European Journal of Obstetrics and Gynecology 280 (2023) 198–199

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.journals.elsevier.com/european-journal-of-obstetrics-and-gynecology-and-reproductive-biology

Short communication

The effect of low-dose aspirin on platelet function during pregnancy compared to placebo: An explorative study. A letter to the Editor

The Editor

We read with interest Bij de Weg et al.'s, recent mechanistic report on the inhibitory effect of Aspirin on platelet function in patients with pre-eclampsia [1]. Compared to placebo, this study found that 80 mg of generic Aspirin demonstrated significant inhibitory effect on platelet function as evidenced by surrogate markers of platelet function (Verify Now® Aspirin Reaction Units [450.5 vs 648.0, $p = 0.017$]; Chronolog LTA [9.5% vs 94.5%, $p = 0.009$]; serum thromboxane B_2 (TXB_2) levels [11.9 ng/mL versus 175.9 ng/mL, $p = 0.030$] [1]. Despite the relatively small sample size of this exploratory study, its point estimates appear consistent with what has been reported from other studies examining Aspirin pharmacodynamics in different morbidities other than pregnancy [2].It is noteworthy that Bij de Weg et al.'s study did not provide information on the Aspirin formulation used in the study; although it still remains uncertain if enteric coating of aspirin would have significantly impacted the point estimate of platelet inhibition reported in that study. Enteric coating of Aspirin has recently generated intense mechanistic debate regarding its role in aspirin non responsiveness (as evidence by surrogate markers such as the proportion of TXB_2 inhibition) [3]. Indeed, in a comprehensive proof-of-concept examination of prospectively recruited ethnically diverse patients with ischemic stroke ($N = 42$), we recently reported for the first-time absence of differential aspirin non responsiveness between stroke patients randomized to enteric coated (EC-ASA) vs. those allocated to the plain preparation (P-ASA). In our study, the surrogate marker of Aspirin non responsiveness was the level of residual serum TXB_2 associated with elevated thrombotic risk (<99.0% inhibition or $TXB_2 > 3.1$ ng/ml) within 72 h after three daily Aspirin doses. We found no significant difference between Aspirin non-responders in the P-ASA vs. EC-ASA groups (28.6% vs 23.8%) ($p = 0.726$). Our study was consequent upon earlier concern raised by Bhatt et al. regarding the propensity of Aspirin coating to influence TXB_2 levels in healthy volunteers with type 2 diabetes mellitus [4]. Although the key driver to incomplete inhibition of TXB_2 levels in this study was attributed to impaired absorption, it's probable link with enteric coating remains a probability. Bij de Weg et al.'s exploratory report has therefore provided a reassuring mechanistic framework to support Aspirin responsiveness (or be it through the agency of a surrogate marker) in a cohort of pregnant patients. Recently, questions have been raised regarding the potential role of single nucleotide polymorphisms (SNP) of gene encoding proteins involved in the biodisposition of Aspirin in pregnancy. In a recent composite study design involving an initial cross-sectional study and subsequent genome-wide association *meta*-analysis, Mone et al. established that no SNP was significantly associated with Aspirin response in pregnancy [5]. As has been evident in the general population, going forward in addition to real-patient outcome studies, a determination of bioequivalence between Aspirin formulations may be necessary in the Bij de Weg et al.'s, patient cohort (pregnant women at 2nd and 3rd trimesters of pregnancy). This is in addition, to other areas of pharmacodynamic uncertainties highlighted in Fig. 1.

Funding

The authors declare that no funding was received for the present study.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Dr. Mohammed I Danjuma reports was provided by Hamad Medical Corporation.

https://doi.org/10.1016/j.ejogrb.2022.12.013
Received 22 November 2022; Accepted 6 December 2022
Available online 9 December 2022
0301-2115/© 2022 Published by Elsevier B.V.

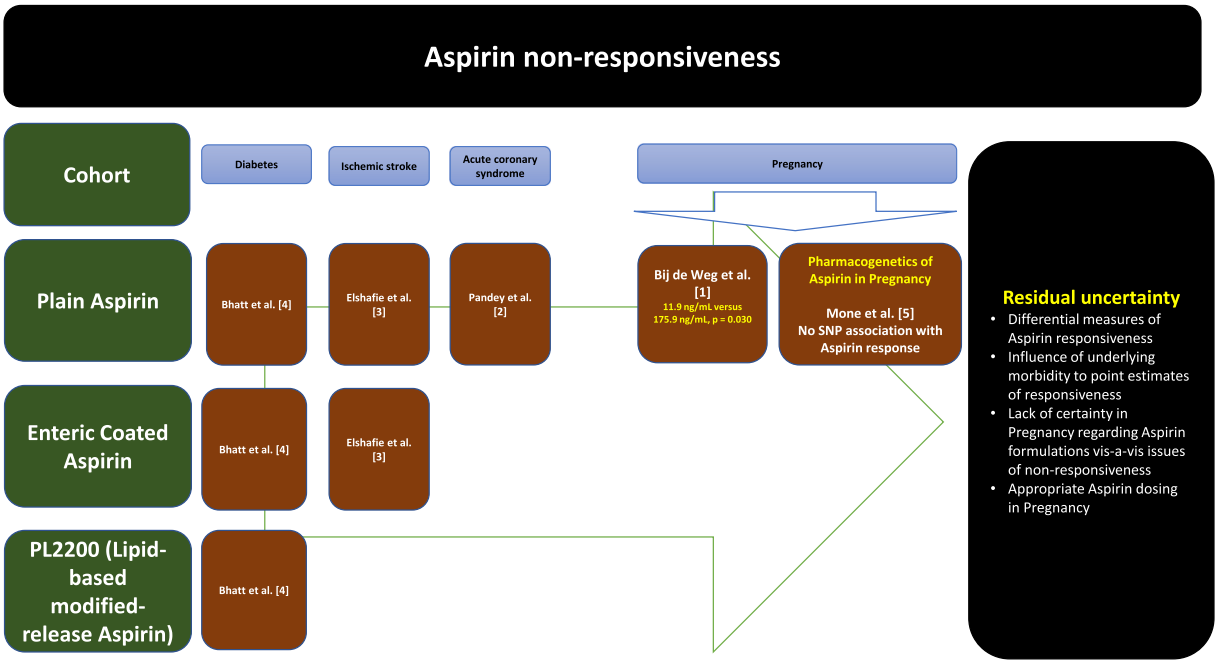

Fig. 1. Schematic representation of current evidence as it related to point estimates of aspirin responsiveness in pregnancy.

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