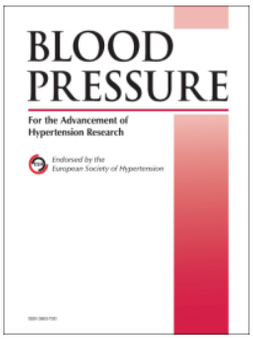

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RESEARCH ARTICLE

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Effects of Dan Shen (*Salvia miltiorrhiza*) on blood pressure management in hypertensive patients: a randomized controlled trial

Pan Li[a], Zonghua Jiang[a], Linfei Dong[b], Shifeng Wang[a], Jiangli Qi[a] and Longhong Zhu[a]

[a]Department of Neurology, Ganzhou Hospital-Nanfang Hospital, Southern Medical University, Ganzhou City, Jiangxi Province, China; [b]Department of General Practice, Ganzhou Hospital-Nanfang Hospital, Southern Medical University, Ganzhou City, Jiangxi Province, China

ABSTRACT

Objective: This randomised, double-blind, placebo-controlled trial aimed to evaluate the efficacy and safety of *Salvia miltiorrhiza* (Dan Shen) in the management of primary hypertension.

Methods: From April 2023 to September 2024, 320 patients aged 30–75 years with diagnosed primary hypertension were enrolled at Ganzhou Hospital of Southern Medical University (Ganzhou People's Hospital). Patients were randomised to receive either intravenous *Salvia miltiorrhiza* (20 mL diluted in 200 mL of 5% glucose daily for 12 weeks) or a placebo with identical appearance and administration. Primary outcomes included changes in blood pressure measured by 24-h ambulatory blood pressure monitoring (ABPM). Secondary outcomes included symptom scores, lipid and glucose profiles and health-related quality of life (QoL) assessed using validated laboratory measures and the SF-36 questionnaire.

Results: A significant reduction in systolic and diastolic blood pressure (DBP) was observed in the intervention group from week 4, reaching 136.78 ± 10.28 and 85.36 ± 8.37 mmHg by week 12, respectively – both significantly lower than in the control group ($p < 0.01$). Symptom scores for headache, dizziness and fatigue decreased by 1.2, 1.1 and 1.2 points ($p < 0.01$), with no significant changes in the control group. Lipid profiles improved notably: total cholesterol (TC), LDL-C and triglycerides (TGs) declined by 9.8%, 10.7% and 17.1%, respectively, while HDL-C increased by 17.0% (all $p < 0.05$). Fasting glucose levels fell by 4.3% ($p < 0.05$). QoL, assessed *via* SF-36, improved significantly, particularly in vitality (+20.9) and physical functioning (+18.6). Adverse events (AEs) were mild to moderate, mainly gastrointestinal discomfort and dizziness, and did not result in dropout. Treatment adherence was high, with 94.2% of participants completing at least 80% of the protocol.

Conclusion: Dan Shen significantly reduced both systolic and DBP, alleviated hypertension-related symptoms, improved lipid and glucose metabolism, and enhanced QoL in patients with primary hypertension.

PLAIN LANGUAGE SUMMARY

- Dan Shen effectively lowers blood pressure in hypertension patients.
- It improves symptoms and metabolic profiles safely.
- Enhances quality of life with mild, manageable side effects.

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Hypertension; *Salvia miltiorrhiza*; blood glucose; lipid metabolism; phytotherapy; cardiovascular risk factors

Introduction

Hypertension remains a leading global health concern, affecting over 1.3 billion people and contributing significantly to cardiovascular morbidity and mortality [1–3], especially in low- and middle-income countries [4]. Although standard antihypertensive drugs – such as ACE inhibitors and calcium channel blockers – are effective in reducing blood pressure, their long-term use is often limited by drug resistance, adverse effects and patient non-adherence [5,6]. As a result, complementary and alternative therapies with better safety profiles are increasingly being explored.

Salvia miltiorrhiza (Danshen), a traditional Chinese medicine, has demonstrated promising cardiovascular protective properties. Modern pharmacological investigations have elucidated that its principal

CONTACT Longhong Zhu zhulonghong@126.com 7th Floor, Inpatient Department, 18 Meiguan Avenue, Ganzhou City 341000, Jiangxi Province, China

bioactive constituents, including tanshinones and salvianolic acids, exert pleiotropic effects such as vasodilation, anti-inflammation, anti-oxidation and improvement of endothelial function [7,8]. Moreover, recent *in vivo* studies have indicated that Danshen significantly reduces blood pressure, improves hemodynamics and attenuates vascular remodelling [9]. However, robust, high-quality randomised controlled trials (RCTs) in clinical settings remain scarce. Consequently, definitive clinical evidence supporting Danshen as an effective adjunctive therapy for hypertension remains insufficient, and existing findings are, in some instances, inconsistent.

