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Nitric Oxide Levels in Primary Hypertension Patients Receiving Wet Cupping Therapy

Nurhayani[1*], Dwi Pudjonarko[2], Nurahmi[3], Misriyani[4]
[1]Daya Hospital City of Makassar, Indonesia
[2]Faculty of Medicine, Diponegoro University, Semarang, Indonesia
[3]Department of Clinical Pathology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia
[4]Department of Medical Education, Faculty of Medicine, University of Alkhairaat, Palu, Indonesia
[*]Authors Correspondence: nurhayaniagus81@gmail.com/08115003131

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ABSTRACT
Wet cupping has been shown in several studies to lower blood pressure in hypertensive patients. However, the mechanism of action remains unknown, limiting its use as a complementary non-pharmacological treatment. This study aims to examine the effect of wet cupping on systolic blood pressure, diastolic blood pressure, and nitric oxide levels in hypertensive patients. The study employed a quasi-experimental method with a pretest and post-test design, including a control group. The sample consisted of 40 individuals, they were diagnosed with primary grade I hypertension. The participants were divided into two groups (treatment and control). The intervention group received wet cupping therapy twice, at a 28-day interval, while continuing their antihypertensive medication. The control group only consumed antihypertensive medication. The study revealed a significant decrease in systolic and diastolic blood pressure but no significant increase in nitric oxide levels. After the intervention, the systolic blood pressure in the intervention group decreased by 17.69 mmHg (p=0.010), compared to a decrease of 5.87 mmHg (p=0,108) in the control group, with a difference of (p=0.010). The diastolic blood pressure in the treatment group decreased by 11.56 mmHg (p=0.000), compared to a decrease of 0.73 mmHg (p-0.570) in the control group, with a difference of (p=0.001). The nitric oxide levels in the intervention group increased by 2.5 µmol/L (p=0.530), compared to a decrease of 0.47 µmol/L (p=0.116), in the control group, with a difference of (p=0.539). It can be concluded that wet cupping therapy reduces systolic and diastolic blood pressure but does not significantly increase nitric oxide levels in the blood of hypertensive patients.

INTRODUCTION

Hypertension is a chronic disease that affected 1.28 billion individuals in 2019. Indonesia accounts for 51.3 million cases, with a prevalence in adults aged 30-79 years reaching 40%. This figure is 5% higher than the global prevalence of 30.5% and the prevalence in the Southeast Asian region, which is 3%.[1-3] This figure is a cause for significant concern in Indonesia, given that statistical evidence indicates a 144% increase over the past two decades. The potential for various complications and the threat of being the main cause of death represent a significant burden for sufferers, underscoring the need for alternative treatments that can help prevent the worsening of the condition.[4] Conversely, Furthermore, the average hypertensive patient also experiences a decrease in productivity due to their illness, which has an impact on their socioeconomic life. Additionally, they require high nominal medical expenses.[5]

Impaired vasodilation, stemming from endothelial dysfunction, serves as an initial indicator of hypertension. The vascular endothelium produces nitric oxide from L-arginine through the NO synthase enzyme. This molecule inhibits platelet adhesion and aggregation, facilitating blood vessel relaxation. Disruption in bioavailability or excessive degradation leads to decreased endothelial homeostasis.[6,7]

The management of hypertension by the WHO and the Ministry of Health emphasises pharmacological intervention and lifestyle improvement through non-pharmacological means. The combination of these approaches is expected to assist patients in enhancing their quality of life by successfully controlling blood pressure and preventing complications.[4] Controlled blood pressure is the primary treatment target for hypertensive patients. This can be achieved through dietary adjustments, reduced salt intake, exercise, maintaining an ideal body weight, avoiding smoking, and reducing stress. Data indicates a success rate of up to 30% with these methods.[8]

Wet cupping therapy, adapted from Middle Eastern medicine and Traditional Chinese Medicine (TCM), has been abandoned by many countries due to the transition to modern medicine. However, this practice has regained popularity after being observed among athletes and celebrities worldwide.[9] In Indonesia, it is common among certain groups and has been increasingly adopted over the years as an alternative for hypertension. Although no research explicitly mentions the growth of cupping use, the 2020 health profile report states that the growth of traditional health providers, which includes cupping therapy, has increased by 130 health centres from all over Indonesia.[10] Data from a cupping clinic in Makassar City yearly increase in visits particularly after the COVID-19 pandemic. Several hospitals have begun integrating cupping with modern medicine through traditional and herbal medicine departments. Patient decisions, apart from being influenced by specific religious beliefs, are also based on the findings of several studies that have uncovered numerous health benefits of cupping, particularly in pain management.[11,12]

