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The Evaluation of the Glucose-Lowering Effect of Bloodletting Therapy in Type 2 Diabetes Mellitus

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Objective: This study uses a quantitative method to evaluate bloodletting therapy's impact on lowering blood glucose levels and improving metabolic parameters in patients with type 2 diabetes mellitus (T2DM). Method: This randomized, controlled clinical trial included 110 patients diagnosed with T2DM who met the study's inclusion criteria. Participants were randomly assigned to a control group (standard medication) and an experimental group (standard medication plus bloodletting therapy). Both groups received medicine according to the Mongolian Clinical Practice Guidelines for T2DM treatment. The experimental group additionally underwent bloodletting therapy on Day 6 of the study, following a 5-day preparation period during which they consumed 2.0 grams of a "3-seed decoction" (twice daily). The bloodletting procedure involves drawing blood from the posterior antebrachial vein (100-150 mL). The study evaluated primary outcomes, including fasting blood glucose and HbA1c levels, and secondary outcomes, such as insulin levels, C-peptide concentrations, and lipid profiles (total cholesterol, triglycerides, LDL, and HDL) at baseline, Day 30, and Day 60. **Results:** The experimental group demonstrated significant improvements in metabolic parameters. BMI levels decreased from 30.45±4.48 at baseline to 29.09±3.60 at Day 60 ($P < 0.05$), and HbA1c decreased from 9.2 ± 2.46% to 8.49 ± 1.85% ($P< 0.05$). Furthermore, significant reductions were observed in insulin levels (from 43.38 ± 14.12 to 25.61 ± 4.8 pmol/L; $P= 0.0001$) and C-peptide levels (from 4.9 to 4.2 ng/mL; $P= 0.0004$). The lipid profile also showed improvements, with a reduction in LDL cholesterol and triglycerides compared to the control group, although these changes were not statistically significant at Day 60. **Conclusion:** Integrating bloodletting therapy into the treatment regimen for T2DM provides additional benefits, including significant reductions in blood glucose, HbA1c, insulin, and C-peptide levels. Bloodletting therapy, when used in combination with standard pharmacotherapy, could offer a cost-effective and clinically beneficial treatment option for managing type 2 diabetes.

Keywords: Bloodletting, Type 2 Diabetes Mellitus, Glucose, Insulin, C-Peptide, Blood Lipid Profile

Introduction

Diabetes is a chronic metabolic disease characterized by elevated levels of blood glucose, which leads over time to severe damage to the heart, blood vessels, eyes, kidneys, and nerves. The most common is type 2 diabetes, usually in adults, which occurs when the body becomes resistant to insulin or doesn't make enough insulin.[1] Diabetes mellitus affects over 530 million people globally, with 10.5% of adults aged 20-79 living with the condition. Type 2 diabetes (T2DM) accounts for approximately 98% of all diabetes cases, and 1 in 11 adults is at risk of developing the disease. Globally, every 30 seconds a person with diabetes loses a limb, and 70–80% of all diabetes-related deaths occur in low- and middle-income countries. The economic burden of diabetes is substantial, with an estimated 10% of global health expenditure (about 760 billion USD in 2019) directed toward diagnosing and treating the disease.

In Mongolia, as of 2019, the prevalence of diabetes among adults aged 20–79 was 99.3 per 1,000 individuals, with an estimated 1,330 deaths attributed to diabetes annually. These statistics highlight the importance of strengthening the prevention and control of diabetes in Mongolia.[2]

Type 2 diabetes is often associated with lipid metabolism disturbances, including dyslipidemia, which exacerbates the risk of cardiovascular complications.[3] A 2002 study by Piia P. Simonen, et al. have shown that elevated blood glucose levels increase cholesterol synthesis, contributing to the heightened cardiovascular risk observed in diabetic patients.[4] Specifically, individuals with T2DM often exhibit elevated triglyceride levels and reduced high-density lipoprotein (HDL) cholesterol levels, further promoting the development of atherosclerosis and increasing the risk of coronary artery disease, ischemic stroke, and peripheral arterial disease.[5-7] Dyslipidemia is a recognized risk factor for diabetic retinopathy, underscoring the importance of comprehensive lipid management in diabetes care.[8]