To address this gap, we conducted a randomised, double-blind, placebo-controlled trial to evaluate the efficacy and safety of Dan Shen in patients with primary hypertension. Specifically, we aimed to assess its impact on blood pressure, symptom relief, cardiovascular risk markers (lipid and glucose levels), quality of life (QoL) and adverse events (AEs). This study intends to provide robust clinical evidence to support the potential integration of Dan Shen into personalised hypertension care.

Methods

General information

This randomised, double-blind, placebo-controlled clinical trial was designed to evaluate the efficacy of *Salvia miltiorrhiza* (Dan Shen) in the management of primary hypertension. Between April 2023 and September 2024, 320 patients diagnosed with hypertension were recruited from Ganzhou Hospital of Southern Medical University (Ganzhou People's Hospital). The study protocol was approved by the institutional ethics committee, and all participants provided written informed consent prior to enrolment.

All procedures conformed to the ethical standards outlined in the Declaration of Helsinki and were overseen by the research center's ethics committee. Participants were fully informed regarding the study objectives, procedures, potential risks and their rights. They retained the right to withdraw from the trial at any point without consequence. Data collection and management were conducted using a validated electronic data capture (EDC) system to ensure accuracy and data integrity.

Sample size estimation was based on preliminary clinical observations and pre-trial data. Assuming a two-sided significance level (α) of 0.05 and a statistical power of 80%, the minimum required sample size was calculated to be 107 participants per group. Accounting for an anticipated dropout rate of 20%, the target enrolment was increased to 128 participants per group, for a total of 256 participants. Sample size calculations were performed by a certified statistician using PASS 2021 software (NCSS, LLC, Kaysville, UT) [10].

Inclusion criteria were as follows: (1) adults aged 30–75 years with a diagnosis of primary hypertension according to the 2017 Chinese Hypertension Guidelines (systolic blood pressure [SBP] ≥ 140 mmHg and/or diastolic blood pressure [DBP] ≥ 90 mmHg); (2) no history of severe comorbidities or hypertension-related complications (e.g. coronary artery disease, heart failure, chronic kidney disease); (3) no prior use of Dan Shen or related investigational treatments; and (4) no evidence of hepatic or renal insufficiency, diabetes or pregnancy.

Exclusion criteria included: (1) significant cardiovascular or chronic systemic diseases (e.g. heart failure, coronary artery disease); (2) recent use of anticoagulants (e.g. warfarin, aspirin); (3) pregnancy or lactation; (4) known hypersensitivity to *Salvia miltiorrhiza* or its constituents; (5) participation in other clinical trials or prior exposure to similar investigational agents; and (6) cognitive impairment, dementia or active psychiatric disorders.

Randomisation, grouping and interventions

Randomisation was performed using a computer-generated random number sequence, created by an independent statistician. Participant allocation was conducted *via* a centralised randomisation system to ensure allocation concealment and eliminate selection bias. Eligible participants were assigned in a 1:1 ratio to either the experimental group (receiving *Salvia miltiorrhiza* injection) or the control

group (receiving placebo), as illustrated in Figure 1. To preserve blinding, investigators, participants and outcome assessors were unaware of group assignments.

The Dan Shen injection and placebo were identical in appearance, packaging, labelling, and administration protocol. A designated pharmacist, blinded to allocation, prepared and dispensed the interventions. All treatment records were entered into an encrypted EDC system. Independent third-party audits were regularly conducted to ensure data authenticity and compliance with protocol standards.

Both groups received standard clinical care, including lifestyle counselling and electrolyte management. The intervention group was administered *Salvia miltiorrhiza* injection (manufactured by Hangzhou Zhongda Qingchunbao Pharmaceutical Co., Ltd.; approval no. Z33020177), at a dose of 20 mL diluted in 200 mL of 5% glucose solution, delivered *via* intravenous infusion once daily for 12 consecutive weeks [11,12]. The control group received an identical placebo solution, administered in the same volume and frequency over the same treatment duration.

To ensure ethical compliance and patient safety, the routine use of antihypertensive, antiarrhythmic or lipid-lowering medications was generally not permitted during the study period. In cases of markedly elevated blood pressure (e.g. systolic ≥180 mmHg or diastolic ≥110 mmHg) or the onset of a hypertensive emergency, immediate clinical intervention was permitted at the discretion of the attending physician to ensure patient safety. Emergency management included the short-term administration of rapid-acting antihypertensive agents, such as nifedipine (Bayer Pharmaceuticals; National Drug Approval No. HJ20171342; 10 mg/tablet), with detailed documentation of the drug name, dosage, administration time and clinical response. All such incidents were promptly reported to the ethics committee by the

