Low Dose Aspirin for Prevention of Pre-eclampsia in Women at High Risk

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Purpose/Objectives/Hypothesis

To assess the treatment efficacy of low dose prophylactic aspirin (75-150 mg) in pregnant women at high risk for preeclampsia after 11 weeks of gestation compared to placebo in an attempt to reduce incidence of preeclampsia

Background/Introduction

Preeclampsia is a disorder of pregnancy associated with new-onset hypertension, which occurs most often after 20 weeks of gestation and frequently near term.

It is estimated that 4.6% of pregnancies worldwide are complicated by preeclampsia.

Usually accompanied by new-onset proteinuria, hypertension, and other signs or symptoms of preeclampsia such as right upper quadrant, epigastric pain, or headaches

Design

We conducted a PubMed search using key words: “Pre-eclampsia”, “aspirin”, and “randomized controlled trial”. A total of 133 articles were reviewed. These results were narrowed to eleven randomized clinical trials. This is a evidence based review of four randomized clinical trials

Major Inclusion Criteria

Inclusion criteria were females from 11 weeks of gestation or later with high risk for preeclampsia

Major Exclusion Criteria

Exclusion criteria included unconscious or severely ill status, learning difficulties or serious mental illness, major fetal abnormality identified at the time that scanning was performed at 11 to 13 weeks of gestation, regular treatment with aspirin within 28 days before screening, bleeding disorder such as VWB disease, peptic ulceration, hypersensitivity to aspirin, long-term use of NSAIDs, and participation in another drug trial within 28 days before screening, history of chronic illness, multiple gestations, smoking, abnormal uterine artery doppler, abnormal serum level of pregnancy-associated

Result Tables

STUDY 1

Table 2. Outcomes According to Trial Group.

Outcome	Aspirin Group (N = 798)	Placebo Group (N = 822)	Odds Ratio (95% or 99% CI)*
Primary outcome: preterm preeclampsia at <37 wk of gestation — no. (%)	13 (1.6)	35 (4.3)	0.38 (0.20–0.74)
Secondary outcomes according to gestational age			
Adverse outcomes at <34 wk of gestation			
Any — no. (%)	32 (4.0)	53 (6.4)	0.62 (0.34–1.14)
Preeclampsia — no. (%)	3 (0.4)	15 (1.8)	0.18 (0.03–1.03)
Gestational hypertension — no. (%)	2 (0.3)	2 (0.2)	1.02 (0.08–13.49)
Small-for-gestational-age status without preeclampsia — no./total no. (%)†	7/785 (0.9)	14/807 (1.7)	0.53 (0.16–1.77)
Miscarriage or stillbirth without preeclampsia — no. (%)	14 (1.8)	19 (2.3)	0.78 (0.31–1.95)
Abruption without preeclampsia — no. (%)	1 (0.1)	3 (0.4)	0.36 (0.02–7.14)
Spontaneous delivery without preeclampsia — no. (%)	12 (1.5)	12 (1.5)	1.07 (0.37–3.10)
Adverse outcomes at <37 wk of gestation			

STUDY 2

Table 2
Comparison of the incidence of preeclampsia and early-onset preeclampsia between the aspirin and placebo groups.

Variables	Placebo group (n = 284)	Aspirin group			χ^2 Value	Pearson	P for trend
		Group A	Group B	Group C			
All pregnancies (n = 1105)							
With pre-eclampsia (%)	51(18.0 %)	37(13.6 %)	28 (10.1 %)	26 (9.6 %)	10.237	−0.111	0.001
No pre-eclampsia (%)	233(82.0 %)	235(86.4 %)	250 (89.9 %)	245 (90.4 %)			
Pre-eclampsia (n = 142)							
Early-onset (%)	14 (27.5 %)	5 (13.5 %)	2 (7.1 %)	1 (3.8 %)	8.996	−0.243	0.003
Late-onset (%)	37 (72.5 %)	32 (86.5 %)	26 (92.9 %)	25 (96.2 %)			

Mantel-Haenszel chi square test was used to determine whether there was a linear relationship between different aspirin doses and the onset of preeclampsia and preeclampsia.

