



Effectiveness of soak feet therapy using warm water with Epsom salt and lemongrass oil on change of magnesium levels, nitric oxide (no) and blood pressure in pregnant women with hypertension

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Abstract

Background: The maternal mortality rate due to hypertension in pregnancy is 14% of 289,000 deaths (WHO, 2015), and in Indonesia 25.8%. In Central Java Province in 2017 32.97% and Banjarnegara District 23.8%. Warm water foot bath therapy with Epsom Salt and Lemongrass Oil is a complementary effort in managing hypertension because the content of MgSO₄ compounds in Epsom Salt and Citronella from Lemongrass Oil is able to exert effects on changes in blood pressure through the influence of Magnesium and Nitric Oxide (NO) biomarkers.

Objective: To explain the effect of foot bath therapy using warm water, Epsom Salt, and Lemongrass Oil on changes in biomarkers and blood pressure in pregnant women with hypertension.

Methods: Quasy experiment with pretest-posttest with control group design. The research subjects were pregnant women with hypertension according to the inclusion and exclusion criteria of 40 respondents. Data analysis using Paired-t Test, One Way Anova and Multiple Linear Regression with a significance level <0.05.

Results: There is a therapeutic effect of warm foot soaking with Epsom Salt 1% for 3 days on increasing Mg, NO, and blood pressure levels with p value <0,05.

Conclusion: There is an effect of foot bath therapy using warm water, Epsom Salt, and Lemongrass Oil on changes in biomarkers and blood pressure in pregnant women with hypertension.

Keywords: soak feet, Epsom salt, lemongrass oil, magnesium, nitric oxide, blood pressure, pregnant women

1. Introduction

Hypertension is a condition of an increase in blood pressure both systolic and diastolic from normal values. An empirical diagnosis of hypertension can be made by measuring systolic blood pressure ≥ 140 mmHg and diastolic ≥ 90 mmHg ^[1, 2]. Hypertensive conditions that are no less important to be treated immediately are hypertension in pregnancy (HDK), considering that these conditions contribute significantly to maternal and perinatal morbidity and mortality ^[3].

According to the World Health Organization (WHO) in 2015 around 14% of the 289,000 maternal deaths were caused by pregnancy hypertension ^[4]. According to the Basic Health Research (Riskesdas) in 2013 the prevalence of hypertension in pregnancy in Indonesia was 25.8% ^[5]. The maternal mortality rate in Central Java Province in 2017 was 88.05 / 100,000 live births with the biggest cause of death was hypertension in pregnancy (32.97%) ^[6]. Some districts in Central Java in 2017 that are ranked top for maternal deaths are Banjarnegara District as the fifth rank with MMR of 137.7 / 100,000 live births ^[6, 7]. The second largest cause of maternal death in Banjarnegara District in 2017 is hypertension in pregnancy of 23.8% ^[7]. One of the contributors to maternal deaths in Banjarnegara District in 2017 is the Kalibening Health Center with a total of 2 cases (9.2%) of the total 21 deaths. The cause of maternal death in Puskesmas Kalibening is hypertension in pregnancy by 50% ^[7].

Pregnant women with hypertension are at risk of developing (cerebrovascular disorders, cerebral edema, liver rupture, kidney failure, heart failure) which is a complication of preeclampsia, HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count), to death. Risks that occur in fetuses with hypertensive mothers are premature birth and fetal growth disorders (IUGR), until the occurrence of stillbirth ^[8]. Various factors(multifactorial)the background of the HDK be things that need attention to be resolved so that the circumstances that led to the emergency can be avoided so as to reduce maternal morbidity and mortality ^[9]. Physiological changes that occur in pregnant women will affect a variety of changes in all body regulatory systems, including changes in the pharmacokinetics and pharmacodynamics of the drugs consumed. The effect of physiological changes in pregnancy on pharmacokinetics and pharmacodynamics of drugs used during pregnancy is related to changes in gastrointestinal motility that affect changes in gastric emptying time which implicitly affects changes in absorption of drugs especially those given orally, including hypertensive drugs in pregnancy ^[10]. Teratogenic factors and the effects of using pharmacological therapies such as the occurrence of overshoot hypotension and hypoperfusion placentalthat can affect fetal growth are also issues to consider in the use of hypertension drugs in pregnancy ^[11].