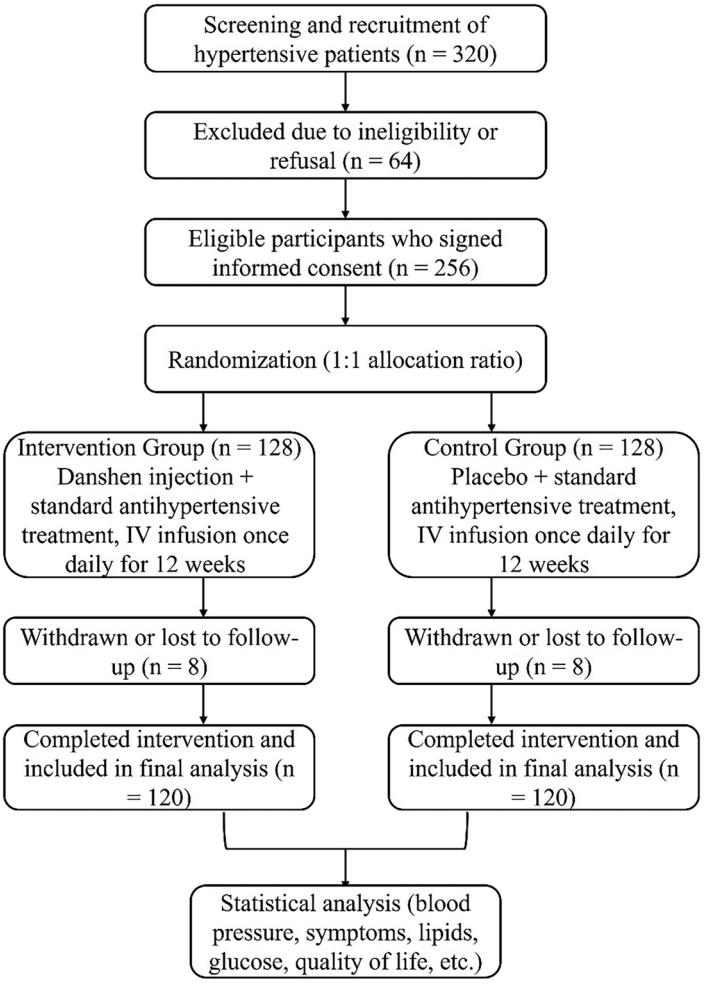

Figure 1. CONSORT Flow diagram of the randomised, double-blind, placebo-controlled clinical trial evaluating the efficacy of *Salvia miltiorrhiza* (Danshen) in patients with essential hypertension. *n* indicates the number of patients at each stage. All dropouts were voluntary and ethically managed.

study monitor and were incorporated into the safety analysis. In addition, a hypertension risk warning mechanism was established for this trial, whereby dynamic blood pressure monitoring was conducted at every follow-up visit to proactively identify and manage potential AEs.

Outcome measures

Blood pressure assessment

Blood pressure was continuously monitored using 24-h ambulatory blood pressure monitoring (ABPM), both before and after the 12-week treatment period. Measurements were obtained with the Oscar 2 ABPM device (Meditech, Hungary), which recorded blood pressure readings every 15 min over a 24-h cycle. Primary endpoints included changes in SBP and DBP. Treatment efficacy was defined as either a reduction in SBP ≥ 10 mmHg or normalisation of BP to <140/90 mmHg.

Symptom improvement

Hypertension-related symptoms – including headache, dizziness and fatigue – were assessed using a standardised symptom severity scale. Each symptom was rated by participants on a 4-point scale: 0 = none, 1 = mild, 2 = moderate and 3 = severe. Participants self-reported scores at baseline and after the intervention to evaluate symptom changes over time.

Blood lipid and blood glucose levels

Fasting venous blood samples were collected for the assessment of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TGs) and fasting blood glucose (FBG). Laboratory analyses were conducted using standardised protocols. According to the American Diabetes Association (ADA) criteria, normal fasting glucose is defined as <100 mg/dL (<5.6 mmol/L) [13]. Dyslipidemia was diagnosed based on the Chinese Guidelines for the Prevention and Treatment of Dyslipidemia in Adults, with thresholds defined as TC > 6.22 mmol/L, LDL-C > 4.14 mmol/L or TG > 2.26 mmol/L [14].

Quality of life assessment

Health-related QoL was evaluated using the Short Form-36 (SF-36) questionnaire, a validated instrument comprising 36 items across eight domains: physical functioning, role limitations due to physical health, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems and mental health. Scores for each domain range from 0 to 100, with higher scores indicating better QoL and functional status [15].

Follow-up and data collection

Participants underwent biweekly follow-up assessments throughout the 12-week treatment period to monitor safety and adherence. Each follow-up included inspection of the infusion site, measurement of vital signs (including blood pressure), symptom scoring, laboratory testing (lipids and glucose), quality-of-life assessment and documentation of any AEs.