Bloodletting has been reported to significantly reduce triglyceride levels, particularly in individuals with elevated baseline triglycerides. For example, in a clinical study, bloodletting reduced triglyceride levels from 287 mg/dL to 133 mg/dL ($P< 0.001$), accompanied by a reduction in ferritin levels.[9] Furthermore, traditional medical practices, such as bloodletting, have long been believed to remove "bad blood" and improve overall health. According to the ancient text Bider Ombo Sutra, et al. bloodletting therapy is integral in promoting health by "separating" harmful substances from the body, thereby improving circulation and optimizing the quality of blood.[10] Tserendagva Dalkh, et al. also demonstrated that bloodletting treatment reduces blood viscosity and enhances the metabolic function of water and minerals, contributing to improved blood composition in chronic hepatitis patients.[11] In this study, we evaluated the bloodletting treatment of Mongolian Traditional Medicine for DM2 patients while using blood-thinning medication for the first time in Mongolia. Given the potential benefits of bloodletting in regulating blood lipids and glucose metabolism, this study aims to evaluate the impact of bloodletting therapy on lipid metabolism and glucose control in patients with type 2 diabetes.

Materials and Methods

Study Design and Participants

This randomized, controlled clinical trial was conducted over two years, from January 2022 to December 2023, based at the Mongolian-Japanese Hospital and the Central Hospital of Mongolian Traditional Medicine of MNUMS. Initially, f 120 self-referred participants with a confirmed diagnosis of T2DM within the last five years were recruited.

The inclusion criteria of the study were:

- Diagnosed within last 5 years
- Aged between 20 and 70 years old
- Fasting glucose > 6.1 mmol/L
- Random blood glucose ≥ 11.1 mmol/L
- HbA1c > 6.5%

The exclusion criteria of the study were:

- Allergic to herbal medicines and its preparations
- Use of drugs that could interfere with the study results in the prior month or during the study
- Daily alcohol consumption
- Smoking more than one pack of cigarettes per day
- Presence of acute or other chronic diseases requiring treatment
- Liver or kidney dysfunction
- Pregnancy or lactation
- Participation in other clinical studies in the prior month or being a blood donor
- Use of insulin therapy for glucose control

After initial screening, 10 participants were excluded, and 110 participants met the inclusion criteria and were randomized into two groups using simple randomization by a computer-generated random digit table.

- Experimental Group: 56 participants (mean age: 55±9 years; BMI: 30.45±4.48 kg/m^2),
- Control Group: 54 participants (mean age: 55±9 years; BMI: 29.76±5.00 kg/m^2).

The control group received standard pharmacological treatment according to clinical guidelines for T2DM. This included the prescription of glucose-lowering drugs (metformin, gliclazide, glimepiride), blood thinners, and statins by their endocrinologists. All participants received 1000 mg mof etformin, gliclazide 30 mg, or glimepiride 1 mg dof aily. Aspirin 100 mg or atorvastatin 20 mg were prescribed for the control group patients.[12]

Experimental Group

The experimental group received both standard treatments for diabetes, taking either 1000 mg metformin, gliclazide 30 mg, glimepiride 1 mg daily, and additional bloodletting therapy. Bloodletting therapy was performed on Day 6 of the study following a preparatory period of five days. During the preparatory phase, participants consumed 2.0 grams of "3-seed decoction" twice daily. The decoction was prepared by adding 2 grams of a powdered 3-seed powder into 200 mL of boiling water, allowed to cool to a lukewarm temperature, and consumed.

On Day 6, participants underwent a single bloodletting procedure, in which 100–150 mL of venous blood was removed via bloodletting from the posterior antebrachial vein. The procedure followed the guidelines for bloodletting treatment issued by the Ministry of Health of Mongolia (effective March 25, 2021).[13] Blood pressure and pulse oximeter were measured before and after the intervention. Participants were monitored for 30 minutes in a separate waiting room post-treatment. Treatment results were evaluated thrice on days 0, 30, and 60 using the following primary and secondary outcome criteria.

Primary and Secondary Outcomes

- Primary Outcomes: The primary endpoints included the following measures:
  - Blood glucose levels (fasting glucose),
  - Glycated hemoglobin (HbA1c).
- Secondary Outcomes: Secondary endpoints included:
  - Insulin levels,
  - C-peptide levels,
  - Lipid panel (total cholesterol, LDL, HDL, triglycerides).

Laboratory Analyses

All laboratory tests were conducted at the accredited laboratory of the Mongolian-Japanese Hospital of MNUMS, Mongolia. Biochemical parameters were analyzed three times during the study: at baseline (Day 0), 30 days (Day 30), and 60 days (Day 60), using a full-automatic analyzer (BM-6010).

