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Role of L-Arginine in Pre-Eclampsia

Yasmeen Amin[1], Naureen Javed[1], Sidrah Akram[1], Bushra Ashraf[1], Shazia Batool[1]

[1]Department of Obstetrics and Gynaecology, Allied Hospital-2, Faisalabad, Pakistan.

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Correspondence to: Yasmeen Amin, Department of Obstetrics and Gynaecology, Allied Hospital-2, Faisalabad, Pakistan.
Email: yasmeenamin2017@gmail.com

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ABSTRACT

Introduction: Although the precise mechanism is yet unknown, L-arginine has been shown to be useful against preeclampsia by reducing systemic symptoms. L-arginine remodeling activities are thought to improve the uterine spiral arteries, which are thought to be compromised during preeclampsia. Such research was not before carried out within our general community. Therefore, we wish to investigate the outcomes of the L-arginine group of pregnant patients who are at high risk. My research will be useful in treating preeclampsia in high-risk pregnancies by employing L-arginine. **Materials & Methods:** The current study conducted at Department of Obstetrics and Gynaecology, Unit 3 DHQ/ Allied Hospital 2 Faisalabad from 7 Sep 2023 to 07 March 2023. There were 100 high-risk pregnancies with ages ranging from 20 to 35 years old (50 in each group). Patients having a history of H/O renal illness and diabetes were not included. Patients receiving a placebo were placed in Group B, while those receiving L-arginine were placed in Group A. Women in group A received 300 grams of L-arginine (Amino Whey Sachet) once daily until delivery, while women in group B received a homologous placebo (starch) once daily until delivery. Data from both groups were recorded. **Results:** The study's age range was 20 to 35 years old, with a mean age of 27.17 ± 4.18 years. The average age of the women in groups A and B was 27.18 ± 4.17 and 27.16 ± 4.17 years, respectively. 173 patients, or 74.57% of the total, were in the 20–30 age range. 44 (88.0%) of the patients in group A (L-arginine) and 33 (66.0%) of the patients in group B (placebo) in my study showed efficacy, with a p-value of 0.009, which is statistically significant. **Conclusion:** This study concluded that L-Arginine is very effective in the prevention of preeclampsia in high-risk Pregnancies.

INTRODUCTION

Worldwide, hypertensive disorders of pregnancy impact up to 10% of pregnancies, including the 3%–5% of pregnancies that are made worse by preeclampsia. Preeclampsia is the term for new-onset hypertension that appears after 20 weeks of pregnancy and is accompanied by proteinuria or indications of liver or uterine damage. Preventative measures only considerably lower a woman's risk of preeclampsia, and risk variables that have been identified are insufficient in predicting when it will occur despite its prevalence [1-3]. It is an important cause of maternal and neonatal illness and mortality worldwide, especially in underdeveloped nations. In India, the incidence of preeclampsia amongst the hospital patients is roughly 7-10% of all prenatal admissions [2]. Although the actual etiology of preeclampsia is not established, poor placentation and endothelial dysfunction are considered the basic hallmarks of preeclampsia [3]. It is a multisystem illness that affects the maternal kidneys, liver, brain, coagulation system and particularly the placenta [4]. Given that preeclampsia is a condition that essentially affects every organ system in the mother, it has a variety of clinical features and requires close interdisciplinary collaboration for diagnosis, treatment, and prevention [5]. Hypertension and proteinuria (protein in urine ≥0.3 g/24 h (1+ dipstick) on two occasions ≥4 h apart) or edema are symptoms of pre-eclampsia (PE) [2]. It is a major cause of maternal and neonatal morbidity and mortality, complicating between 2% and 8% of pregnancies [3]. Maternal and perinatal health are both significantly impacted by pre-eclampsia and eclampsia, especially in developing nations. They cause more than six million perinatal deaths and nearly a third of a million deaths in low- and middle-income environments. According to a recent systemic review of world mortality, Pakistan has the third-highest burden of maternal, fetal, and child death and is the sixth most populous country. In Pakistan, eclampsia is responsible for 34% of maternal mortality among patients treated to tertiary care facilities [4]. Even with the numerous advancements in contemporary medicine around the world, preeclampsia is still difficult to grasp in terms of both its exact etiology and treatment. However, data points to a central role for widespread endothelial dysfunction (ED) in the pathophysiology of preeclampsia [5]. Preeclampsia may result from low concentrations of these nitric oxide levels because of their reduced bioavailability [6].

All living forms' proteins contain the amino acid L-arginine. It falls within the category of conditionally essential or semi-essential amino acids. Despite not being an essential amino acid according to the above definition,

L-arginine is still a necessary amino acid. Nitric oxide is formed using L-arginine as a precursor [7]. Therefore, it makes sense that L-arginine supplementation would reduce this occurrence by acting as a donor of nitric oxide [8]. Although the precise mechanism is yet unknown, L-arginine has been shown to be useful against preeclampsia by reducing systemic symptoms. L-arginine remodeling processes are thought to help improve the uterine spiral arteries, which are thought to be compromised during preeclampsia [9]. In order to determine if L-arginine or a placebo is more effective at preventing pre-eclampsia in high-risk pregnancies, Taj N undertook a study. The study had 130 female participants in total. Group A consisted of 65 patients who were in the L-arginine group, while Group B consisted of 65 patients who were in the placebo group. It was shown that both groups were effective. Efficacy was 92.3% in the L-arginine group and 69.2% in the placebo group (p<0.000).