Adherence to treatment was defined as receiving at least 80% of the scheduled 84 intravenous infusions (i.e. ≥67 infusions). Any participant experiencing moderate-to-severe AEs – such as injection-site infections, persistent fasting hyperglycaemia (≥7.0 mmol/L) or allergic reactions – was withdrawn from treatment, and all clinical findings, interventions and outcomes were meticulously documented. Data were collected at baseline and at the end of the 12-week intervention for subsequent analysis.

Statistical analysis

All data were managed and validated by a dedicated clinical data management team using a secure EDC system. Statistical analyses were performed using SPSS version 22.0 (IBM Corp., Chicago, IL)

[16]. Continuous variables were reported as mean ± standard deviation (mean ± SD). Between-group comparisons were analysed using independent sample t-tests, while within-group changes were assessed using paired t-tests.

Categorical variables were expressed as frequencies and percentages [*n* (%)], and compared using the chi-square (χ^2) test. For repeated measurements over time, repeated measures analysis of variance (ANOVA) or linear mixed-effects models were employed to assess treatment effects. A two-sided *p* value <0.05 was considered statistically significant.

Results

Study population and baseline characteristics

A total of 320 patients with primary hypertension were screened. Among them, 256 eligible participants were randomised into the intervention group ($n = 128$) and the control group ($n = 128$). During the 12-week study period, 12 participants withdrew due to personal reasons or AEs – 5 from the intervention group and 7 from the control group – resulting in 244 participants completing the study (123 in the intervention group and 121 in the control group). At baseline, there were no statistically significant differences between the two groups in demographic and clinical characteristics, including age, sex, body mass index (BMI), baseline SBP and DBP, lipid and glucose levels, symptom scores and comorbidities (all $p > 0.05$), indicating good baseline comparability (Table 1).

Blood pressure changes

In the intervention group, mean SBP decreased significantly from 150.96 ± 12.92 mmHg at baseline to 136.78 ± 10.28 mmHg at week 12 ($p < 0.001$), with statistically significant reductions observed as early as week 4. Similarly, DBP declined from 92.80 ± 9.44 mmHg to 85.36 ± 8.37 mmHg over the same period ($p < 0.001$). The reductions in both SBP and DBP were sustained throughout the intervention.

Conversely, the control group did not exhibit significant within-group changes in either SBP or DBP during the 12-week follow-up (all $p > 0.05$). Between-group comparisons revealed statistically significant differences in both SBP and DBP at weeks 4, 6, 8, 10 and 12 (all $p < 0.05$), favouring the intervention group (Figure 2 and Table 2).

Improvement in hypertension-related symptoms

Participants in the intervention group experienced significant improvements in hypertension-related symptoms, including headache, dizziness and fatigue. At week 12, mean symptom scores had decreased by 1.3, 1.2 and 1.1 points, respectively, compared to baseline ($p < 0.01$ for all). In contrast, the control group showed no significant changes in these symptom domains over the same period ($p > 0.05$) (Table 3).

Table 1. Baseline characteristics of patients in the experimental and control Groups.

Characteristic	Control group ($n = 121$)	Experimental group ($n = 123$)	Statistic	*p* Value
Age (years)	57.19 ± 8.26	57.70 ± 9.22	$t = -0.45$	0.650
Male, *n* (%)	65 (54.17)	73 (60.83)	$\chi^2 = 1.09$	0.296
Body mass index (kg/m^2)	26.30 ± 3.46	25.90 ± 3.23	$t = 0.92$	0.361
Baseline systolic BP (mmHg)	152.50 ± 11.89	150.04 ± 12.61	$t = 1.55$	0.122
Baseline diastolic BP (mmHg)	92.76 ± 9.46	92.95 ± 8.23	$t = -0.16$	0.873
Blood lipids (total cholesterol, mmol/L)	5.32 ± 1.05	5.41 ± 1.01	$t = -0.74$	0.463
Blood glucose (fasting, mmol/L)	5.28 ± 0.67	5.20 ± 0.65	$t = 0.88$	0.381
Diabetes mellitus, *n* (%)	10 (8.33)	17 (14.17)	$\chi^2 = 2.04$	0.15
Dyslipidemia, *n* (%)	57 (47.50)	49 (40.83)	$\chi^2 = 1.08$	0.30
Chronic kidney disease, *n* (%)	5 (4.17)	7 (5.83)	$\chi^2 = 0.35$	0.55