Pharmacological management of hypertension in pregnancy

so far is mostly done through oral therapy such as Labetalol, Methyldopa and Nifedipine therapy. Pharmacological management has become a standard of service in dealing with hypertension in pregnancy, but the side effects of each of these drug therapies need to be considered. A study by Xie *et al* analyzed the comparison of the effects of labetalol with methyldopa on the poor infant prognosis of pregnant women with hypertension. They concluded that compared with the use of methyldopa, the use of labetalol had a longer hospital stay during infancy and worse neonatal outcomes such as the occurrence of hypoglycemia as an effect of drug use [12].

Another study conducted by Giannubilo *et al* to assess the effects of nifedipine and labetalol on maternal and fetal prognosis. They found more cases of IUGR in infants with mothers treated with labetalol (38.8%) compared with nifedipine use (15.5%) [10, 13]. They conclude that antihypertensive therapy in pregnancy using labetalol has the potential to change the behavior of the fetus towards efforts to treat hypertension in a lighter direction as a form of compensation [10]. The disrupted effects of fetal growth (IUGR) are caused by the pharmacological effects of labetalol which adversely affect uteroplacental metabolism so that it affects the transfer of nutrients in the placenta, or decreases perfusion pressure in the intervillous space [10, 13]. Another drug used as an antihypertensive agent in pregnancy is a type of drug that works as a calcium antagonist / Calcium Channel Blockers (CCB), nifedipine. Nifedipine is a CCB from dihydropyridine derivatives that is most widely used for hypertension in pregnancy as a second-line therapy in non-severe hypertension by working to block the flow of calcium across the cell membrane, thereby supporting smooth muscle relaxation [10]. Nifedipine as the most appropriate antihypertensive drug in pregnancy still has side effects. The results of a study conducted by Chan *et al* evaluated the safety of pregnant women from the effects of CCB used during pregnancy. In 269 relevant reports, the highest side effects among women who were given more than 60 mg of the total dose of nifedipine reported a number of side effects such as headaches, flushing, nausea, and vomiting up to 19%, 51%, 9%, and 18% of each study reported. Other side effects are associated with significant morbidity, such as tachycardia (33%), hypotension (39% of RCTs or controlled observational studies with nifedipine > 60 mg total dose) [14]. The problem as an effect of the pharmacological therapy of antihypertensive drugs used in pregnancy, it is important to consider other non-pharmacological therapies as an alternative effort or supporting effort in dealing with pregnancy hypertension so as not to lead to worse potential diagnoses. One of the therapies non-pharmacological in the management of hypertension today is foot bath therapy which is part of water therapy (Hydrotherapy) which according to several studies has been proven to be able to reduce blood pressure. The results of previous studies by Wulandari *et al*, and Nopriani *et al* concluded that there was a relationship between decreased blood pressure and administration of foot bath therapy [15, 16]. Based on the research of Evlan-Tas *et al*. Concluded that Water Immersion/ soaking for 3 hours divided in 3 days can produce hemodynamic changes [17]. Average diastolic blood pressure levels decrease significantly during immersion caused by an increase in central blood volume. This resulted in stroke volume and cardiac output increased and decreased

systemic vascular resistance, as well as the system renin-angiotensin and the sympathetic nervous system activity suppressed resulting in decreased blood pressure [17].