Statistical Analyses

Data analysis was performed using Stata 17.0 software. The results were presented as means (± standard deviation). Comparisons between groups at each time point (Day 1, 30, and 60) were performed using:

- Independent T-tests for between-group comparisons
- Repeated measures ANOVA for comparisons of contin uous variables among two groups at three different time points.
- Two-way mixed ANOVA for Comparison Glucose and Fat Analysis Measurements by Group
- Paired T-tests were used to assess within-group chang es pre and post-treatment.

A P-value of <0.05 was considered statistically significant.

Research Ethics Issue

The Research Ethics Committee of the Mongolian National University of Medical Sciences approved the study protocol on December 24, 2021 (Approval № 2021/3-13). The study was conducted by the principles of the Declaration of Helsinki. Informed consent was obtained from all participants before the study.

Results

A total of 110 patients were included in the study, 64 of whom were women and 46 of whom were men. The mean age of the participants in the experimental group was 54.95 ± 9.50 years, while in the control group, it was 54.51 ± 9.77 years. The two groups had no statistically significant differences regarding age, weight, height, BMI, blood glucose levels, HbA1c, cholesterol, triglycerides, HDL, and LDL levels at baseline ($P \geq 0.05$, Table 1).

Blood Glucose and HbA1c Changes

In the experimental group, laboratory tests after 60 days demonstrated significant improvements in BMI and HbA1c levels. Specifically, HbA1c decreased from 9.20±2.46% at baseline to 8.49± 1.85 % ($P< 0.05$), and BMI reduced from 30.45 ± 4.48 to 29.09 ± 3.60 ($P< 0.05$). In contrast, the control group showed no statistically significant changes in blood glucose or HbA1c at the 30-day or 60-day follow-up points ($P \geq 0.05$, Table 2,3).

Table 1. Baseline characteristics of the study subjects

Characteristics	Experimental Group (n=56)	Control Group (n=54)	P-value
(n=54)	P-value	54.51±9.77	0.80
Height	164.57±23.70	163.96±8.09	0.85
Weight	84.65±15.61	79.90±14.55	0.09
BMI	30.45±4.48	29.76±5.006	0.44
Glucose	10.36±3.44	9.19±3.37	0.07
HbA1c	9.11±2.56	8.34±2.19	0.08
T-Chol	5.43±1.13	5.51±0.94	0.68
TG	2.54±2.50	2.03±1.04	0.16
HDL	1.24±0.25	2.65±1.39	0.30
LDL	3.40±0.96	3.53±0.79	0.46

Data are presented as mean ± SD. Bold values denote statistical significance at the P< 0.05 level. Note: SD, standard deviation. Using independent samples t-tests.

Table 2. Effects of the experimental group on blood glucose level, HbA1C, and lipid parameters in patients with type 2 diabete

Variables	Experimental group (n=56)								
	0	30	P-value	0	60	P-value	30	60	P-value
Weight	81.86±12.49	80.8±12.4	0.034*	81.86±12.49	81.05±13.12	0.318	80.81±12.42	81.05±13.12	0.99
BMI	29.26±3.28	163.96±8.09	0.03*	29.26±3.28	29.09±3.60	0.99	28.85±3.33	29.09±3.58	0.868
Glucose	10.59±4.30	79.90±14.55	0.237	10.59±4.30	9.26±3.61	0.138	9.39±3.37	9.26±3.61	0.99
HbA1C	9.20±2.46	29.76±5.006	0.005*	9.20±2.46	8.49±1.85	0.009*	8.73±2.18	8.49±1.85	0.188
Tchol	5.35±1.14	9.19±3.37	0.424	5.35±1.14	5.41±1.18	0.99	5.04±1.32	5.41±1.85	0.14
TG	2.02±1.19	8.34±2.19	0.99	2.02±1.19	1.96±1.45	0.99	1.98±1.49	1.96±1.45	0.99
HDL	1.27±0.26	5.51±0.94	0.99	1.27±0.26	1.23±0.29	0.847	1.24±0.31	1.23±0.29	0.99
LDL	3.48±1.09	2.03±1.04	0.219	3.48±1.09	3.48±0.94	0.99	3.13±1.08	3.48±0.94	0.095

*0- Pre-treatment performance, 30-Results 30 days after treatment, 60- Results days after treatment, *P< 0.05*

Table 3. Effects of the control group on blood glucose level, HbA1C, and lipid parameters in patients with type 2 diabetes