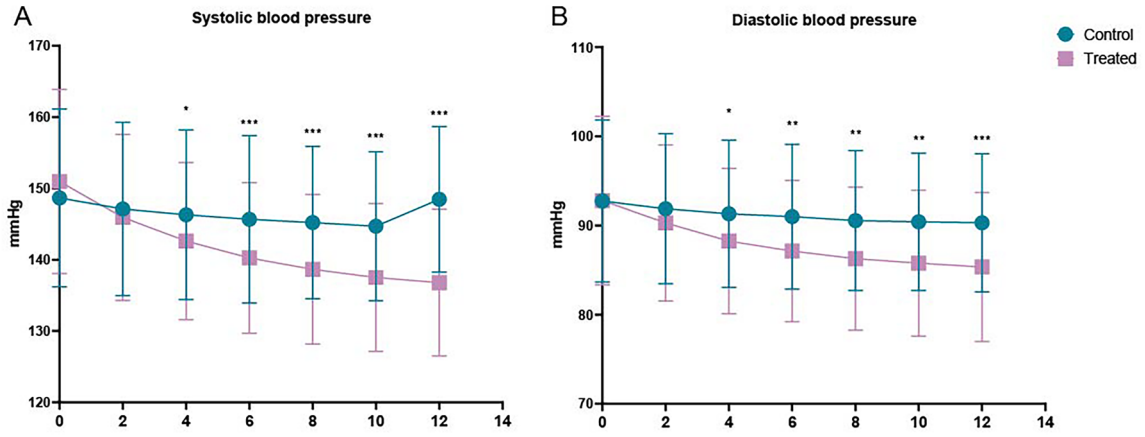

Figure 2. Time-course changes in blood pressure over 12 weeks. (A) Systolic blood pressure (SBP); (B) Diastolic blood pressure (DBP). Data are presented as mean ± SD. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ compared with the control group at the corresponding time point.

Table 2. Comparison of systolic and diastolic blood pressure before and after 12 weeks of treatment in the experimental and control groups (x ± s).

	Systolic BP (SBP, mmHg)		*p* Value (experimental *vs.* control)	Diastolic BP (DBP, mmHg)		*p* Value (experimental *vs.* control)
Time point	Control	Experimental		Control	Experimental	
Baseline	148.66 ± 12.48	150.96 ± 12.92	0.82	92.76 ± 9.09	92.80 ± 9.44	0.91
Baseline	148.46 ± 10.20 ($p = 0.12$)	136.78 ± 10.28 ($p < 0.001$)	< 0.001	90.32 ± 7.75 ($p = 0.14$)	85.36 ± 8.37 ($p < 0.001$)	<0.001

Table 3. Comparison of hypertension-related symptoms before and after 12 weeks of treatment in the experimental and control groups (x ± s).

Symptom	Baseline score (control group)	12-Week score (control group)	Baseline score (experimental group)	12-Week score (experimental group)	*p* Value (experimental *vs.* control)
Headache	1.92 ± 0.71	1.96 ± 0.66 ($p = 0.12$)	2.00 ± 0.84	0.77 ± 0.42 ($p < 0.01$)	0.02
Dizziness	1.84 ± 0.64	1.48 ± 0.58 ($p = 0.20$)	1.81 ± 0.73	0.70 ± 0.27 ($p < 0.01$)	0.03
Fatigue	2.00 ± 0.68	2.05 ± 0.72 ($p = 0.60$)	2.02 ± 0.99	0.81 ± 0.44 ($p < 0.01$)	0.04

These findings suggest that *Salvia miltiorrhiza* not only improved blood pressure control but also alleviated common subjective symptoms associated with hypertension.

Lipid and blood glucose levels

During the intervention period, participants in the experimental group exhibited significant improvements in both lipid profiles and FBG levels. After 12 weeks of treatment (TC, LDL-C and TG levels decreased by 9.6% ($p < 0.01$), 11.8% ($p < 0.01$) and 11.1% ($p < 0.05$), respectively, compared to baseline. Concurrently, HDL-C increased by 14.3% ($p < 0.01$). Between-group analysis confirmed that the elevation in HDL-C was significantly greater in the experimental group than in the control group ($p < 0.05$). Furthermore, FBG levels in the experimental group exhibited a continuous decline over the 12-week treatment period, decreasing from 5.29 ± 0.70 mmol/L at baseline to 5.06 ± 0.50 mmol/L at week 12, with the reduction reaching statistical significance ($p < 0.05$). In contrast, no significant change in FBG was observed in the control group, with values shifting from 5.37 ± 0.73 to 5.23 ± 0.76 mmol/L ($p > 0.05$) (Table 4 and Figure 3). These findings suggest that *Salvia miltiorrhiza* may exert a beneficial effect on metabolic homeostasis in addition to blood pressure regulation.