Water therapy which is part of services SPA that is legal in Indonesia is regulated in the Republic of Indonesia Government Regulation No. 8 of 2014. Utilization of water in foot bath therapy is used as the main modality in helping to maintain and improve client health [18]. Principles in water treatment is the utilization of the physical properties of water (buoyancy of water / buoyancy), hydrostatic pressure, and viscosity properties of water, as well as hydrodynamic nature / water flow and thermodynamic (heat and cold) [18]. Scientifically warm temperatures have physiological and psychological effects on the body so that they affect relaxation and comfort reactions [18, 15]. The effects of relaxation stimulate the nervous system in the legs resulting in an active parasympathetic nerve resulting in a decrease in blood pressure [16].

The implementation of foot bath therapy can be combined / mixed using natural ingredients / products from plants / plants, essential oils / essential oils, minerals, salt, mud, and aromatic fragrances [18]. Natural ingredients that can be combined with water therapy include Epsom Salt. Epsom Salt is a heptahydrate sulphate mineral ($MgSO_4 \cdot 7H_2O$) which has the same compound structure as $MgSO_4$ [19]. $MgSO_4$ compounds contained in Epsom salts have been known to be useful in the health world as anti-drugs convulsant in handling cases of hypertension in pregnancy, especially in preeclampsia / Eclampsia. $MgSO_4$ is one of the chemical mediators that influence the pathophysiological factors of hypertension in pregnancy [20].

Pathophysiological factors of hypertension in pregnancy one of which is a decrease in levels of Nitric Oxide (NO) due to dysfunction of endothelial cells in blood vessels. NO is a substance called Endothelium Derived Relaxing Factors (EDRFs) in endothelial cells that function as vasodilators of blood vessels [21]. The results Ishaku *et al*, showed that administration of $MgSO_4$ intravenous able to activate placental endothelial function through mechanically increasing A2AAR and iNOS as well as Transport L-Arginine so that it triggers an increase in Nitric Oxide Synthase (NOS) and NO levels as blood vessel vasodilators which results in a decrease in blood pressure [22]. Another study by Surjadi analyzed $MgSO_4$ therapy for vasodilation due to the effect of elevated levels (NO) in pregnant women with preeclampsia showing that there was an increase in NO levels associated with an increase in magnesium concentration (Mg) [20]. Magnesium compounds are indirectly involved in the biochemical process of contraction, modulating vascular smooth muscle tone and contractility by influencing the concentration and availability of calcium ions resulting in vasodilation effects and decreased blood pressure [23].

Another ingredient that can be used in water therapy is Lemongrass Oil/ lemongrass oil. The main ingredients are alcohol monoterpenes, namely linalool and geraniol which are found in citronella oil which have analgesic, calming and balancing activities, stimulants, vasodilator and hypotensive effects [15]. The relaxing effect can help lower blood pressure through the nerve olfactory to be sent to the limbic system. Stimulants sent to the limbic system will stimulate the hypothalamus which will then stimulate the vagus nerve. The vagus nerve will transmit parasympathetic impulses to the heart and there will be a decrease in the

frequency and contractility of the heart [24]. Various studies on the effect of therapeutic foot soak, use of MgSO₄ and citronella oil to the decrease in blood pressure has been shown to significantly, however pemanfaatan Epsom salts and lemongrass oil directly through immersion foot as an alternative in the management of hypertension in pregnancy need to be demonstrated empirically through measurements biomarker that play a role in blood pressure are Magnesium and NO compounds.

2. Methods

This type of research uses the research Quasy Experiment by using a pre-test – post-test with control group design. This study arranged four groups: three intervention groups that were given soak feet therapy using warm water with Epsom Salt 1% and Lemongrass Oil for 10 drops with a duration of 15 minutes in each group in pregnant women with hypertension, while the control group was given intervention with therapy using warm water without any combination. Soak feet therapy using warm water with Epsom Salt 1% and Lemongrass Oil given for 3 days. Measurement of blood pressure using mercury spigmomanometer instruments and stethoscopes, then for examination of magnesium (Mg) and nitric oxide (NO) levels by taking intravenous blood as much as 3 cc to be sent to the Kalibening Laboratory for centrifuge.