We conclude that L-arginine plays a significant effect in preventing pre-eclampsia in high-risk pregnant individuals and in lessening the severity of pre-eclampsia [10]. Such research was not before carried out within our general community. Therefore, we wish to investigate the outcomes of the L-arginine group of pregnant patients who are at high risk. L-arginine will be useful in my research to treat preeclampsia in high-risk pregnancies.

MATERIALS AND METHODS

Selected for this randomized controlled trial were 100 (50 in each group) women of age 20-35 years with singleton high risk pregnancy (presence of anyone of following; preeclampsia in previous pregnancy, blood pressure >140/90 mmHg on 2 occasions and family h/o high blood pressure) of gestational age < 20 weeks and parity 0-4. By using WHO sample size calculator for two proportions, power of the study= 80%, level of significance =5%, anticipated proportion in L-arginine group (P1) = 92.3%10, anticipated proportion in placebo group (P2) = 69.2%10. Calculated sample size was 100 (50 in each group). Patients who refused informed permission, had a history of diabetes, or had a history of kidney illness were not included.

All patients who visited the OPD in succession were included once the research proposal was approved by the "Ethical Review Committee" in accordance with the inclusion and exclusion criteria. Consent was obtained with knowledge. Using a table of random numbers, randomization was carried out. Patients receiving a placebo were placed in Group B, while those receiving L-arginine were placed in Group A. Women in group A received 300 grams of L-arginine (Amino Whey Sachet) once daily till delivery, while women in group B received a homologous placebo (starch) once daily until delivery. Data from both groups were recorded. All of the pain data was gathered using a specially created proforma.

IBM-SPSS Version 25, a statistical analysis application, was used to evaluate the data. For qualitative factors including efficacy and family history of hypertension, frequency and percentage were calculated. For quantitative characteristics such as age, parity, gestational age, duration of chronic hypertension, and BMI, the mean ±SD was displayed. The effectiveness of both groups was compared using the chi square test.

RESULTS

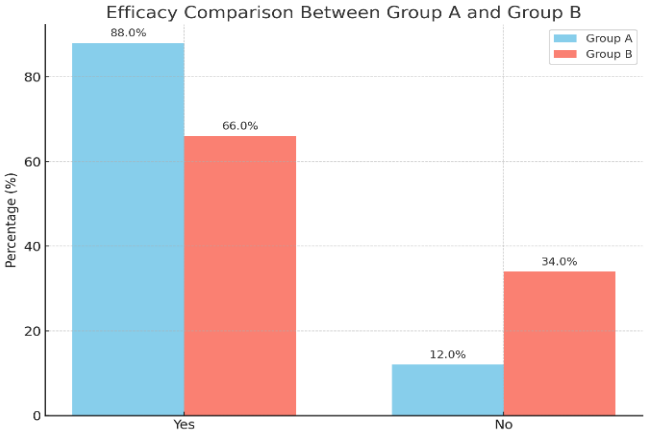
The study's age range was 20 to 35 years old, with a mean age of 27.17 ± 4.18 years. The average age of the women in groups A and B was 27.18 ± 4.17 and 27.16 ± 4.17 years, respectively. As can be seen, 173 (74.57%) of the patients were between the ages of 20 and 30. Pregnancy duration was 15.13 ± 2.01 weeks on average. 2.11 ± 1.05. was the mean parity. A mean height of 162.33 ± 11.45 cm was recorded. A mean weight of 72.34 ± 5.64 kg was recorded. Group B's mean BMI was 28.34 ± 3.13 kg/m2, while group A's was 28.60 ± 2.98 kg/m2. HTN lasted an average of 3.11 ± 1.07 years. 44 (88.0%) of the patients in group A (L-arginine) and 33 (66.0%) of the patients in group B (placebo) in my study showed efficacy, with a p-value of 0.009, which is statistically significant (Table 1).

Table 1

Comparison of Efficacy of L-Arginine versus Placebo in the Prevention of Preeclampsia in High-Risk Pregnancies.

Variable		Group A (n=50)		Group B (n=50)		P-value
		Frequency	%age	Frequency	%age	
Efficacy	Yes	44	88.0	33	66.0	0.009
	No	06	12.0	17	34.0	

Figure 1



DISCUSSION

The semi-essential amino acid L-arginine has drawn interest as a potential preventive agent for pregnancy-related hypertension disorders. Vasodilation and nitric oxide synthesis depend on L-arginine. The body's natural L-arginine production may not be enough to meet the increased demand for nitric oxide during pregnancy, which could result in endothelial dysfunction and impaired vascular balance. Supplemental L-arginine may help prevent preeclampsia since clinical evidence indicates that it can improve endothelial function and lower blood pressure [10].