Quality of life

QoL was evaluated using the SF-36 questionnaire. After 12 weeks of intervention, participants in the experimental group showed significant improvements across all SF-36 dimensions. Compared to

baseline, scores for physical functioning, role functioning, bodily pain, vitality, social functioning, emotional role and mental health were all significantly increased ($p < 0.01$ for each domain). Notably, the most marked improvements were observed in the vitality and physical functioning domains, with mean increases of 22.1 and 15.6 points, respectively – both significantly greater than those observed in the control group ($p < 0.05$). In contrast, the control group demonstrated no statistically significant changes in any QoL dimension over the same period ($p > 0.05$) (Table 5). These results highlight the positive impact of *Salvia miltiorrhiza* on both subjective well-being and functional status in patients with hypertension.

Safety and adverse events

A total of 13 AEs were reported in the experimental group, yielding an incidence rate of 11%, compared to 9% in the control group. All AEs were classified as mild to moderate in severity, and no participant discontinued the intervention due to adverse effects. In the experimental group, the most common AEs included gastrointestinal symptoms such as abdominal distension and nausea (5 cases, 38.5%), followed by dizziness (4 cases, 30.8%), fatigue (2 cases) and mild headache (2 cases). The control group exhibited a comparable AE profile, with gastrointestinal discomfort (4 cases), dizziness (3 cases) and minor fatigue or headache (2 cases each). Most AEs occurred within the first 4 weeks of treatment, were transient, and resolved spontaneously within one to two weeks, without requiring medical intervention or affecting treatment outcomes.

With regard to infusion-site complications, a single case of mild erythema and swelling at the injection site was observed in the intervention group (0.8%). No signs of phlebitis or infection were noted, and the symptoms resolved completely within three days after local care. However, no clinically

Table 4. Comparison of lipid and blood glucose levels before and after 12 weeks of treatment in the experimental and control groups ($x \pm s$).

Indicator	Baseline value (control group)	12-Week value (control group)	Baseline value (experimental group)	12-Week value (experimental group)	*p* Value (experimental *vs.* control)
Total cholesterol (TC)	5.20 ± 0.87	5.17 ± 0.75 ($p = 0.5$)	5.28 ± 0.87	4.76 ± 0.81 ($p < 0.01$)	0.02
LDL cholesterol (LDL-C)	3.52 ± 0.57	3.51 ± 0.50 ($p = 0.3$)	3.27 ± 0.69	2.92 ± 0.60 ($p < 0.01$)	0.01
HDL cholesterol (HDL-C)	1.29 ± 0.31	1.30 ± 0.30 ($p = 0.85$)	1.41 ± 0.31	1.65 ± 0.31 ($p < 0.01$)	0.03
Triglycerides (TGs)	1.79 ± 0.69	1.82 ± 0.65 ($p = 0.6$)	1.87 ± 0.67	1.55 ± 0.49 ($p < 0.05$)	0.04
Fasting blood glucose (FBG)	5.37 ± 0.73	5.23 ± 0.76 ($p = 0.8$)	5.29 ± 0.70	5.06 ± 0.50 ($p < 0.05$)	0.05

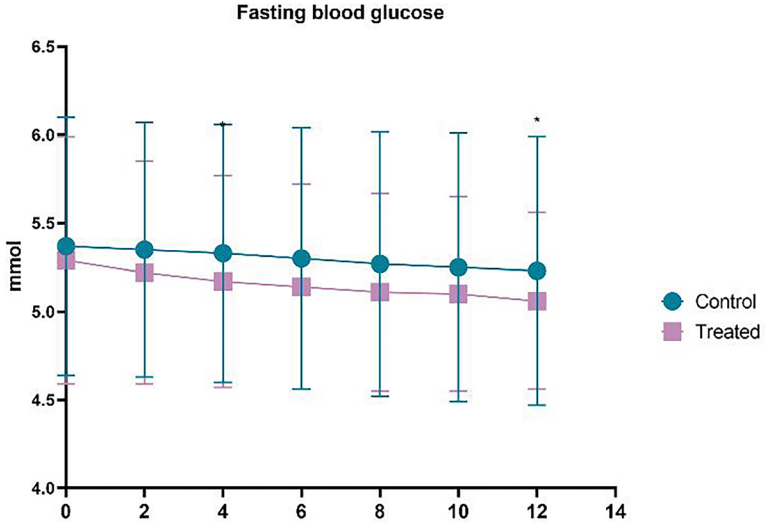

Figure 3. Longitudinal changes in fasting blood glucose (FBG) over 12 weeks in the experimental and control groups. *$p < 0.05$ compared with the control group at the corresponding time point.

Table 5. Comparison of quality of life scores before and after 12 weeks of treatment in the experimental and control groups (x ± s).

