Gao Y, Yang Z, Cai H, et al. Gender- and age specific differences in the association of hyperuricemia and hypertension: a cross sectional study. Int J Endocrinol 2019; 2019: 7545137.*
26. *Cho EJ, Lee HY, Sung KC, Park S, Sohn IS, Park CG, Choi DJ, Ha JW, Ahn YK, Shin J, et al. Comparison of 24-hour ambulatory central blood pressure reduction efficiency between fixed amlodipine or up-titrated hydrochlorothiazide plus losartan: the k-central study. Am J Hypertens 2019; 32: 992-1002.*
27. *Aftab RA, Khan A, Adnan A, Sulaiman S, Khan T. Safety and efficiency of losartan 50 mg in reducing blood pressure among patients with post-diagnosis ultraviolet hypertension: a randomized control trial. Sci Rep 2017; 7: 17741.*
28. *Masajtis-Zagajewska A, Majer J, Nowicki M. Losartan and eprosartan induce a similar effect on the acute rise in serum uric acid concentration after an oral fructose load in patients with metabolic syndrome. J Renin Angiotensin Aldosterone Syst 2021; 2021: 2214978.*
29. *Wang Z, Cui T, CI X, Zhao F, Sun Y, Li Y, Liu R, Wu W, Yi X, Liu C. The effect of polymer of uric acid transporters on uric acid transport. J Nephrol 2019; 32: 177-187.*
30. *Borghi C, Tykarski A, Widecka K, Filipiak KJ, Domienik KAR, Owicz J, Kostka Jeziorny K, Varga A, Jaguszewski M, Narkiewicz K, Mancia G. Expert consultation for the diagnosis and treatment of patient with hyperuricemia and high cardiovascular risk. Cardiol J 2018; 25: 545-563.*