Variables	Control group (n=54)								
	0	30	P-value	0	60	P-value	30	60	P-value
Weight	77.79±13.17	77.48±13.76	0.69	77.79±13.17	77.01±13.14	0.123	77.48±13.76	77.01±13.14	0.398
BMI	28.95±4.73	28.79±4.98	0.366	28.95±4.73	28.70±4.77	0.19	28.79±4.98	28.70±4.77	0.99
Glucose	9.16±3.41	8.89±3.59	0.99	9.16±3.42	8.11±2.79	0.014*	8.89±3.59	8.11±2.80	0.057
HbA1C	8.38±2.20	8.20±2.10	0.253	8.38±2.20	7.996±1.73	0.065	8.20±2.10	7.996±1.73	0.153
Tchol	5.51±0.95	5.50±0.93	0.99	5.51±0.95	5.54±0.98	0.99	5.50±0.93	5.54±0.98	0.99
TG	2.03±1.06	1.97±1.19	0.99	2.03±1.06	1.91±1.46	0.99	1.97±1.19	1.91±1.46	0.99
HDL	1.27±0.30	1.26±0.28	0.99	1.27±0.30	1.37±0.64	0.639	1.26±0.28	1.37±0.64	0.55
LDL	3.48±1.09	2.03±1.04	0.99	3.48±1.09	3.50±0.69	0.99	3.55±0.81	3.48±0.94	0.99

*0- Pre-treatment performance, 30-Results 30 days after treatment, 60- Results days after treatment, *P< 0.05*

Lipid Profile and Other Laboratory Parameters

On the 30th day post-treatment, the experimental group showed a significant reduction in LDL cholesterol, measuring 3.17 ± 0.99 mmol/L (P= 0.0261), which was statistically lower than the control group's level of 3.55 ± 0.81 mmol/L.

Although the experimental group's blood glucose, HbA1c, cholesterol, and triglyceride levels were reduced compared to the control group, no other statistically significant differences were observed (Table 2,3).

At the 60-day follow-up, the control group demonstrated a statistically significant reduction in BMI. However, in the experimental group, blood glucose, HbA1c, cholesterol, LDL, and triglyceride levels showed a trend toward improvement compared to the control group, although these differences did not reach statistical significance (Table 4).

Table 4. Comparisons of the effect of the experimental group and control group on diabetes

Variables	30th day after treatment			60th day after treatment		
	Experimental group (n=56)	Control Group (n=54)	P-value	Experimental group (n=56)	Control Group (n=54)	P-value
BMI	30.74±5.55	29.51±5.25	0.2473	30.74±5.50	28.54±4.7	0.0479*
Glucose	9.15±3.16	8.84±3.58	0.6131	8.97±3.75	8.11±2.79	0.1657
HbA1c	8.38±2.02	8.16±20.9	0.5633	8.1±1.83	7.99±1.72	0.7559
Tchol	5.138±1.23	5.50±0.92	0.0741	5.24±1.17	5.54±0.98	0.1408
TG	2.128±1.47	1.96±1.18	0.5106	1.96±1.27	1.91±1.46	0.8343
HDL	1.316±0.36	1.26±0.28	0.393	1.36±0.33	1.37±0.64	0.8908
LDL	3.17±0.99	3.55±0.81	0.0261*	3.42±0.91	3.50±0.69	0.5841

*Data are presented as mean ± SD. Bold values denote statistical significance at the P< 0.05 level. Note: SD, standard deviation. using independent samples t-tests. *P< 0.05*

A two-factor ANOVA test found no statistically significant differences between groups or measurements. The lipid-related indicators, including cholesterol, triglycerides, HDL, and LDL, showed no significant statistical differences between the two groups. This suggests that bloodletting has a comparable effect to statin treatment, which reduces these indicators. (Table 5)

Insulin and C-Peptide Analysis

Further analysis was conducted in a subgroup of 20 patients with T2DM to investigate the blood glucose-lowering effect of bloodletting therapy. When studying the results of bloodletting treatment on blood insulin and C peptide, the insulin level decreased from 25.441±20.91 mmol/l to 18.336±8.45 mmol/l with statistically significant results (P> 0.0252) (Table 5). After the bloodletting treatment, insulin levels significantly reduced from 43.38 ± 14.12 mmol/L to 25.61 ± 4.8 mmol/L (P= 0.0001). Similarly, C-peptide levels decreased from 4.9 to 4.2 (P= 0.0004), showing statistically significant reductions.

Interestingly, insulin levels increased post-treatment in this subgroup, from 2.246 mmol/L to 2.81 mmol/L, showing a significant rise (P= 0.0003). However, C-peptide levels showed a trend toward an increase, which did not reach statistical significance (Table 6, Figures 1 and 2).

