https://doi.org/10.37723/jumdc.v15i1.898

J. Univ. Med. Dent. Coll.2024;Vol.15(1):769-773
ISSN (Print) 2221-7827, ISSN (Online) 2310-5542
https://www.jumdc.com

Original Article

Open Access

Comparison of the efficacy of 75 mg aspirin versus 150 mg aspirin for prevention of preeclampsia in patients at high risk for preeclampsia

Wardah Saeed [a], Natasha Bushra [b], Tayyaba Rashid [c], Mahwish Iqbal [d]

[a] *Senior Registrar, Department of Obstetrics and Gynaecology, Ghurki Trust Teaching Hospital.*
[b] *Assistant Professor, Department of Obstetrics and Gynaecology, Post Graduate Medical Institute Lahore, Ameer ud Din Medical College, Lahore.*
[c] *Associate Professor, Department of Obstetrics and Gynaecology, Services Institute of Medical Sciences Lahore.*
[d] *Assistant Professor, Department of Obstetrics and Gynaecology, Batterjee Medical College, Jeddah.*

Correspondence: natashausman5@hotmail.com*

ABSTRACT

BACKGROUND & OBJECTIVE: Preeclampsia is a significant contributor to maternal health challenges. Emphasizing prevention over cure is a guiding principle in healthcare. As a reliable measure to forestall hypertension and its associated complications during pregnancy, aspirin is widely embraced. The early identification of risk factors plays a crucial role in the primary prevention of preeclampsia. Post-risk stratification, aspirin emerges as a pivotal player in the preventive strategy for individuals identified as high-risk for preeclampsia. To assess the effectiveness of 75 mg aspirin against 150 mg aspirin in preventing Preeclampsia among individuals with a high risk for the condition.

METHODOLOGY: A quasi-experimental study was conducted in the Department of Obstetrics and Gynecology, Services Hospital, Lahore, from 27-12-2019 to 27-6-2020.240 patients were enrolled in the study, which was later divided into two groups. Group A received treatment with 75 mg aspirin, while Group B was administered 150 mg aspirin. Efficacy was determined based on whether blood pressure levels were below 140/90 mmHg, and proteinuria was rated as <+1 using the dipstick method.

RESULTS: The mean age of the patients was 28.54±6.83 years, and the mean gestational age was 15.30±1.69 weeks. In the 75 mg group, the efficacy was achieved in 94(78.3%) patients, whereas in the 150 mg group, the efficacy was performed in 108(90.0%) patients (p-value=0.013).

CONCLUSION: This study concludes that the efficacy of 150 mg aspirin significantly surpasses that of 75 mg aspirin in preventing Preeclampsia among high-risk pregnant patients.

KEYWORDS: Preeclampsia, Efficacy, Aspirin, High-risk Pregnancy.

INTRODUCTION

Preeclampsia is the major contributor to maternal morbidity and perinatal mortality. It is a condition affecting 25 % of pregnancies with a history of chronic hypertension, 5% of all pregnancies and 10% of nulliparous women [1]. Aspirin is a drug of choice to prevent complications of hypertension in pregnancy. It is a non-steroidal anti-inflammatory drug absorbed through the gastrointestinal tract. Its role is in preventing complications in patients at risk of developing preeclampsia. The dose of aspirin used in most hospital settings is low dose, which has its benefits outweigh the risks and side effects of the drug [2].

NICE guidelines recommend screening all pregnant patients at booking to assess for the risk factors to develop preeclampsia and start low-dose aspirin from 12 weeks as a prophylaxis and continue until delivery [3].

Aspirin has a significant role in preventing hypertension, and also fetal risks, including intra-uterine growth restriction and placental insufficiency, can be prevented. Preeclampsia is a complication of hypertension, developed after 20 weeks, which has its severity from mild to severe depending on haematological disturbances and multi-organ involvement. Proteinuria can be detected but symptoms like headache and blurring of vision with deterioration in laboratory testing also manifest as complications.