The initial belief of the relationship was based on an experiment that found cupping dilates topical capillaries and increases blood flow in the skin. Blood vessels in the cupping area dilate by releasing vasodilators such as adenosine, noradrenaline and histamine, leading to increased circulation.[13] Another study revealed that increased levels of NO synthase, an enzyme that produces NO from l-argin, were higher around the acupoints of rat skin. In line with this evidence, it is also explained that endothelial dysfunction and decreased NO production can affect the development of atherosclerosis. Mice with eNOS deficiency showed more atherosclerotic lesions, whereas mice with eNOS excess showed reduced lesion formation.[14]

This evidence strengthens the reason why the blood pressure of hypertensive patients who receive cupping can be controlled and affects their quality of life.[12] However, given the many doubts about cupping therapy other than for familiar therapies such as pain management.[15-17] These conditions encourage the need for more research to prove that cupping is feasible as a complementary hypertension that can be accounted for in non-pharmacological management. Further research is required to elucidate the relationship between cupping and the reduction of patient blood pressure through the enhancement of nitric oxide bioavailability in individuals who undergo wet cupping.

MATERIAL AND METHOD

This study employed a quasi-experimental design with a pre-and post-test with control group design. The treatment's influence was assessed by comparing pre- and post-test values. The study population comprised hypertensive patients who made outpatient visit from July to December 2020 at clinics and hospitals in Makassar City. The sample consisted of individuals aged 36-60 years, consuming anti-hypertensive medications, non-smokers, and not consuming alcohol or herbs with high nitrate content. Exclusions were made for patients with a history of kidney disease and/or diabetes mellitus, insomnia, anemia, a history of blood clotting disorders, undergoing nitrate therapy, or being pregnant. Forty respondents were initially involved based on the hypothesis test calculation for the mean of two independent populations. Subjects were consecutively selected, with 9 of them dropping out during the study, resulting in data analysis involving only 16 individuals in the treatment group and 15 in the control group.

Patients' nitric oxide levels were obtained by venous blood sampling. Sample collection and examination were performed by laboratory assistants from Prodia Laboratory in Makassar. The samples were stored at a temperature of (-200c) and the analysis of the examination results was done simultaneously at the end of the study, namely at the beginning of the fifth week. Subsequently, the data from the laboratory examinations were subjected to analysis to ascertain the discrepancies in the augmentation of nitric oxide levels between the treatment and control groups, employing the Paired T-test. To ascertain the discrepancy in the mean values prior to and following the intervention, the independent T-test and Mann-Whitney U-test were employed. This research has been granted ethical clearance by the Ethics Commission Health Research Faculty of Community Health Diponegoro University (No. 266/EA/KEPK-FKM/2020).

RESULTS

The baseline characteristics of the respon-dents were statistically homogeneous, except for nitric oxide levels. There were no significant differences between the two groups of respondents in terms of age, BMI, systolic blood pressure, diastolic blood pressure, and quality of life, with a p-value greater than 0.05. However, in terms of nitric oxide levels, the two groups exhibited statistically different charac-teristics (p-value 0.017) (Table 1).

After the intervention in the treatment group, the mean serum nitric oxide levels increased from 26.01 μmol/L to 28.51 μmol/L, showing an increase of 2.5 μmol/L with a p-value of 0.530. In contrast, in the control group, the levels decreased from 38.86 μmol/L to 33.39 μmol/L, indicating a decrease of 0.47 μmol/L with a p-value of 0.116. The statistical test results for the difference in nitric oxide levels between the two groups were not significant, with a p-value= 0.539 (Table 2).

Tabel 1. Analysis of Responden Charateristics

Variable	Treatment		Control		p-value
	Mean ± SD	Median (Min-Max)	Mean ± SD	Median (Min-Max)	
Age	47.83 +7.36	49 (33-63)	48.35 + 9.09	46 (35–64)	0.849[a]
BMI	26.13 + 4.74	25.37 (18.73-37.78)	24.64 + 3.14	25.61 (18.73–29.97)	0.258[b]
Systolic Blood Pressure	137.39 + 10.47	140 (120-150)	131.35 + 0.25	132.50 (110-148)	0.087[c]
Diastolic Blood Pressure	84.06 + 5.87	83 (70-90)	80.75 + 7.30	80 (70-97)	0.136[d]
Nitric Oxide Levels	25.97 + 10.73	25.10 (9.62-55.38)	36.59 + 4.92	33.72 (16.74-1.30)	0.017[e]
Quality of Life	56.50 + 15.94	53.59 (26.45- 86.19)	58.12 + 3.53	68.50 (8.58 – 96.30)	0.803[f]
Duration of Diagnosis	5.55 + 3.59	5 (1-12)	5.65 + 3.72	5 (1-12)	0.931[g]