Discussion

Currently, 14 classes of drugs are available to treat type 2 diabetes mellitus, but only 36% of patients with type 2 diabetes achieve glycemic control with the currently available therapies. Therefore, new treatment options are desperately needed.[14] Diabetes mellitus presents a significant financial burden on healthcare systems worldwide. As of 2019, 10% of the global health expenditure (approximately 760 billion USD) was dedicated to diagnosing and treating diabetes.[15,16] This does not constrain national economies, healthcare systems, patients, and their families.[16-18] In Mongolia, a study by Michael. G, et al. revealed that the average annual expenditure for treating type 2 diabetes was 600,000 MNT, while the country's minimum wage was only 420,000 MNT. This discrepancy creates financial hardship for both patients and healthcare providers.[19]

Table 5. Comparison of sugar and fat analysis measurements by group

Variables		Partial SS	df	MS	F	P-value
BMI	Model	228.6992	5	45.73983	1.62	0.1549
	Measurement	35.98355	2	17.99178	0.64	0.5298
	Group	198.2332	1	198.2332	7.01	0.0085
	Measurement#Group	12.81662	2	6.408311	0.23	0.7973
Glucose	Model	208.7528	5	41.75056	3.48	0.0044
	Measurement	110.2816	2	55.14082	4.59	0.0108
	Group	73.33596	1	73.33596	6.11	0.014
	Measurement#Group	23.00515	2	11.50257	0.96	0.3848
HbA1c	Model	44.86578	5	8.973157	2.06	0.0694
	Measurement	26.56619	2	13.28309	3.06	0.0483
	Group	10.83336	1	10.83336	2.49	0.1153
	Measurement#Group	6.508415	2	3.254208	0.75	0.4737
T-Chol	Model	8.508563	5	1.701713	1.45	0.2071
	Measurement	1.869711	2	0.934855	0.79	0.4526
	Group	4.576326	1	4.576326	3.89	0.0494
	Measurement#Group	1.933778	2	0.966889	0.82	0.4405
TG	Model	15.17874	5	3.035748	1.25	0.2873
	Measurement	7.086075	2	3.543037	1.45	0.2351
	Group	4.805578	1	4.805578	1.97	0.1612
	Measurement#Group	2.943759	2	1.47188	0.6	0.5472
HDL	Model	0.898653	5	0.179731	1.22	0.3008
	Measurement	0.821166	2	0.410583	2.78	0.0635
	Group	0.012798	1	0.012798	0.09	0.7687
	Measurement#Group	0.069389	2	0.034695	0.23	0.7908
LDL	Model	5.69358	5	1.138716	1.49	0.1932
	Measurement	0.953646	2	0.476823	0.62	0.537
	Group	2.971483	1	2.971483	3.88	0.0496
	Measurement#Group	1.679804	2	0.839902	1.1	0.335

Analysed Two-way mixed analog.

Table 6. Effect of expermintal group on insulin and C-peptide in patients with type 2 diabetes

Variables	Measurement	N	Mean±SD	P-value
C Peptide	Before	20	3.668±1.445	0.4824
	After	20	3.539±0.896	
Insulin	Before	20	25.441±20.916	0.0252*
	After	20	18.336±8.447	

*Data are presented as mean ± SD. Bold values denote statistical significance at the P< 0.05 level. Note: SD, standard deviation. Using paired samples t-tests. *P< 0.05*