STUDY 3

Table 6
Rates of preeclampsia, intrauterine growth restriction, and preterm delivery in women treated with aspirin vs placebo

Variables	Aspirin (n = 43)	Placebo (n = 43)	aOR (95% CI)	p
PE	27 (62.8%)	38 (88.4%)	0.23 (0.07–0.73)	0.013
Preterm delivery	6 (14%)	1 (2.3%)	9.78 (0.90–105.89)	0.061

Data presented as number (percentage%). Adjusted odds ratio was adjusted for maternal age, parity, and number of previous pregnancies complicated by PE.
IUGR = intrauterine growth restriction, PE = preeclampsia.

STUDY 4

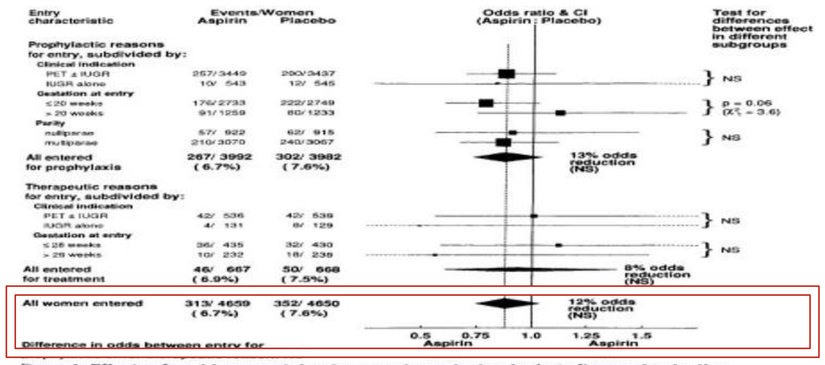

Figure 1: **Effects of aspirin on proteinuric pre-eclampsia developing after randomisation**

Validity Table of Studies

Author	Randomized	Concealed Randomization	ITT	Baseline Characteristics	Equal Treatment	Blinded	Follow Up	Results	Study Sites
Gu et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes (555/580 patients or 95.69%)	Statistically Significant	1 Center (China)
Abdi et al.	Yes, using Random Allocation software	N/a	No	Yes	Yes	No	Yes (87/90 patients or 96.7%)	Statistically Significant	1 Center (Iran)
The Lancet plus Collaborative Group	Yes, using central 24-hr service at the Clinical Trial Service Unit at Oxford	Yes	Yes	Yes	Yes	Double Blinded, Placebo-Controlled Trial	Yes (7845/8915 patients or 88%)	Not Statistically Significant	213 Centers
Rolnik et al.	Yes, using 1:1 ratio with Web-based system	Yes	Yes	Yes	Yes	Double Blinded, Placebo Controlled Trial	Yes (1620/1776 patients or 91.21%)	Statistically Significant	13 Centers (US, Europe, H.K.)

Results and Recommendation

Authors	NNT	P-Value
Gu et al.	12	P = 0.001
Abdi et al.	4	P = 0.013 (CI 0.07-0.73)
The Lancet plus Collaborative Group	N/A	N/a
Rolnik et al.	37	P = 0.004 (CI 0.20-0.74)

Clinical Recommendation	SOR	References
Pregnant women at high risk for preeclampsia should be started on prophylactic dose of ASA (75-150 mg) in an attempt to reduce incidence of preeclampsia after 11 weeks of gestation	B	Gu et al. Abdi et al. The Lancet plus Collaborative Group Rolnik et al.

Future Study Directions

Do women with specific risk factors benefit more from ASA prophylaxis?
Which dosage is the optimal dose that maximizes effectiveness while simultaneously reduces adverse effects?
Are other platelet inhibitors as effective in preeclampsia prevention?

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References

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