3. Results

Table 1: Distribution of frequency respondents’ pregnant women with hypertension by age, gestational age, profession and psychic demographic data

Variable	Intervention 1		Intervention 2		Intervention 3		Control		P value
	F	%	F	%	F	%	F	%	
Age									
<20 years	1	10%	1	10%	2	20%	1	10%	0.994
20-35 years	7	70%	7	70%	6	60%	7	70%	
>35 years	2	20%	2	20%	2	20%	2	20%	
Gestational Age									
Trimester II	4	40%	4	40%	5	50%	5	50%	0.939
Trimester III	6	60%	6	60%	5	50%	5	50%	
Profession									
Work	2	20%	3	30%	2	20%	3	30%	0.912
No Work	8	80%	7	70%	8	80%	7	70%	
Psychic									
Normal	8	80%	7	70%	8	80%	8	80%	0.934
Mild stress	2	20%	3	30%	2	20%	2	20%	
Moderate stress	0	0%	0	0%	0	0%	0	0%	
Stress is quite heavy	0	0%	0	0%	0	0%	0	0%	
Severe stress	0	0%	0	0%	0	0%	0	0%	

*Chi-Square Test

Description:

Intervention 1: soak feet of warm water with Epsom salt and Lemongrass oil

Intervention 2: soak feet of warm water with Epsom Salt

Intervention 3: soak feet of warm water with Lemongrass Oil

Intervention 4: soak feet with warm water

Based on the table above, it shows that the average age, gestational age, profession and psychological level of respondents of pregnant women with hypertension

pregnancy in the intervention group and the control group there is no significant difference which means the same or homogeneous with p value > 0.05.

Table 2: Analysis of differences in mean values of magnesium (Mg), nitric oxide (NO), systolic and diastolic blood pressure between the intervention group and control group

Variable	Groups				P value
	Intervention 1	Intervention 2	Intervention 3	Intervention 4	
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	

Mg levels	0.173 ± 0.157	0.170 ± 0.162	0.019 ± 0.119	0.030 ± 0.129	0.026
NO Levels	10.29 ± 8.593	10.157 ± 8.842	2.342 ± 7.351	2.541 ± 8.00	0.043
BPS	-10.80 ± 7.083	-8.10 ± 7.866	-2.00 ± 6.146	-0.30 ± 4.967	0.003
BPD	-8.80 ± 4.962	-7.30 ± 6.129	-2.70 ± 5.186	-1.10 ± 3.212	0.004

*One Way Anova

Description:

Intervention 1: soak feet of warm water with Epsom salt and Lemongrass oil

Intervention 2: soak feet of warm water with Epsom Salt

Intervention 3: soak feet of warm water with Lemongrass Oil

Intervention 4: soak feet with warm water

Based on the table above, showed that the average content of magnesium (Mg), levels of nitric oxide (NO), systolic and diastolic blood pressure between the treatment and control groups were different and a significant value with p-

value <0.05. So, it can be concluded that there is an effect of warm water foot bath therapy with Epsom Salt 1% for 3 days on reducing blood pressure through increased levels of magnesium (Mg) and nitric oxide (NO).

Table 3: Comparison of mean values of magnesium (Mg), nitric oxide (NO), systolic and diastolic blood pressure between the intervention group and control group

Variable	Intervention 1 & 2	Intervention 1 & 3	Intervention 1 & 4	Intervention 2 & 3	Intervention 2 & 4	Intervention 3 & 4
	P value	P value	P value	P value	P value	P value
Mg levels	0.964	0.022	0.033	0.025	0.036	0.866
NO levels	0.970	0.037	0.042	0.040	0.045	0.957
BPS	0.367	0.005	0.001	0.046	0.012	0.569
BPD	0.505	0.010	0.001	0.046	0.009	0.478

*Post Hoc Test

Description:

Intervention 1: soak feet of warm water with Epsom salt and Lemongrass oil

Intervention 2: soak feet of warm water with Epsom Salt

Intervention 3: soak feet of warm water with Lemongrass Oil

Intervention 4: soak feet with warm water

Based on the table above, shows the most influential therapy towards changing magnesium levels (Mg) is a therapy for soaking feet with warm water using Epsom Salt (intervention 2). Then the most influential therapy for changes in levels nitric oxide (NO) is foot bath therapy with warm water using Epsom Salt (intervention 2). Furthermore, the most influential therapy for changes in systolic blood pressure is foot bath therapy with warm water using Epsom Salt and Lemongrass Oil (intervention 1), while the most influential therapy for changes in diastole blood pressure is foot bath therapy with warm water using Epsom Salt and Lemongrass Oil (intervention 1).

Table 4: Effect of differences in the magnesium (Mg) and nitric oxide (NO) levels on systolic and diastolic blood pressure

Variable		P value
BP systolic	Sig. F	0.000
	R	0.825
	R2 square	0.663
	F Hitung	39.404
	(Constan)	-0.098
BP dyastolic	Koefisien regresi Kadar Mg	-6.758
	Koefisien regresi Kadar NO	-0.483
	Sig. F	0.000
	R	0.780
	R2 square	0.588
	F Hitung	28.815
	(Constan)	-1.297
	Koefisien regresi Kadar Mg	-19.236
	Koefisien regresi Kadar NO	-0.282

*Multiple Linear Regression Test

Based on the table above, known the significance value F of 0.000 is smaller than 0.05, so it can be concluded that magnesium and Nitric Oxide levels simultaneously or

jointly affect the systolic and diastolic blood pressure.

4. Discussion

4.1 Characteristics of respondents

Based on the results of the statistical test Chi-square in table 1, it can be seen that the characteristics of respondents by age indicate that there are no significant differences between the intervention groups 1,2,3 and control of the age criteria of respondents. In other words, each group has the same age proportion with a p value of 0.994. The respondent characteristics based on gestational age showed that gestational age between the intervention group 1,2,3 and control had the same proportion with p value of 0.939. Based on job characteristics, the p value is 0.912, which means that there is no difference in the proportion between jobs between the intervention group 1,2,3 and control. Based on the psychological state it is known that the psychological state between the intervention group 1,2,3 and control has the same proportion with a p value of 0.934. From the resulting characteristic data it can be concluded that the characteristics of respondents based on age, gestational age, occupation, and physical condition between the intervention groups 1,2,3 and control have the same proportion so that it can be considered not to influence the relationship between the interventions given to the research results in each group.

4.2 Effect of magnesium (Mg) and nitric oxide (NO) levels on systolic and diastolic blood pressure

Based on the results of the study shown in the table above results in the average difference in Mg levels between the intervention group 1,2,3 and the control group had a P value of 0.026. The results of the comparison of the average NO levels between the intervention group 1,2,3 and control obtained a P value of 0.043. In systolic blood pressure, the

mean was obtained between the intervention group 1,2,3 and the control with P value 0,003. In diastolic blood pressure, the mean difference between the intervention group was 1,2,3 and the control with a P value of 0,004. From the above data it can be concluded that there are significant differences in the average Magnesium (Mg) levels, Nitric Oxide, systolic and diastolic blood pressure between the intervention groups 1,2,3, and controls. Based on post hoc follow-up tests, it was concluded that the most influential therapy for changes in Mg and NO levels was foot bath with warm water using Epsom Salt (intervention 2) while the most influential therapy for changes in systolic and diastolic blood pressure was foot bath with warm water using Epsom Salt and Lemongrass Oil (intervention 1).