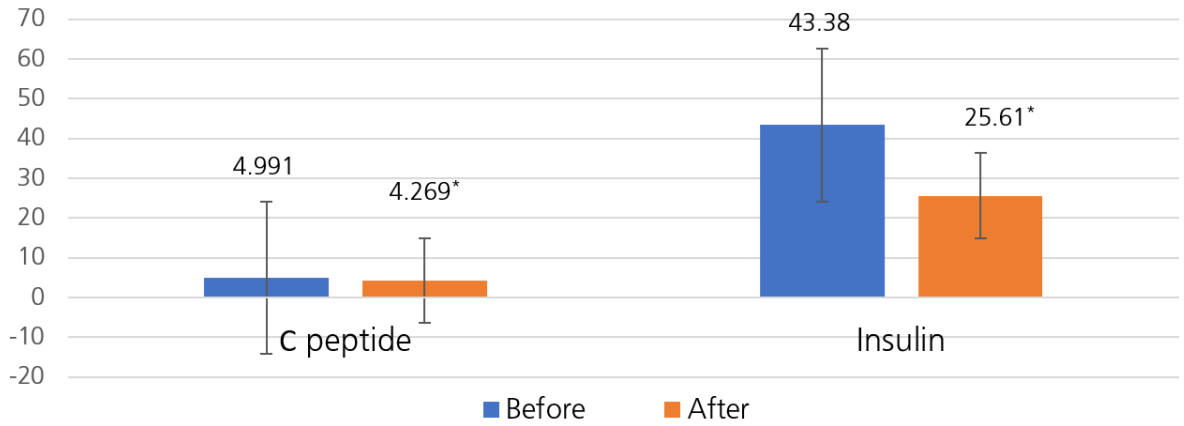

Figure 1. The effect of bloodletting therapy on elevated blood insulin and c-peptide in patients with type 2 diabetes.
Data are presented as mean ± SD. Bold values denote statistical significance at the P< *0.05 level. Note: SD, standard deviation. Using paired samples t-tests.* *P< *0.05*

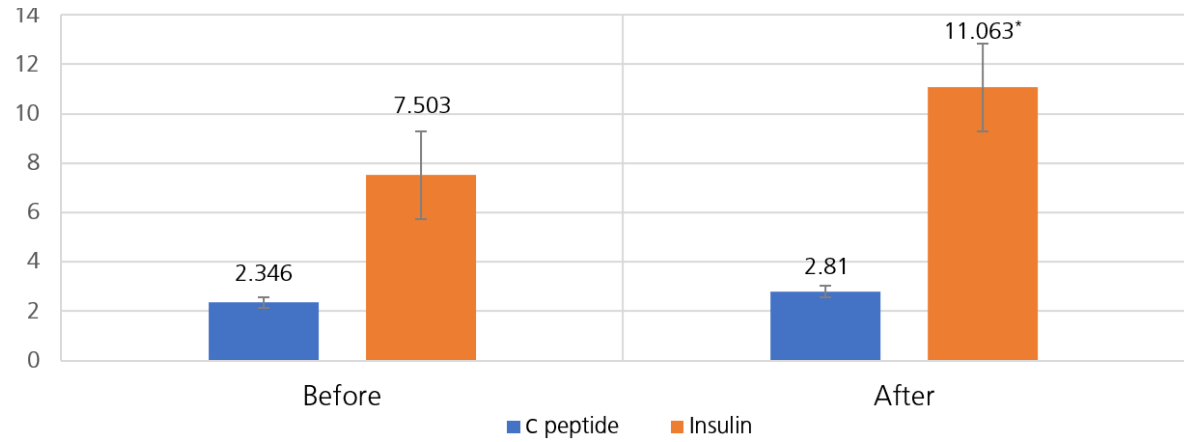

Figure 2. The effect of bloodletting therapy on normal and reduced blood insulin and c-peptide in patients with type 2 diabetes
Data are presented as mean ± SD. Bold values denote statistical significance at the P< *0.05 level. Note: SD, standard deviation. Using paired samples t-tests.* *P< *0.05*

Our study aimed to evaluate the effects of bloodletting therapy on blood glucose, HbA1c, and lipid metabolism in patients with type 2 diabetes. The results suggest that bloodletting, in combination with standard pharmacological treatment, can provide a beneficial adjunct therapy for improving metabolic control in these patients.

Our findings are consistent with earlier studies on the potential benefits of bloodletting in diabetes management. For instance, José Manuel Fernández-Real's survey in 2002 showed that bloodletting (500 ml of blood) resulted in decreased insulin levels and a modest reduction in HbA1c after one month, mirroring the clinical improvements observed in our study.[20]

In a 2017 study by Angelique Dijkstra. et al, 12 non-diabetic donors (52.2%) and 10 type 2 diabetic donors (58.8%) significantly reduced HbA1c after donating blood. The most considerable reduction was observed in the non-diabetic group at 11.9% and in the type 2 diabetes group at 12.0%.[21]

In our study, the experimental group showed significant reductions in blood glucose (from 10.59 ± 4.30 mmol/L to 9.26 ± 3.61 mmol/L) and HbA1c (from 9.20 ± 2.46% to 8.49 ± 1.85%) after 60 days of bloodletting treatment. This reduction was statistically significant (P <0.001), indicating that bloodletting can complement standard diabetes treatment in lowering fasting blood glucose and HbA1c.

The International Diabetes Federation (IDF) treatment guidelines recommend a combination of diet therapy, exercise, and pharmacotherapy to manage type 2 diabetes. Our study supports the integration of bloodletting therapy as an adjunctive treatment to pharmacotherapy, particularly in improving blood glucose control and HbA1c levels.

Lipid abnormalities, including elevated cholesterol and triglyceride levels, are common in patients with type 2 diabetes

and contribute to an increased risk of cardiovascular disease (CVD).