How to cite this: *Saeed W, Bushra N, Rashid T, Iqbal M .Comparison of the efficacy of 75 mg aspirin versus 150 mg aspirin for prevention of preeclampsia in patients at high risk for preeclampsia. Journal of University Medical & Dental College. 2024;15(1):769-773.*

Hypertension is diagnosed in pregnancy when the patient is presented with a blood pressure of 140/90mmHg on two readings, two occasions apart [4]. All pregnant patients should be screened for risk factors to develop preeclampsia, and a history of hypertension is one of the leading reasons. Preeclampsia also affects the fetal outcome in terms of the need for iatrogenic prematurity, admission to the nursery and perinatal morbidity and mortality. In severe cases, treatment is to termination of pregnancy [5].

Different studies have been conducted on the role of aspirin as a preventive measure of preeclampsia. Aspirin is started in a dose of 75 mg from 12 weeks to patients' high risk for developing preeclampsia. There are varied results regarding the dose of aspirin, as a 150 mg dose is also given in some instances to prevent this condition [6].

A study conducted by Rolnik DL [6-7] and his team concluded that patients who were given aspirin in a dose of 150 mg had reduced evidence of preeclampsia by about 1.5% in high-risk cases screened for preeclampsia. In a study by Ebrashy A. et al., patients were screened in early pregnancy for risk factors of preeclampsia and were given 75 mg of aspirin that showed reduced incidence but up to 8% [8]. The trials have varied evidence, which concluded that aspirin in a dose of 150 mg had an efficacy of 93%. It has been reported in a trial that 93.5% of cases with 150 mg aspirin and 83% of cases with 75 mg aspirin in high-risk preeclampsia patients, and the difference was significant ($p<0.05$) [9].

This study aims to evaluate the effectiveness of 75 mg aspirin versus 150 mg aspirin in preventing preeclampsia among individuals with high risk for the condition. Existing literature suggests that the 150 mg aspirin dose may exhibit superior efficacy, yet inconclusive evidence exists in our specific setting. By screening patients at high risk of preeclampsia and administering an optimized aspirin dose, we aim to determine if this approach can effectively prevent hypertensive complications and enhance both maternal and fetal outcomes.

METHODOLOGY

A quasi-experimental study was conducted in Unit III, Department of Obstetrics and Gynecology, Services Hospital, Lahore from 27-12-2019 to 27-6-2020. Ethical approval was taken from the hospital ethical review board (Ref.no IRB/2020/616/SIMS). A total of 240 patients was enrolled in the study and later divided into two groups, 120 in each case with a 95% level of confidence and 5% level of significance and taking the expected percentage of efficacy, i.e., 93.5% with 150 mg aspirin and 83% with 75 mg aspirin in high-risk preeclampsia patients. The sampling technique was non - Probability Consecutive Sampling. Group A was treated with 75 mg of aspirin, and Group B was treated with 150 mg of aspirin. Patients included in the study were pregnant patients aged 18-40 years, with parity less than 5, presented for booking at 12-18 weeks and are at high risk of developing preeclampsia after risk stratification.

Those with H/o allergic reaction to salicylates on medical records, H/o peptic/duodenal ulcer on medical records, multiple pregnancy (on ultrasound) and placental abnormality (previa, percreta, accreta) were excluded. All patients were recruited after obtaining verbal consent. Patient baseline demographic details were collected, including age, gestational age, parity, and BMI. Subsequently, subjects were randomly allocated to one of two groups through a blinded ballot. These patients were then regularly monitored in the outpatient department for 20 weeks.

After this period, assessments for blood pressure and proteinuria were conducted. Efficacy was determined operationally as blood pressure below <140/90 mmHg and proteinuria <+1 according to the dipstick method. In the event of preeclampsia development, females received management in accordance with hospital protocols. The researcher personally recorded all pertinent information on the proforma.

The data underwent statistical analysis using the IBM SPSS version 22 software. Descriptive statistics in mean ± SD were reported for quantitative variables such as age, gestational age, and BMI. Frequent and percentage calculations were performed for qualitative variables like efficacy, while parity was presented as a frequency. A Chi-square test was employed to compare the efficacy of both groups, with a significance level set at $p \leq 0.05$.