Source: Primary Data, 2020

p-value a,b,e,f,g: Independent t-test; p-value c,d: Mann-Whitney

Tabel 2. Analysis of Serum Nitric Oxide Levels After Intervention

Nitric Oxide Levels	Treatment Group	Control Group	p-value
Mean ± SD	2.5 ± 15.57	- 0.48 ± 17.38	0.539[a]
Δ Before – After Intervention	0.530[b]	0.116[c]	

Source: Primary Data, 2020
Δ difference, a: Mann whitney b: Paired t-test c: Wilcoxon

The mean systolic blood pressure of hypertensive patients in the treatment group before the intervention was 139.19 and decreased to 121.50 mmHg after cupping therapy, indicating a decrease of 17.69 mmHg with a p-value of 0.001. In contrast, the control group exhibited a decrease from 131.87 mmHg to 126.00 mmHg, representing a decrease of 5.87 mmHg with a p-value of 0.108. The statistical test results for the difference in systolic blood pressure between the two groups were significant, with a p-value=0.010 (Table 3).

After the intervention in the treatment group, the mean diastolic blood pressure decreased from 83.63 mmHg to 78.06 mmHg, indicating a decrease of 11.56 mmHg with a p-value of 0.00. In contrast, the control group showed a decrease from 80.33 mmHg to 79.60 mmHg, representing a decrease of 0.73 mmHg with a p-value of 0.570. The statistical test results for the difference in diastolic blood pressure between the two groups were significant, with a p-value=0.001 (Table 4).

Table 3. Difference in Systolic Blood Pressure of Patients After Intervention

Systolic Blood Pressure	Treatment Group	Control Group	p-value
Mean ± SD	17.69 ±14.79	5.87 ± 12.944	0.010[a]
Δ Before – After Intervention	0.010[b]	0.108[c]	

Source: Primary Data, 2020
Δ difference, a: Mann whitney; b,c: Wilcoxon

Table 4. Difference in Diastolic Blood Pressure of Patients After Intervention

Dyastolic Blood Pressure	Treatment Group	Control Group	p-value
Mean ± SD	11.56 ± 7.42	0.73 ± 8.79	0.001[a]
Δ Before – After Intervention	0.001[b]	0.570[c]	

Source: Primary Data, 2020
Δ difference, a: Independent t-test; b,c: Wilcoxon

DISCUSSION

A decrease in blood nitric oxide levels is one of the early indicators of hypertension. Evaluated nitric oxide levels in hypertensive patients were found to be 25.14 µmol/L ± 16.74, while in normotensive individuals, the levels were 55.28 µmol/L ± 25.73.50. Vasodilation impairment resulting from reduced nitric oxide levels due to endothelial dysfunction in hypertension can be alleviated by the body's natural response to inflammation from the wound caused by cupping.[6,18] An increase in NO synthase levels, the enzyme that produces NO from I-arginine around the cupping wound site, occurs. Another theory suggests that topical capillary dilation in the cupping area leads to increased blood flow in the skin area. This process releases vasodilators such as adenosine, norepinephrine, and histamine, thereby increasing circulation.[13]

However, these statements are not consistent with the findings of this study. The nitric oxide levels of the cupping intervention respondents increased by 2.5 µmol/L (p=0.530), but this increase was not statistically significant. This discrepancy may be influenced by the NOS3 gene polymorphism. Its effect on blood pressure varies among individuals depending on ethnic groups, fat intake, and the patient's diet.[19] These factors are confounders that were not controlled in this study, in addition to the initial non-homogeneous nitric oxide level data of the respondents in both groups.

