Adenosine diphosphate and thromboxane A_2 platelet activation in type II diabetes mellitus

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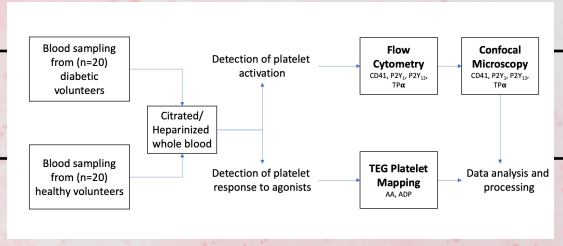
Introduction

- Type II Diabetes Mellitus has become a global health concern and is associated with the increased risk for thrombotic events, including myocardial infarction and stroke.[1]
- Platelets play an important role in the development of a blood clot through activation, aggregation and the formation of a fibrin network.
- Adenosine diphosphate (ADP) and thromboxane A_2 (TXA_2) are two potent platelet activators and were found to be up regulated in diabetic patients, but platelet activation through these agonists has not been well defined.[2]

The aim of this study was to elucidate whether diabetic platelets are more reactive towards ADP or TXA_2, compared to healthy platelets and whether platelets in diabetic populations are primed for activation by these agonists by expressing more receptors.



Methods:

Flow Cytometry, Confocal Microscopy: Analyse receptor expression for ADP ($P2Y_1$ and $P2Y_{12}$) and TXA_2 (TP) on platelet surfaces after stimulation (thrombin and collagen) or no stimulation .

TEG Platelet Mapping: Test platelet activation in response to ADP and TXA_2.

Results

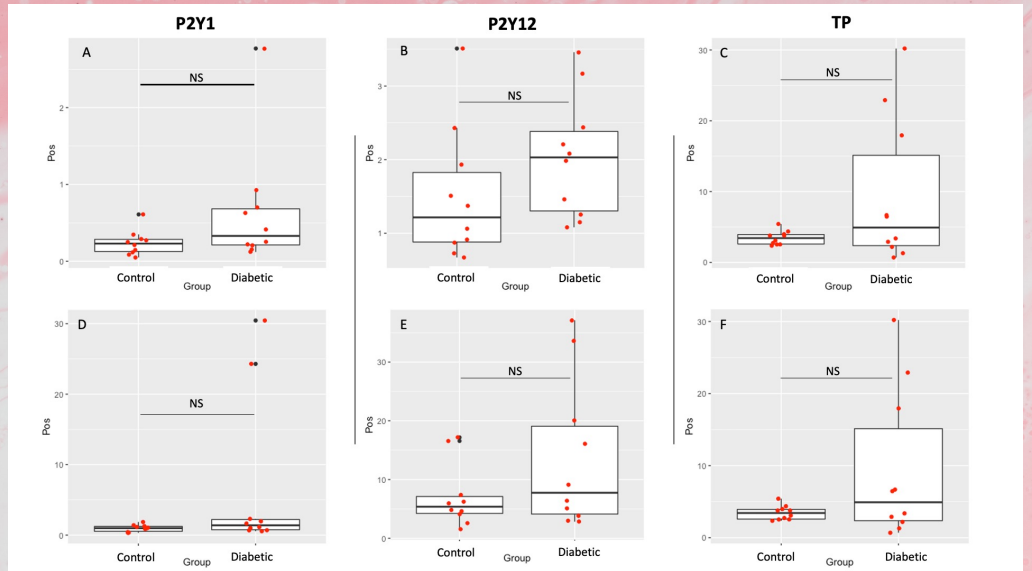


Figure 1: Flow cytometry results of percentage positivity for P2Y1, P2Y12 and TP
A-C: Unstimulated; D-F: Stimulated. Data expressed as median and IQR. P< 0.05

Table 1: Variables for TEG Platelet Mapping and percentage platelet aggregation

	Control (n=9)	Diabetic (n=9)	P-value
MA_{Kaolin} (Thrombin)	63.7 (3.10)	70.3 (2.88)	**0.0002533**
MA_{Fibrin}	18.4 (6.62)	36.8 (17.30)	**0.01332**
MA_{ADP}	44.5 (11.59)	59.9 (8.40)	**0.003077**
MA_{AA}	41.1 (11.38)	47.1 (15.54)	0.3652
% Agg ADP	53.2 (28.66)	69.5 (36.73)	0.3111
% Agg AA	46.3 (30.54)	17.3 (58.26)	0.2105

Abbreviations: MA, Maximal amplitude; ADP, Adenosine diphosphate; AA, Arachidonic acid; Agg, aggregation. Values expressed as mean and SD. P< 0.05

- **Flow cytometry data (n=10):** no significant difference between control and diabetic platelet receptor expression in stimulated or unstimulated samples.
- **TEG data (n=8):** significant difference in maximal (MA) amplitude (mm) of the clot between groups for kaolin treated samples, fibrin and ADP.

Discussion and conclusion:

- TEG data shows diabetic patients might have a risk for bigger thrombi (MA_{Kaolin}), greater fibrin formation (MA_{Fibrin}) and increased sensitivity to ADP (MA_{ADP}).
- Preliminary data shows diabetic platelets do not express more receptors for $P2Y_1$, $P2Y_{12}$ and TP thus, greater ADP sensitivity might indicate increased signalling through these receptors.

References: 1. Pretorius L, Thomson GJA, Adams RCM, Nell TA, Laubscher WA, Pretorius E. Platelet activity and hypercoagulation in type 2 diabetes. Cardiovasc Diabetol. 2018 Nov 2;17(1):141. 2. Offermanns S. Activation of platelet function through G protein-coupled receptors. Circ Res. 2006 Dec 8;99(12):1293–304.

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