In a 2013 study by Julia Braun.et al, the P-value for total cholesterol was 0.046, and the P-value for glucose was 0.046 when examining whether glucose could be used instead of total cholesterol as a risk factor for CVD. The model with glucose had better risk predictability.[22]

In our study, on the 0 th day post-treatment, the experimental group showed a significant reduction in LDL cholesterol, measuring 3.17 ± 0.99 mmol/L (P= 0.0261), which was statistically lower compared to the control group's level of 3.55 ± 0.81 mmol/L. Although there were improvements in triglycerides and total cholesterol, these did not reach statistical significance, which could be due to the sample size or the short duration of the study.

The effect of bloodletting on lipid profiles is consistent with previous studies. For example, a survey by Heshu Sulaiman Rahman in 2020 showed that bloodletting significantly reduced triglycerides, LDL cholesterol, and fasting blood glucose levels.[18] Similarly, our study observed improvements in cholesterol (from 5.45 ± 1.14 mmol/L to 5.04 ± 1.23 mmol/L) and triglycerides (from 2.02 ± 1.19 mmol/L to 1.96 ± 1.45 mmol/L) in the experimental group. These changes may help mitigate cardiovascular risk in diabetic patients.

Insulin and C-Peptide Reduction

Another important aspect of our study was the effect of bloodletting on insulin and C-peptide levels. In patients with type 2 diabetes, elevated insulin levels often accompany insulin resistance. Bloodletting reduces insulin levels, potentially reflecting an improvement in insulin sensitivity. In the experimental group, insulin levels decreased significantly from 43.38 ± 14.12 mmol/L to 25.61 ± 4.8 mmol/L (P= 0.0001), and C-peptide levels also reduced from 4.9 to 4.2 (P< 0.0004). These reductions are consistent with the hypothesis that bloodletting may help regulate insulin secretion and improve pancreatic function.

Interestingly, patients who initially had elevated insulin and C-peptide levels showed a decrease in insulin post-treatment (from 25.44 to 18.336 mmol/L, P< 0.001), similar to findings in earlier studies, such as Fernández-Real's, et al. where bloodletting led to a reduction in plasma insulin.

In contrast, patients with lower baseline insulin levels showed a slight increase in insulin post-treatment (from 2.246 mmol/L to 2.81 mmol/L, P= 0.0003). This suggests that bloodletting may help normalize insulin levels and support the pancreas's endocrine function.

The precise mechanisms underlying the therapeutic effects of bloodletting remain unclear. However, several potential explanations have been proposed. Bloodletting may reduce oxidative stress, improve microcirculation, or enhance the metabolic clearance of glucose and lipids, all of which could contribute to the observed clinical improvements. Additionally, reducing insulin and C-peptide levels may suggest decreasing systemic inflammation, a key feature of insulin resistance and type 2 diabetes.

While our study provides promising evidence of the benefits of bloodletting for managing type 2 diabetes, several limitations should be considered. First, the study duration was relatively short (60 days), and it is unclear whether the observed improvements in blood glucose, HbA1c, and lipid parameters would be sustained over the long term. Second, the sample size was relatively small, which may have limited the statistical power to detect differences in certain parameters, such as triglycerides and cholesterol. Future studies with larger sample sizes and more extended follow-up periods are needed to confirm these findings and explore the long-term effects of bloodletting therapy.

Given the positive results observed in this study, future research should aim to include bloodletting therapy in clinical guidelines for managing type 2 diabetes. Combining bloodletting with other treatment modalities, such as pharmacotherapy, exercise, and dietary interventions, may be beneficial to provide a more comprehensive approach to diabetes management. Furthermore, studies investigating the underlying mechanisms of bloodletting in metabolic regulation are warranted to understand better how this ancient therapy can be optimized for modern clinical practice.

Conclusion

This study suggests that bloodletting therapy may be a valuable adjunct treatment for type 2 diabetes. It demonstrated significant reductions in blood glucose, HbA1c, insulin, and specific lipid parameters, indicating that bloodletting could help improve metabolic control and reduce cardiovascular risk. The incorporation of bloodletting into standard treatment regimens for type 2 diabetes may provide an alternative therapeutic option for patients seeking complementary or alternative treatments.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this study. The funders we're not involved in the study design, data collection, analysis, decision to publish, or preparation of the manuscript.