Supplementing to increase nitric oxide synthesis seems like a sensible approach, given the critical role that nitric oxide bioactivity—or lack thereof—plays in the endothelial dysfunction that characterizes hypertension. L-arginine supplementation has enhanced endothelium-dependent vasodilation in hypercholesterolemic individuals. In both hypertension and cardiovascular

disorders, this dysfunction and the resulting decreased nitric oxide activity are important markers of the underlying pathophysiology. Because hypertension individuals' circulatory systems dilate their epicardial arteries and respond less well to nitric oxide-based agonists, their vascular pressure regulation may be disrupted. Since it serves as the primary substrate for the synthesis of endothelial nitric oxide, L-arginine is necessary [11].

This study was carried out to compare the effectiveness of L-arginine and a placebo in preventing preeclampsia in high-risk pregnancies. The study's age range was 20 to 35 years old, with a mean age of 27.17 ± 4.18 years. The average age of the women in groups A and B was 27.18 ± 4.17 and 27.16 ± 4.17 years, respectively. 173 patients, or 74.57% of the total, were in the 20–30 age range. With a p-value of 0.009, which is statistically significant, 44 (88.0%) patients in group A (L-arginine) and 33 (66.0%) patients in group B (placebo) in my study showed efficacy. In order to determine if L-arginine or a placebo is more effective at preventing pre-eclampsia in high-risk pregnancies, Taj N undertook a study. The study had 130 female participants in total. Group A consisted of 65 patients who were in the L-arginine group, while Group B consisted of 65 patients who were in the placebo group. Both groups were found to be effective. Efficacy was 92.3% in the L-arginine group and 69.2% in the placebo group ($p<0.000$). We conclude that L-arginine plays a significant effect in preventing pre-eclampsia in high-risk pregnant individuals and in lessening the severity of pre-eclampsia [12].

Four of the included studies demonstrated that, in comparison to the placebo group, L-arginine significantly lowered blood pressure and prevented preeclampsia [13–16]. Another study, however, found that while L-arginine supplementation decreased the use of several antihypertensive drugs, it had no statistically significant effect on the total drop in blood pressure in women with mild chronic hypertension. However, the small sample size and exclusion of patients with severe chronic hypertension were the study's limitations [17]. In one study, the use of L-arginine supplemented with antioxidant vitamins as an intervention significantly decreased the incidence of preeclampsia in high-risk pregnant women. Nevertheless, the study was unable to determine how L-arginine, when paired with vitamins, would lower the risk of preeclampsia [18]. Our review's findings supported earlier research [13,15,17], which found that L-arginine is beneficial in lowering the risk of preeclampsia.

Together with our results, a 2016 study by Pulido et al. indicates that consuming L-arginine can reduce the incidence of preeclampsia by 26% [19]. L-arginine is better than a placebo at lowering the risk of preeclampsia, according to a recent meta-analysis of ten studies (OR: 0.36, 95% CI: 0.17–0.77) [20]. According to research by Vadillo et al., arginine insufficiency may be the cause of preeclampsia [21]. The positive biological activity of L-arginine in pregnancies impacted by growth limits and hypertension diseases was supported by a 2023 systematic review of 51 studies, 25 of which involved humans and 26 of which involved animals. According to the review, L-arginine is a safe intervention that may enhance the results for both the mother and the fetus, especially when moderate clinical abnormalities are present [22].

Facchinetti F. et al.'s findings provide some credence to the current study's theory that preeclampsia is characterized by a disturbance of the L-arginine-Nitric Oxide pathway [23]. It's possible that our findings are similar to a study by Rytlewski K. et al. that found that supplementing with L-arginine reduced blood pressure in preeclamptic women by increasing nitric oxide bioavailability and/or endothelial production [24]. A study on nitric oxide during pregnancy and delivery by Hudicek-Martincic G. et al. supports the current study's findings. It discovered that larger levels of nitric oxide are used in pathological pregnancy situations, such as IUGR, preeclampsia, and premature labor [25].

A further example by Khetsuriani T. et al. demonstrated that during pregnancy, the concentration of free nitric oxide dropped by 10%, which is in line with the findings of the present investigation [26]. The nitric oxide pathway in preeclampsia was investigated in a study by Buhimschi IA et al., using rats given NG-nitro-L-arginine (L-NAME), a nitric oxide synthase inhibitor utilized as an animal model for preeclampsia. Their results showed that preeclampsia is caused by nitric oxide deficiency, which is in line with our current research [27].

A study by Hladunewich MA et al. that examined the impact of L-arginine treatment on preeclampsia produced contradictory findings. There were no appreciable variations in blood pressure between the two groups, even though postpartum serum arginine levels significantly increased [28].

CONCLUSION

According to the study's findings, L-arginine effectively prevents preeclampsia in high-risk pregnancies. Therefore, in order to prevent preeclampsia and the morbidity and death of the mother, we advise that high-risk gravid females be given L-arginine.

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