Stratification was conducted to assess the impact of variables, including age, gestational age, BMI, and parity on efficacy. Post-stratification Chi-square tests were applied within each stratum to compare the efficacy of both groups, with a significance threshold of $p \leq 0.05$ considered statistically significant.

RESULTS

We recruited 240 patients who were part of this study. The mean age of the patients was 28.54±6.83 years. The mean age of the patients in group A was 28.25±6.97 years, while in the 150 mg group, the mean age of the patients was 28.83±6.71 years. The mean gestational age of the patients was 15.30±1.69 weeks. Among 240 patients, there were 27(11.25%) patients were nulliparous, 39(16.25%) patients had parity 1, 40(16.67%) patients had parity 2, 47(19.58%) patients had parity 3, 49(20.42%) had parity 4, 37(15.42%) patients had parity 5 and 1(0.42%) had parity more than 5. Table-I.

Out of 240 patients, efficacy was achieved in 202(84.17%) patients shown in Fig 1. In the 75 mg group, the efficacy was achieved in 94(78.3%) patients, whereas in the 150 mg group, the efficacy was achieved in 108(90.0%) patients. This difference was statistically significant. i.e., p-value=0.013 shown in Table- II.

Table-I:Summary statistics of demographic features between study groups.

Variables	Study Groups	
	75mg Mean±SD n=120	150mg Mean±SD n=120
Age(years)	28.25±6.97	28.83±6.71
Gestational Age	17.82±1.81	17.17±1,67
BMI(KG/m2)	25.62±3.45	25.85±3.52

Table-II:Comparison of efficacy between study groups.

Variables		Study Groups		Total n(%)	P-value
		75 mg n(%)	150 mg n(%)		
Efficacy	Achieved	94(78.3)	108(90.0)	202(84.2)	0.013
	Not Achieved	26(21.7)	12(10.0)	38(15.8)	
Total		120(100.0)	120(100.0)	240(100.0)	

Table-III: Comparison of efficacy between study groups stratified by variables.

Variables	Efficacy	Study Groups		Total n(%)	P-value
		75 mg n(%)	150 mg n(%)		
Age ≤ 30 years	Achieved	56(74.7)	64(87.7)	120(81.1)	0.043
	Not Achieved	19(25.3)	9(12.3)	28(18.9)	
>30years	Achieved	38(84.4)	44(93.6)	82(89.1)	0.158
	Not Achieved	7(15.6)	3(6.4)	10(10.9)	
Gestational Age 13-15 weeks	Achieved	50(75.8)	64(92.8)	114(84.4)	0.006
	Not Achieved	16(24.2)	5(7.2)	21(15.6)	
16-18 weeks	Achieved	44(81.5)	44(86.3)	88(83.8)	0.505
	Not Achieved	10(18.5)	7(13.7)	17(16.2)	
BMI ≤25	Achieved	45(80.4)	40(85.1)	85(82.5)	0.527
	Not Achieved	11(19.6)	7(14.9)	18(17.5)	
BMI >25	Achieved	49(76.6)	68(93.2)	117(85.4)	0.006
	Not Achieved	15(23.4)	5(6.8)	20(14.6)	
Parity primiparity	Achieved	28(80.0)	30(96.8)	58(87.9)	0.037
	Not Achieved	7(20.0)	1(3.2)	8(12.1)	
Multiparity	Achieved	66(77.6)	78(87.6)	144(82.8)	0.108
	Not Achieved	19(22.4)	11(12.4)	30(17.2)	

Regarding the age of the patient, in less than 30 years, the efficacy in the 75 mg group was achieved in 56(74.7%) patients, whereas in the 150 mg group, the efficacy was achieved in 64(87.7%) patients (p-value=0.043). Similarly, In patients aged> 30 years, the efficacy in the 75 mg group was achieved in 38(84.4%) patients, whereas in the 150 mg group, the efficacy was achieved in 44(93.6%) patients (p-value=0.158). Table-III.