In addition, it was found that magnesium and Nitric Oxide levels simultaneously or jointly affected the systolic blood pressure with the degree of association in the strong correlation category. The percentage effect of Mg and NO levels on systolic blood pressure was 66.3%, while the remaining 33.7% of systolic blood pressure was influenced by other variables not examined. Each increase in Mg levels by 1 mmol / L will reduce systolic blood pressure by 6.758 mmHg and each increase in NO levels by 1 mmol / L will reduce systolic blood pressure by 0.483 mmHg, so it can be concluded that the influence of Mg is greater than NO in affect changes in systolic blood pressure. Meanwhile, the diastolic blood pressure changes found that magnesium and Nitric Oxide levels simultaneously or jointly affect diastole blood pressure with the degree of relationship in the category of strong correlation. The percentage effect of Mg and NO levels on diastole blood pressure was 58.8%, while the remaining 41.2% diastole blood pressure was influenced by other variables not examined. Each increase in Mg levels by 1 mmol / L will reduce diastole blood pressure by 19.236 mmHg and each increase in NO levels by 1 mmol / L will reduce diastole blood pressure by 0.282 mmHg, so it can be concluded that the influence of Mg is greater than NO in affect changes in diastolic blood pressure.

In line with the theory of the relationship between Mg and Mg NO stating that plays a role in dilating Adenine A2A receptor (A2AAR) during the formation of NO in the endothelial cells of blood vessels. This receptor will activate Endogenous Nucleoside Adenosine which plays a role on L-Arginine Transport in the plasma membrane of endothelial cells. L-Arginine transport influences the production of L-Arginine Cationic Amino Acid, where this molecule is a substrate in the formation of NOS. The formation of NO will have an impact on the dilation of blood vessels because in essence the role of NO is as a vasodilator of blood vessels so that blood pressure will decrease [25, 26].

Epsom salts containing magnesium and sulfate are effectively absorbed by the body through the skin so that the levels of magnesium and sulfate in the body will increase as explained in the mechanism of transdermal delivery of therapeutic material in the previous discussion. This can be seen from the increase in the average level of magnesium in respondents after the intervention. An increase in average NO levels after the intervention also occurred in this intervention group. This is also in line with the theory previously explained about the relationship of magnesium with NO.

The body's reaction to foot bath therapy with warm water using Epsom Salt and Lemongrass Oil will simultaneously have a relaxing effect. The warm sensation and magnesium

content found in Epsom salts as well as the citronella content in lemongrass oil all have a relaxing effect in the body. The body's relaxing effect will stimulate the hypothalamic reaction to affect the endocrine system and parasympathetic nervous system. Relaxed body condition, the hypothalamus will also stimulate the production of serotonin which causes the activity of the parasympathetic nervous system and decreased epineprin and no epineprin. In the postganglion, the parasympathetic nerve will bind to acetylcholine which has a relaxing effect on the heart muscle. The effect of relaxation will also affect the condition of the endocrine system which will stimulate the release of Corticotropin Inhibiting Hormone (CIH) which causes the production of Adrenocorticotrophic Hormone (ACTH) in the anterior hyposfisis is inhibited / decreased so that cortisol hormone secretion in the adrenal cortex decreases. Decreased cortisol hormone causes a decrease in epineprin and norepineprin levels which causes a relaxing effect on the heart muscle so that peripheral resistance and cardiac output decrease which causes vasodilation of blood vessels and decreased blood pressure [27].

5. Conclusion

Based on the results of research on the effect of foot bath therapy with warm water using Epsom Salt and Lemongrass Oil on changes in levels of Magnesium (Mg), Nitric Oxide (NO), and Blood Pressure in pregnant women with hypertension at Kalibening Banjarnegara Health Center, it can be concluded as follows:

- 5.1 There is an effect of foot bath therapy using water warm, Epsom Salt, Lemongrass Oil to changes in biomarkers and blood pressure in pregnant women with hypertension
- 5.2 There is an effect therapeutic foot soak with warm water, Epsom Salt, Lemongrass Oil for 3 days against increased levels of Magnesium (Mg), Nitric Oxide (NO), and drop in Blood Pressure
- 5.3 There is an effect therapeutic foot soak use warm water with Epsom Salt for 3 days to increase levels of Magnesium, NO, and drop in Blood Pressure
- 5.4 No effect of feet soak therapy using warm water with Lemongrass Oil for 3 days on increasing levels of Magnesium, Nitric Oxide (NO), and drop in Blood Pressure
- 5.5 No effect of foot bath therapy use warm water butted ma 3 days for increasing levels of Magnesium, NO, and drob in blood pressure
- 5.6 The most influential therapy for increasing Mg and NO levels is foot bath therapy with warm water using Epsom Salt
- 5.7 The most influential therapy for decreasing systolic and diastolic blood pressure is foot bath therapy with warm water using Epsom Salt and Lemongrass Oil

6. References

1. Cunningham FG, Leveno JK, Bloom LS, Houth CJ, Rouse JD, Spong YC, *et al.* *Obstetri Williams*. 23rd ed. Jakarta: EGC, 2013.
2. Leveno K, Cunningham FG, Giant FNM. *Obstetri Williams Panduan Ringkas*. 21st ed. (Yudha EK, Subekti NB, eds.). Jakarta: EGC, 2012.
3. Nelson-piercy C. Hypertension in pregnancy Key points. *Medicine (Baltimore)*. 2018; 18(5):10-13. doi: 10.1016/j.mpmed.2018.09.010