Quality of life dimension	Baseline value (control group)	12-Week value (control group)	Baseline value (experimental group)	12-Week value (experimental group)	p-value (experimental *vs.* control)
Physical function	61.92 ± 15.80	62.85 ± 16.85 ($p = 0.45$)	58.71 ± 17.63	77.30 ± 14.46 ($p < 0.01$)	0.02
Role function	61.66 ± 16.12	59.77 ± 15.87 ($p = 0.67$)	57.86 ± 16.02	74.72 ± 14.68 ($p < 0.01$)	0.03
Bodily pain	57.14 ± 18.11	56.38 ± 15.63 ($p = 0.48$)	52.54 ± 15.91	69.40 ± 15.86 ($p < 0.01$)	0.05
General health	53.15 ± 15.98	54.82 ± 13.26 ($p = 0.72$)	54.30 ± 16.49	68.48 ± 11.20 ($p < 0.01$)	0.06
Vitality	53.04 ± 17.15	51.39 ± 17.77 ($p = 0.73$)	52.10 ± 16.71	73.02 ± 14.10 ($p < 0.01$)	0.01
Social function	62.02 ± 18.48	64.40 ± 14.97 ($p = 0.62$)	62.12 ± 14.78	72.87 ± 14.55 ($p < 0.01$)	0.04
Emotional role	60.40 ± 17.28	57.48 ± 17.24 ($p = 0.77$)	57.87 ± 21.05	72.72 ± 15.01 ($p < 0.01$)	0.07
Mental health	61.89 ± 15.77	60.78 ± 15.04 ($p = 0.69$)	61.63 ± 15.72	76.74 ± 14.89 ($p < 0.01$)	0.06

diagnosed phlebitis occurred in either group during the 12-week period. Systematic assessment of injection-site reactions was performed weekly by study nurses using a standardised grading scale, and no severe or cumulative complications were recorded. For metabolic safety, one participant in the intervention group exhibited a transient elevation in fasting plasma glucose at week 4 (6.2 mmol/L), which remained below the diagnostic threshold for diabetes. No intervention was required and levels normalised upon subsequent testing. No similar metabolic events were noted in the control group.

Among the 240 patients who completed the study, 226 (94.2%) achieved ≥80% adherence to the treatment protocol. In the experimental group, 113 out of 120 participants (94.2%) met this adherence criterion. These findings indicate that the intravenous administration of *Salvia miltiorrhiza* was feasible, well-tolerated, and associated with a high level of treatment compliance in this patient population.

Discussion

This study is the first to systematically evaluate the efficacy of *Salvia miltiorrhiza* (Danshen) injection in patients with primary hypertension through a rigorously designed randomised, double-blind, placebo-controlled clinical trial. Our findings demonstrated that Danshen treatment led to a mean reduction of approximately 14 mmHg in SBP and 7 mmHg in DBP over a 12-week period, with statistically significant differences emerging as early as week 4 compared to placebo ($p < 0.01$). The antihypertensive effect was sustained throughout the study duration. In addition to blood pressure reduction, Danshen markedly improved hypertension-related symptoms, significantly decreased levels of TC, LDL-C, and TGs, while increasing HDL-C. FBG levels were also significantly reduced. Health-related QoL, as assessed by the SF-36 questionnaire, improved across multiple domains, most notably in vitality and physical functioning. These improvements were not observed in the placebo group. Moreover, the incidence of AEs was lower in the Danshen group, supporting its favourable safety profile. These results not only confirm the independent antihypertensive properties of Danshen – consistent with prior findings using compound Danshen preparations (e.g. a 13.8 mmHg reduction in SBP) – but also underscore its potential for integrated modulation of multiple metabolic pathways [17].

The antihypertensive effects of Danshen are likely mediated through its multi-target, synergistic mechanisms of action. Previous studies have shown that Danshen can modulate the Th17/Treg cell balance and favourably alter gut microbiota composition [18]. Its aqueous extracts have been reported to suppress vascular inflammation and fibrosis by attenuating the ROS/TLR4/NF-κB signalling pathway, thereby reducing oxidative stress [19]. Additionally, Danshen enhances endothelial nitric oxide synthase (eNOS) expression and nitric oxide (NO) production, contributing to vasodilation and endothelial function restoration. Leung et al. further demonstrated that Danshen regulates vascular tone by modulating voltage-gated K^+ channels and TRPC/Ca^{2+} pathways [20]. Our observations of rapid blood pressure reduction and concomitant improvements in metabolic parameters are consistent with these

mechanistic insights. The antioxidative and anti-inflammatory properties of Danshen appear particularly relevant in the context of hypertension, a condition frequently accompanied by endothelial dysfunction and elevated oxidative stress [21,22]. Excessive reactive oxygen species (ROS) generation impairs vasodilation and increases peripheral resistance. Danshen mitigates this damage by reducing ROS production, protecting endothelial cells from oxidative injury, promoting NO synthesis and suppressing vasoconstrictive factors such as endothelin-1 [23,24]. These concerted actions improve vascular compliance and decrease peripheral vascular resistance, thereby contributing to its potent antihypertensive effects.