The selection of cupping as an intervention in the study was based on several previous research findings that indicated its effectiveness in reducing blood pressure.[20,21] Specifically, Aleyidi (2019) stated that there was a decrease in systolic pressure by 2.8 mmHg in hypertensive patients who underwent cupping intervention after the second intervention within a 4-week range. Similar studies conducted by Syahrumdani et al. (2021) also found the same result, with patient systolic blood pressure significantly decreasing (p=0.01 and 0.03).[22] Besides these results, they also found that the total cholesterol levels of the respondents decreased by 5.41, which is thought to be one of the reasons for the decrease in systolic and diastolic pressure. This reaction is likely due to the hematological system

mechanism that significantly affects the coagulation pathway control by increasing blood flow and organ oxygenation.[21] Another theory states that the reduction in arterial blood volume due to cupping incisions, as well as capillary dilation due to the negative pressure of the cup, leads to increased local blood flow.[12,22]

The data analysis of systolic and diastolic blood pressure yielded consistent results, showing a significant decrease in systolic blood pressure by 17.69 mmHg (p=0.010) among respondents who underwent wet cupping intervention twice a 28-day interval. This is in line with the results of the significant difference between the intervention and control groups (p=0.001). However, there was a noticeable difference in the systolic pressure decrease by 14.89 mmHg compared to the previous study by Aleyidi, where they found a decrease in systolic pressure of only 2.8 mmHg. This difference could be attributed to the quantity and duration of cupping applications by the respondents. The effectiveness of cupping has been previously studied in 2019, and both of these factors significantly influenced the cupping outcomes.[23] Considering these results, cupping is likely a non-pharmacological complementary treatment for hypertension, with the clinical consideration that a stable and continuous 12 mmHg decrease in blood pressure in hypertensive patients can prevent 1 death out of every 11 treated patients.

From these results, a significant increase in blood nitric oxide levels does not accompany the decrease in blood pressure among respondents undergoing wet cupping. However, these results should be addressed. The mechanism of this decrease is likely due to a positive response associated with the improvement in the quality of life of patients following cupping compared to before.[12,24]

CONCLUSION AND RECOMMENDATION

Based on this study, we can conclude that wet cupping therapy significantly reduces blood pressure in hypertensive patients. However, it does not significantly impact increasing nitric oxide levels. Further research is recommended for more accurate results. Homogenizing the treatment and control groups, especially regarding nitric oxide levels, needs to improve controlling respondent bias.

AUTHOR CONTRIBUTIONS

Conceived and designed the experiments by DP; NY performed the experiments, analyzed the data and wrote the manuscript; NR interpreted the respondent's laboratory results; MY made corrections to the manuscript and perfected the writing results. The authors read and approved the final manuscript. DP = Dwi Pudjonarko; NY = Nurhayani; NR = Nurahmi; MY = Misriyani.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Kario, K., Okura, A., Hoshide, S. & Mogi, M. The WHO Global Report 2023 on Hypertension Warning the Emerging Hypertension Burden in Globe and Its Treatment Strategy. *Hypertension Research*. 2024;47:1099–1102. https://doi.org/10.1038/s41440-024-01622-w
2. WHO. Hypertension. World Health Organization; 2023. https://www.who.int/news-room/fact-sheets/detail/hypertension#Overview
3. WHO Team. Hypertension Indicators for Improving Quality and Coverage of Services. World Health Organization; 2021. https://www.who.int/publications/i/item/9789240037120
4. WHO Western Pacific Region. Diagnosis and Management for Patients with Hypertension. World Health Organization; 2023. https://www.who.int/publications/i/item/9789240081062
5. Etika, T., Pristianty, L. & Ratna Hidayati, I. Analisis Cost of Illness pada Pasien Hipertensi Peserta BPJS Rawat Jalan di Puskesmas Banyuanyar. *Pharmaceutical Journal of Indonesia*. 2020;6(1):41–46. https://doi.org/10.21776/ub.pji.2020.006.01.7
6. Kurniawan, A. & Yanni, M. Pemeriksaan Fungsi Endotel pada Penyakit Kardiovaskular. *Jurnal Human Care*. 2020;5(3):638-649. http://dx.doi.org/10.32883/hcj.v5i3.817