4. World Health Organization. World Health Statistic 2015. Geneva: WHO, 2015.
5. Kementerian Kesehatan RI. Pusat Data Informasi Kementerian Kesehatan RI Hipertensi. Heal Educ Behav. 2014; 2(4):328-335. doi:10.1177/109019817400200403
6. Dinas Kesehatan Provinsi Jawa Tengah. Profil Kesehatan Provinsi Jawa Tengah Tahun 2017. Semarang: Dinas Kesehatan Jateng, 2017.
7. Dinas Kesehatan Kabupaten Banjarnegara. Profil Kesehatan Kabupaten Banjarnegara Tahun 2017. Banjarnegara, 2017.
8. Easterling TR. Pharmacological management of hypertension in pregnancy. Semin Perinatol. 2014; 38(8):1-9. doi: 10.1053/j.semperi.2014.08.016
9. Alexander JM, Wilson KL. Hypertensive Emergencies of Pregnancy. Obstet Gynecol Clin NA. 2013; 40(1):89-101. doi: 10.1016/j.ogc.2012.11.008
10. Clark SM, Dunn HE, Hankins GD V. A review of oral labetalol and nifedipine in mild to moderate hypertension in pregnancy. Semin Perinatol, 2015, 1-8. doi: 10.1053/j.semperi.2015.08.011
11. Plaat F. The Treatment of Hypertension in Pregnancy. Anaesth Intensive Care Med, 2016, 1-4. doi: 10.1016/j.mpaic.2016.11.005
12. Xie RH, Guo Y, Krewski D, *et al.* Association between labetalol use for hypertension in pregnancy and adverse infant outcomes. Eur J Obs Gynecol Reprod Biol. 2014; 175:124-128. doi: https://doi.org/10.1016/j.ejogrb.2014.01.019
13. Giannubilo SR, Bezzeccheri V, Cecchi S, *et al.* Nifedipine versus labetalol in the treatment of hypertensive disorders of pregnancy. Arch Gynecol Obs. 2012; 286(3):637-642. https://link.springer.com/article/10.1007/s00404-012-2371-x.
14. Chan K, Zamora J, Lamont RF, *et al.* Safety concerns for the use of calcium channel blockers in pregnancy for the treatment of spontaneous preterm labour and hypertension: a systematic review and meta-regression analysis. J Matern Neonatal Med. 2016; 23(9):1030-1038. doi: https://doi.org/10.3109/14767050903572182
15. Wulandari P, Arifianto, Sekarningrum D. Pengaruh Rendam Kaki Menggunakan Air Hangat dengan Campuran Garam dan Serai terhadap Penurunan Tekanan Darah Pada Penderita Hipertensi di Wilayah Podorejo RW 8 Ngaliyan. J Keperawatan. 2016; 7(1):43-47. doi: https://doi.org/10.22219/jk.v7i1.3918
16. Nopriani Y, Primanda Y, Makiyah S. N. Efektivitas Kombinasi Relaksasi Otot Progresif dan Rendam Kaki Air Hangat terhadap Tekanan Darah Penderita Hipertensi. Din Kesehat J Kebidanan dan Keperawatan. 2018; 9(2):627-636. https://ojs.dinamikakesehatan.unism.ac.id/index.php/dk-sm/article/view/366.
17. Elvan-Tas, Ayten Franx A, Delprat, Constance Bruinse, Hein W. Koomans HA. Water Immersion in Preeclampsia. Am J Obstet Gynecol. 2016; 195(6):1590-1595. doi: 10.1016/j.ajog.2016.05.007
18. Kementerian Kesehatan RI. Peraturan Menteri Kesehatan Republik Indonesia Nomor 8 Tentang Pelayanan Kesehatan Spa. Jakarta: KEMENKES, 2014.
19. Prystajecky MR, Parent S. Iatrogenic hypermagnesemia following Epsom salt enema. J Acute Med. 2015; 5(3):80-83. doi: 10.1016/j.jacme.2015.06.003
20. Surjadi LM. Kajian Farmakokinetika dan Dampak Farmakodinamika Magnesium Sulfat Pada Penderita Preeklamsia Tinjauan Pengaruh Perbedaan Rute Pemberian MgSO4 Terhadap Perubahan Tekanan Darah Serta Kadar NO dan VEGF Serum, 2015. <http://etd.repository.ugm.ac.id/index.php>.
21. Djanggan S. Disfungsi Endotel Edisi Pertama. Malang: UB Pres; 2015.
22. Ishaku SM, Ismail SM, Kanij S, Babatunde OA, Ara NR. 86 MgSO4 Modulates A2A and A2B Adenosine receptors, eNOS and iNOS Expression, and L-arginine Transport in Human Placental Microvascular Endothelial Cells: Magnesium Sulphate. Pregnancy Hypertens An Int J Women's Cardiovasc Heal. 2016; 6(3):219. doi: 10.1016/j.preghy.2016.08.168
23. Barbagallo M, Dominguez LJ. Magnesium, Oxidative Stress, and Aging Muscle. In: Aging: Oxidative Stress and Dietary Antioxidants. itaty: Elsevier, 2014, 157-166. doi:10.1016/B978-0-12-405933-7.00016-0
24. Widowati I, Harnany A, Sri R. Pengaruh Masase Kaki Dengan Minyak Sereh Wangi Terhadap Penurunan Tekanan Darah Hipertensi Lansia di Kota Pekalongan. Pena J Ilmu Pengetah dan Teknol, 2014, 26(1). doi: <http://dx.doi.org/10.31941/jurnalpena.v26i1.110>
25. Zullino S, Buzzella F, Simoncini T. Nitric oxide and the biology of pregnancy. *Journal Vasc Pharmacol*, 2018, 7(4). doi: 10.1016/j.vph.2018.07.004
26. Bahadoran Z, Mirmiran P, Azizi F, Ghasemi A. Nitrate-rich dietary supplementation during pregnancy: The pros and cons. J Pregnancy Hypertens. 2018; 11(24):44-46. doi: 10.1016/j.preghy.2017.12.010
27. Irfan F, Prabandari YS, Sulistyarini I. Relaksasi Untuk Menurunkan Tingkat Stres dan Tekanan Darah Pada Penderita Hipertensi. J Intervensi Psikol, 2011, 3. doi: <https://dx.doi.org/10.20885/intervensipsikologi.vol3.iss1.art4>