Danshen also exhibits robust lipid-modulating properties. These may be attributed to its ability to inhibit cholesterol biosynthesis, promote HDL-C-mediated reverse cholesterol transport, and enhance lipid metabolism in hepatic and adipose tissues. This may reduce LDL-C accumulation within the vascular wall and delay the progression of atherosclerosis [25,26]. Moreover, the observed reduction in FBG suggests that Danshen may exert glycemic control *via* activation of the AMP-activated protein kinase (AMPK) pathway, suppression of hepatic gluconeogenesis, and improvement of insulin sensitivity [27–29]. These findings provide new evidence supporting its potential role in the management of metabolic syndrome and prediabetes.

QoL was assessed using the SF-36 questionnaire. Compared to the control group, patients receiving *Salvia miltiorrhiza* (Danshen) injection exhibited significant improvements in several domains, particularly in physical functioning, vitality, social functioning and mental health. The most pronounced benefits were observed in the domains of vitality and physical performance. These improvements may be attributable to Danshen's antioxidative and anti-inflammatory effects, as well as its capacity to enhance vascular function. By simultaneously regulating blood pressure, lipid profile and glucose metabolism, Danshen alleviates the overall physiological burden on patients, thereby contributing to enhanced well-being. Furthermore, its putative antidepressant and anxiolytic properties may have contributed to improvements in mental health status [30]. Given that hypertension often coexists with metabolic syndrome, diabetes and dyslipidemia, conventional antihypertensive therapy alone may be insufficient to meet the complex clinical demands of these patients [31]. As a multi-target pharmacological agent, Danshen offers systems-level intervention through coordinated modulation of multiple metabolic pathways [32]. Our study demonstrated that Danshen not only effectively lowers blood pressure but also improves metabolic parameters and health-related QoL. These findings underscore its potential value in patients with hypertension complicated by metabolic disturbances.

Danshen injection exhibited a favourable safety profile, with a high adherence rate (94.2%) and only mild AEs reported. This suggests it is well-tolerated and may be suitable as an adjunctive or alternative treatment for patients with mild-to-moderate hypertension or those with concurrent metabolic disorders. Compared to oral medications, the intravenous formulation of Danshen allows for more precise dose control and a faster onset of action in inpatient settings. Through its anti-inflammatory, antioxidative and renin–angiotensin–aldosterone system (RAAS) modulating effects, Danshen may delay vascular remodelling and reduce the long-term risk of hypertensive complications, ultimately improving clinical outcomes.

Despite the promising findings, this study has several limitations. First, the relatively short follow-up period precludes conclusions regarding the long-term efficacy and safety of Danshen. Future studies with extended observation periods are necessary to confirm the durability of clinical benefits. Second, single-center and small-sample design may introduce selection bias and limit the generalisability of the results. Large-scale, multicentre randomised controlled trials are warranted to validate these observations. Finally, although the multi-target mechanisms of Danshen have been partially elucidated, the specific molecular pathways, key regulatory targets and their differential responses under various metabolic states remain to be fully explored. Multi-omics approaches may provide deeper mechanistic insights to support precision phenotyping and individualised therapeutic strategies.

Conclusion

This study provides robust evidence that *Salvia miltiorrhiza* injection, administered over a 12-week period and in the absence of other antihypertensive or metabolic interventions, significantly reduces

SBP by approximately 14 mmHg and DBP by 7 mmHg. Concurrently, it improves lipid profiles (reductions in TC, LDL-C and TG; increase in HDL-C), lowers FBG, and enhances QoL as assessed by the SF-36 instrument. The findings suggest that Danshen has the potential to exert synergistic, multi-target regulatory effects on both blood pressure and metabolic parameters, positioning it as a promising adjunctive therapy for patients with hypertension and comorbid metabolic abnormalities. However, due to the limitations of a single-centre, small-sample, short-term design, future multicentre studies with larger cohorts and extended follow-up are needed to confirm its long-term efficacy, safety, and underlying mechanisms of action.

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Authors' contributions

Pan Li, Zonghua Jiang and Linfei Dong designed or conceptualised the manuscript and drafted and revised the manuscript. Shifeng Wang, Jiangli Qi and Longhong Zhu designed and conducted the manuscript. Longhong Zhu sought funding. The final version was confirmed by all authors for submission.

Clinical trial number

Not applicable.

Consent for publication

All participants provided written informed consent.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Ganzhou Hospital of Southern Medical University (Ganzhou People's Hospital) (LS-2023-0021). Informed consent was obtained from all the participants. All methods were carried out in accordance with Declaration of Helsinki.

Disclosure statement

The authors declared that they have no conflicts of interest regarding this work.

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Availability of data and material

The datasets used and analysed during this study available from the corresponding author on reasonable request.

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