7. WHO. Global Report on Hypertension the Race against a Silent Killer. World Health Organization; 2023. https://www.who.int/publications/i/item/9789240081062
8. PERHI. Konsensus Penatalaksanaan Hipertensi 2019. Jakarta: Perhimpunan Dokter Hipertensi Indonesia; 2019. https://admin.inash.or.id/cdn/File/Update%20konsensus%202019.pdf
9. Hassan, N., Suleman, R., Al-Azzani, W., Jaber, H. & Mahdi, A. Microparticle Clearance Theory: An Update to the Potential Mechanisms of Action of Cupping Therapy. *Advances in Integrative Medicine*. 2021;8(1):68–72. https://doi.org/10.1016/j.aimed.2020.07.001
10. Kemenkes RI. Profil Kesehatan Indonesia Tahun 2020. Jakarta: Kementerian Kesehatan; 2021. https://media.neliti.com/media/publications/554203-efektivitas-penerapan-vidio-dan-leaflet-c9aab682.pdf
11. Sun, Y., An, Y., Zhou, Y.-J., Wang, X.-Y. & Yu, C.-H. Non-pharmaceutical Chinese Medical Therapies for Degenerative Lumbar Spinal Stenosis: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Complementary Therapies in Medicine*. 2023;74(102949):1-13. https://doi.org/10.1016/j.ctim.2023.102949
12. Nurhayani, N., Pudjanarko, D., Suhartono, S. & Nurahmi, N. Efek Bekam Basah Terhadap Kualitas Hidup Penderita Hipertensi Primer. *Jurnal Epidemiologi Kesehatan Komunitas*. 2022;7(2):538–544. https://doi.org/10.14710/jekk.v7i2.11536
13. Al-Bedah, A. M. N. *et al.* The Medical Perspective of Cupping Therapy: Effects and Mechanisms of Action. *Journal of Traditional and Complementary Medicine*. 2019;9(2): 90–97. https://doi.org/10.1016/j.jtcme.2018.03.003
14. Chambers, J. C., Obeid, O. A. & Kooner, J. S. Physiological Increments in Plasma Homocysteine Induce Vascular Endothelial Dysfunction in Normal Human Subjects. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 1999;19(12):2922–2927. https://doi.org/10.1161/01.ATV.19.12.2922
15. Cramer, H., Kloses, P., Teut, M., et al. Cupping for Patients with Chronic Pain: A Systematic Review and Meta-Analysis. *The Journal of Pain*. 2020;21(9-10):943–956. https://doi.org/10.1016/j.jpain.2020.01.002
16. Shen, W. C. *et al.* Effectiveness of Self-Management of Dry and Wet Cupping Therapy for Low Back Pain: A Systematic Review and Meta-Analysis. *Medicine (United States)*. 2022;101(51). https://pubmed.ncbi.nlm.nih.gov/36595746/
17. Subadi, I., Kusumawardani, M. K., Qorib, M. F., Susilo, I. & Hidayati, H. B. Wet Cupping Therapy Improves MU Opioid Receptor Expression and Pain Threshold in Animal Models of Inflammation. *Anaesthesia, Pain and Intensive Care*. 2019;23(4):348-352. https://doi.org/10.35975/apic.v23i4.1166
18. Talaieva, T.V. Endothelial Dysfunction in the Pathogenesis of Arterial Hypertension: New Diagnostic Methods. *Journal of The National Academy of Medical Sciences of Ukraine*. 2023;29(1-2):73–85. http://journal.amnu.gov.ua/images/pdf/2023-29-1-2/2023-29-1-2-5.pdf
19. Amelia, L., Sukohar, A. & Setiawan, G. Peran Ekspresi Gen Nitrit Oksida Sintase (NOS3) Terhadap Kejadian Hipertensi Esensial. *Majority*. 2018;7(1):263–268.
20. Sormin, T. Pengaruh Terapi Bekam Terhadap Tekanan Darah Penderita Hipertensi. *Jurnal Ilmiah Keperawatan Sai Betik*. 2018;14(2):123-239. https://doi.org/10.26630/jkep.v14i2.1294
21. Lu, S., Du, S., Fish, A., et al. Wet Cupping for Hypertension: A Systematic Review and Meta-Analysis. *Clinical and Experimental Hypertension*. 2018;41(5):474–480. https://doi.org/10.1080/10641963.2018.1510939
22. Syahruramdhani, S., Yuniarti, F. A., Septiana, T. E. & Mustikasari, E. The Effect of Wet Cupping Therapy on Blood Pressure and Total Cholesterol on Healthy Young Male

Adults. *Open Access Macedonian Journal of Medical Sciences*. 2021;9(T4):172–176. https://doi.org/10.3889/oamjms.2021.5854

23. Muflih, M. & Judha, M. Effectiveness of Blood Pressure Reduction Reviewed from Amount of Kop, Duration and Location of Point of Bekam Therapy. *NurseLine Journal*. 2019; 4(1):46-53. https://doi.org/10.19184/nlj.v4i1.9042
24. Kordafshari, G., Reza, M., Ardakani, S., Keshavarz, M. & Esfahani, M. M. Cupping Therapy Can Improve the Quality of Life of Healthy People in Tehran. 2020;37(4):1–5. https://doi.org/10.1016/S0254-6272(17)30164-4