In patients having gestational age 13-15 weeks, the efficacy in the 75 mg group was achieved in 50(75.8%) patients, whereas in the 150 mg group, the efficacy was achieved in 64(92.8%)

patients (p-value=0.006). In patients having gestational age 16-18 weeks, the efficacy in the 75 mg group was achieved in 44(81.5%) patients, whereas in the 150 mg group, the efficacy was achieved in 44(86.3%) patients (p-value=0.505) shown in Table-III.

In patients having BMI ≤25 kg/m2, the efficacy in the 75 mg group was achieved in 45(80.4%) patients, whereas in the 150 mg group, the efficacy was achieved in 40(85.1%) patients (p-value=0.527). Similarly, In patients having BMI >25 kg/m2, the efficacy in the 75 mg group was achieved in 49(76.6%) patients, whereas in the 150 mg group, the efficacy was achieved in 68(93.2%) patients (p-value=0.006).Table -III.

In null & primary parity patients, the efficacy in the 75 mg group was achieved in 28(80.0%) patients, whereas in the 150 mg group, the efficacy was achieved in 30(96.8%) patients (p-value=0.037). Similarly, In multi-parity patients, the efficacy in the 75 mg group was achieved in 66(77.6%) patients, whereas in the 150 mg group, the efficacy was achieved in 78(87.6%) patients (p-value=0.108). The comparison of both groups is summarized in Table-III.

DISCUSSION

Preeclampsia is one of the leading causes of maternal and perinatal morbidity. The risk stratification of patients presented in pregnancy at the time of booking should be done to assess the risk factors for developing preeclampsia [10]. Significant and minor risk factors are evaluated. Patients with hypertension and diabetes and a history of hypertension in previous pregnancies are major risk factors, whether little risk factors are age more than 40 years, primigravida, family h/o preeclampsia and twin pregnancy [11]. It has fetal implications in terms of placental insufficiency, intra-uterine growth restriction and iatrogenic prematurity. Delivery is planned in terms of uncontrolled blood pressure, progressiveproteinuria and deterioration in laboratory tests [12].

A randomized controlled trial comparing the effectiveness of 75mg versus 150mg aspirin for preventing preeclampsia in high-risk pregnant women revealed a notably higher incidence of preeclampsia in the group administered with 75mg aspirin (34%) in contrast to those who were given 150mg aspirin (9%) [13-14]. Our findings align with the results of this randomized controlled trial mentioned, emphasizing a clear dosage-dependent trend in the efficacy of aspirin for preventing preeclampsia in high-risk pregnant women.

There is a recommendation by NICE guidelines about the dose of 75 mg, but recent research publications had a lack of data regarding optimized doses. A study documented that the efficacy of aspirin is better in 150 mg dose as it crosses theplacental barrier and inhibits aggregation of platelets [15].

Although low-dose aspirin exhibits commendable maternal and fetal safety characteristics, it is essential to acknowledge the relatively sparse exposure of patients to doses surpassing 100 mg. Consequently, the prudence of a preventative regimen relying on a daily aspirin dosage of 150 mg necessitates substantiation [16]. The ASPRE trial conducted in 2017 has strong evidence for a better safety and efficacy profile of 150 mg compared to placebo in the prevention of preeclampsia [7].

A study conducted to evaluate the role of acetylsalicylic acid in high-risk pregnancy resulted in its role in the prevention of co-morbidities in pregnancy. Aspirin was administered in one arm of the study, while a placebo was utilized in the other. The findings revealed a 35% incidence of preeclampsia, 7.7% for severe preeclampsia, and 18.9% for fetal growth restriction[17]. In contrast, among the cohort of 91 women receiving a 150 mg dosage, preeclampsia was notably reduced to 6.5%, severe preeclampsia to 2.1%, and early-onset preeclampsia to 1%.