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References

1. Roglic G. WHO Global report on diabetes: A summary. I*nt J Noncommun Dis*. 2016;1(1):3-8. https://doi.org/10.4103/2468-8827.184853
2. Magliano DJ, Boyko EJ. *IDF diabetes atlas*. 2022. https://www.ncbi.nlm.nih.gov/books/NBK581934
3. Simonen P P, Helena K G, Miettinen T A. Diabetes contributes to cholesterol metabolism regardless of obesity. *Dia care*. 2002.25(9):1511-1515. https://doi.org/10.2337/diacare.25.9.1511
4. Feingold K R. *Obesity and dyslipidemia*. 2015. https://europepmc.org/article/NBK/nbk305895/
5. Charlton A, Garzarella J, Jandeleit-Dahm KA, et al. Oxidative stress and inflammation in renal and cardiovascular complications of diabetes. *Bio (Basel)* 2020;10(1):18. https://doi.org/10.3390/biology10010018
6. Harding JL, Pavkov ME, Magliano DJ, et al. Global trends in diabetes complications: a review of current evidence. *Diabetol*. 2019;62:3-16. https://doi.org/10.1007/s00125-018-4711-2
7. Teodoro JS, Nunes S, Rolo AP, et al. Therapeutic options targeting oxidative stress, mitochondrial dysfunction and inflammation to hinder the progression of vascular complications of diabetes. *Front Physiol*. 2019;9:1857. https://doi.org/10.3389/fphys.2018.01857
8. Pappan N, Awosika AO, Rehman A. *Dyslipidemia*. StatPearls. StatPearls Publishing; 2024. https://www.ncbi.nlm.nih.gov/books/NBK560891/
9. Casanova-Esteban P, Guiral N, Andrés E, et al. Effect of phlebotomy on lipid metabolism in subjects with hereditary hemochromatosis. *Metabolism*. 2011;60(6):830-834. https://doi.org/10.1016/j.metabol.2010.07.035
10. Tserendagva D. Essence and waste product secretion pattern, impure blood, blood secretion decoction /tang/ and their correlation. Ulaanbaatar, Mongolia. Munkhiin useg printing;2019.p247-249
11. Oldokh S. Variants of bloodletting vessels and their bioelectric activity matter [dissertation]. Ulaanbaatar, Mongolia. National University of Medicine; 1997
12. MOH. *Clinical practice guidelines for type 2 diabetes mellitus, in order of Health Minister A/96*. Ulaanbaatar 2021, https://moh.gov.mn/uploads/files/f14a0995e970cae49bdd1cd-2deca53d5b6ddebea.pdf.
13. MOH. *Clinical practice guidelines for bloodletting treatment, in order of Health Minister A/152*. Ulaanbaatar 2021, https://www.moh.gov.mn/uploads/files/b457e3e0210de6b0df-c2aa879e9e1465115532e7.pdf
14. Miller BR, Nguyen H, Hu CJ-H et al, New and emerging drugs and targets for type 2 diabetes: reviewing the evidence. *Am Hea Drug Benefits*. 2014:7(8):452-463.
15. Williams R, Karuranga S, Malanda B, et al. Global and regional estimates and projections of diabetes-related health expenditure: Results from the International Diabetes Federation Diabetes Atlas. *Dia Res Clin Pract*. 2020;162:108072. https://doi.org/10.1016/j.diabres.2020.108072
16. Association Diabetes Association. Economic costs of diabetes in the US in 2017. *Dia care*. 2018;41(5):917-928. https://doi.org/10.2337/dci18-0007
17. Yang W, Zhao W, Xiao J, et al. Medical care and payment for diabetes in China: enormous threat and great opportunity. *PLoS One*. 2012. https://doi.org/10.1371/journal.pone.0039513
18. Peters M, Huisman E, Schoonen M, et al. The current total economic burden of diabetes mellitus in the Netherlands. *Neth J Med*. 2017;75(7):281-297.
19. Misheel G, Gantugs.Y. Result of the study of cost estimates for individuals with type 2 diabetes. *J Health Sci*. 2024;3
20. Fernández-Real JM, Penarroja G, Castro A, et al. Blood letting in high-ferritin type 2 diabetes: effects on insulin sensitivity and β-cell function. *Diabetes*. 2002;51(4):1000-1004. https://doi.org/10.2337/diabetes.51.4.1000
21. Dijkstra A, Lenters-Westra E, de Kort W, et al. Whole blood donation affects the interpretation of hemoglobin A1c. *PLoS One* 2017;12(1):e0170802. https://doi.org/10.1371/journal.pone.0170802
22. Braun J, Bopp M, Faeh D. Blood glucose may be an alternative to cholesterol in CVD risk prediction charts. Cardiovasc Diabetol. 2013;12:24. https://doi.org/10.1186/1475-2840-12-24