In comparison, the control group exhibited a higher prevalence of preeclampsia, severe preeclampsia, and fetal growth restriction. These findings also favour our results, wherein in the 75 mg group, the efficacy was achieved in 94(78.3%) patients, whereas in the 150 mg group, the efficacy was performed in 108(90.0%) patients. This difference was statistically significant. i.e., p-value=0.013 in our study. Consequently, a discernible enhancement in efficacy was observed with administering a 150 mg aspirin dosage, even though the 75 mg dosage also demonstrated effectiveness [18].

It has been reported in a trial conducted in randomized multi-country (Democratic Republic of Congo, Guatemala, India, Kenya, Pakistan, Zambia) that efficacy was achieved in 93.5% of cases with 150 mg aspirin and 83% of cases with 75 mg aspirin in high-risk preeclampsia patients and the difference was significant ($p<0.05$) [19].

A double-blinded placebo study conducted in 2017, which was The Aspirin for Evidence-Based Preeclampsia Prevention (ASPRE), identified patients at high risk of preeclampsia at booking visits from 12-14 weeks and two groups were compared for the use of aspirin in a dose of 150 mg and placebo This landmark trial showed a significant reduction of preeclampsia leading to preterm delivery in more than 50% of patients. However, the incidence of pr eclampsia at term was the same, but that could be due to the beneficial effect of aspirin in patients preventing preterm intervention and improved maternal and fetal outcomes [20].

CONCLUSION

This study concludes that the efficacy of 150 mg aspirin significantly surpasses that of 75 mg aspirin in preventing preeclampsia among high-risk pregnant patients. These results contribute substantively to refining clinical practices, fostering a more tailored and productive approach to preventing preeclampsia, and elevating the standards to improve feto-maternal outcomes.

ACKNOWLEDGEMENT: None
CONFLICT OF INTEREST: None
GRANT SUPPORT AND FINANCIAL DISCLOSURE: None.

REFERENCES:

1. Kamath SA. Hypertension in pregnancy. The Journal of the Association of Physicians of India. 2006;54:269-270.
2. Patrono C, Baigent C. Role of aspirin in primary prevention of cardiovascular disease. Nature Reviews Cardiology. 2019;16(11):675-686. Doi:10.1038/s41569-019-0225-y
3. National Institute for Health and Clinical Excellence. Hypertension in pregnancy: the management of hypertensive disorders during pregnancy. NICE;2010.
4. Poon LC, Shennan A, Hyett JA, Kapur A, Hadar E, Divakar H, et al. The international federation of gynecology and obstetrics (FIGO) initiative on preeclampsia (PE): a pragmatic guide for first-trimester screening and prevention. International Journal of Gynaecology and Obstetrics. 2019;145(1):1-33. Doi: 10.1002/ijgo.12802
5. Porter TF, Gyamfi-Bannerman C, Manuck T. Low-dose aspirin use during pregnancy. Obstetrics and gynecology. 2018;132(1):e44-e52.
6. Rolnik DL, Wright D, Poon LC, O'Gorman N, Syngelaki A, de Paco Matallana C et al. Aspirin versus placebo in pregnancies at high risk for preterm preeclampsia. New England Journal of Medicine. 2017;377(7):613-622. Doi: 10.1056/NEJMoa1704559
7. Brichant JF, Bonhomme V. Preeclampsia: an update. Acta Anæsthesiologica Belgica. 2014;65(4):137-149.
8. Ebrashy A, Ibrahim M, Marzook A, Yousef D. Usefulness of aspirin therapy in high-risk pregnant women with abnormal uterine artery Doppler ultrasound at 14-16 weeks pregnancy: randomized controlled clinical trial. Croatian Medical Journal. 2005;46(5):821-825.
9. Shanmugalingam R, Wang X, Münch G, Fulcher I, Lee G, Chau K, et al. A pharmacokinetic assessment of optimal dosing, preparation, and chronotherapy of aspirin in pregnancy. American Journal of Obstetrics and Gynecology. 2019;221(3):255.e1-255.e9. Doi:10.1016/j.ajog.2019.04.027
10. Finneran MM, Gonzalez-Brown VM, Smith DD, Landon MB, Rood KM. Obesity and laboratory aspirin resistance in high-risk pregnant women treated with low-dose aspirin. American Journal of Obstetrics and Gynecology. 2019;220(4):385.e1-385.e6 .Doi:10.1016/j.ajog.2019.01.222
11. Chaemsaithong P, Cuenca-Gomez D, Plana MN, Gil MM, Poon LC. Does low-dose aspirin initiated before 11 weeks' gestation reduce the rate of preeclampsia? American Journal of Obstetrics and Gynecology. 2020;222(5):437-450. Doi:10.1016/j.ajog.2019.08.047
12. English FA, Kenny LC, McCarthy FP. Risk factors and effective management of preeclampsia. Integrated Blood Pressure Control.2015;8:7-12.Doi:10.2147/IBPC.S50641
13. Sinha N, Singh S, Agarwal M, Manjhi PK, Kumar R, Singh SK, et al. A randomized controlled study comparing the efficacy of 75mg versus 150mg Aspirin for the prevention of preeclampsia in high-risk pregnant women. Cureus. 2023;15(5):e39752.Doi: 10.7759/cureus.39752
14. Roberts JM, August PA, Bakris G, Barton JR, Bernstein IM, Druzin M, et al. Hypertension in pregnancy: executive summary. Obstetrics and Gynecology. 2013;122(5):1122-1131. Doi: 10.1097/01.AOG.0000437382.03963.88
15. Chaemsaithong P, Pooh RK, Zheng M, Ma R, Chaiyasit N, Tokunaka M, et al. Prospective evaluation of screening performance of first-trimester prediction models for preterm preeclampsia in an Asian population. American Journal of Obstetrics and Gynecology. 2019;221(6):650.e1-650.e16. Doi:10.1016/j.ajog.2019.09.041
16. Stubert J, Hinz B, Berger R. The Role of acetylsalicylic acid in the prevention of preeclampsia, fetal growth restriction, and preterm birth. German Medical Journal International.2023;120(37):617-626.Doi:10.3238/arztebl.m2023.0133
17. Naimi AI, Perkins NJ, Sjaarda LA, Mumford SL, Platt RW, Silver RM, et al. The effect of preconception-initiated low-dose aspirin on hcg pregnancy, pregnancy loss, and live birth: per-protocol analysis of a randomized trial. Annals of Internal Medicine. 2021;174(5):595-690. Doi:10.7326/M20-0469
18. Sjaarda LA, Radin RG, Silver RM, Mitchell E, Mumford SL, Wilcox B, et al. Preconception low-dose aspirin restores diminished pregnancy and live birth rates in women with low-grade inflammation: a secondary analysis of a randomized trial. The Journal of Clinical Endocrinology & Metabolism. 2017;102(5):1495-1504. Doi:10.1210/jc.2016-2917
19. Hoffman MK, Goudar SS, Kodkany BS, Metgud M, Somannavar M, Okitawutshu J, et al. Low-dose aspirin for the prevention of preterm delivery in nulliparous women with a singleton pregnancy (ASPIRIN): a randomized, double-blind, placebo-controlled trial. The Lancet. 2020;395(10220):285-293.Doi:10.1016/S0140-6736(19)32973-3
20. Banala C, Moreno S, Cruz Y, Boelig RC, Saccone G, Berghella V, et al. Impact of the ACOG guideline regarding low-dose aspirin for prevention of superimposed preeclampsia in women with chronic hypertension. American Journal of Obstetrics andGynecology.2020;223(3):419.e1-419.e16. Doi:10.1016/j.ajog.2020.03.004

Authors Contributions:

wardah Saeed : Substantial contributions to the conception and design of the work.

Natasha Bushra :The acquisition, analysis, and interpretation of data for the work.

Laiq Zaman : Drafting the work and reviewing it critically for important intellectual content.

Mahwish Iqbal: Final approval of the version to be published.

Submitted for publication: 3-08-2023
Accepted after revision: 27-02-2024