A PRELIMINARY STUDY ON PLATELET REACTIVITY IN NORMOTENSIVE SUBJECTS WITH A FAMILY HISTORY OF HYPERTENSION

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INTRODUCTION

- Primary or "essential" hypertension accounts for 90-95% of hypertension worldwide [1].
- Physiologically, the endothelium plays an important role in vascular hemostasis, such as the capacity as a vasodilator and **antithrombotic** [2].

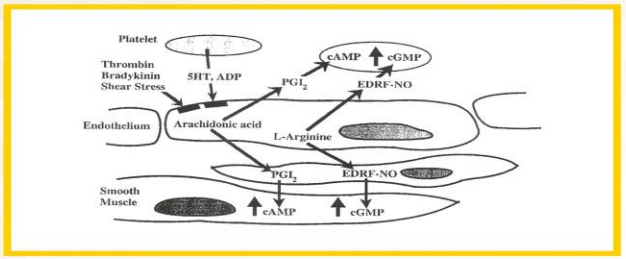

Figure 1. Endothelial cells as thromboregulator [3]

- **Endothelial dysfunction** (ED) is associated with a proinflammatory phenotype, increased oxidative stress, and abnormal modulation of vasoactive pathways, which may lead to impaired endothelium-dependent vasodilation and **thrombotic-prone** [4].
- "The **thrombotic paradox**" means that hypertensive patients have a greater risk to develop thrombosis than to get bleeding [5].
- Normotensive subjects with a family history of hypertension (FHoH) have structural and functional changes in the cardiovascular (CV) system -- > preclinical CV disease state [6].

HYPOTHESIS

- If normotensives subjects with a family history of hypertension already have endothelial dysfunction, thus they will have exaggerated platelets aggregation.

METHODS

- A quasi-experimental, ex vivo, human study.
- Purposive sampling: 20 undergraduate normotensive students from Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta, who comprises of 10 students with an FHoH and other 10 students without an FHoH.
- Normotensive defined as having blood pressure ≤ 140/80 mm Hg measured in sitting position using a non-invasive, oscillometric method, automatic vital sign monitor device TM-2551 P (A & D Co. Ltd., Tokyo, Japan) from the brachial artery of the subjects' dominant hand.
- An FHoH was defined as having mother, father, or both with high blood pressure (systolic blood pressure {SBP} ≥ 140 mm Hg or and diastolic blood pressure {DBP} ≥ 90 mm Hg) based on a self-reported questionnaire.
- The percentage of maximal platelets aggregation in response to adenosine diphosphate (ADP) was measured using the turbidimetric method (Helena Lab.).

RESULTS

Table 1. Group comparison of subjects' characteristics

Characteristics	Normotensive without a FHoH (n = 10)	Normotensive with a FHoH (n = 10)	*P* value
Gender proportion (F:M)	1:1	1:1	-
Age (years)	20,3 ± 1,42	19,8 ± 1,23	0.41
Body mass index (kg/m²)	21,72 ± 1,23	20,36 ± 2,39	0.28
Systolic blood pressure (mmHg)	112 ± 9,49	113,2 ± 7,91	0.76
Diastolic blood pressure (mmHg)	71 ± 5,05	71,6 ± 7,81	0.84
Heart rate (times/minute)	87,7 ± 7,21	82,5 ± 14,79	0.33
Platelets count (10^3/mm³)	326,5 ± 47,92	309,7 ± 57,55	0.49

Note: FHoH = family history of hypertension. F = female. M = male. Data are summarized as a mean ± standard deviation, except for gender proportion.

Table 2. Group comparison of maximal platelets aggregation

Agonist	Normotensive without a FHoH (n = 10)	Normotensive with a FHoH (n = 10)	*p* value
ADP 2 µM	27,56 ± 31	14,74 ± 31,14	0.99
ADP 5 µM	24 ± 64,76	21,97 ± 65,43	0.95
ADP 10 µM	15,47 ± 81,4	10,7 ± 83	0.79

Note: FHoH = family history of hypertension; ADP = adenosine 5'-diphosphate. Maximal platelets aggregation was measured as a percentage (%). Data are summarized as a mean ± standard deviation.

Table 3. Group comparison of the level of maximal platelet aggregation

Agonist	Classification	Normotensive without a FHoH (n = 10)	Normotensive with a FHoH (n = 10)	Nilai *p*
ADP 2 µM	Hypo aggregation	3	2	0.23
	Normal aggregation	5	8	
	Hyper aggregation	2	0	
ADP 5 µM	Hypo aggregation	2	1	0.36
	Normal aggregation	2	5	
	Hyper aggregation	6	4	
ADP 10 µM	Hypo aggregation	1	1	0.87
	Normal aggregation	2	3	
	Hyper aggregation	7	6	

Note: FHoH = family history of hypertension; ADP = adenosine 5'-diphosphate

DISCUSSION

- This study showed that late adolescence-early young adult normotensive subjects with an FHoH have no heightened platelets aggregation in response to different doses of ADP as compared to their counterparts without an FHoH (Table 2 & Table 3).
- ED has been confirmed existed in normotensive subjects with FHoH [7-9].
- The previous study showed that platelet aggregation induced by ADP was significantly higher in men with an FHoH as compared to men without an FHoH, taking low cholesterol and low salt diet [10].
- Akbar [11] reported that platelets from spontaneously hypertensive rats (SHR) had greater platelets aggregation in response to thrombin and prostaglandin E_1 (PGE_1) but lesser platelets aggregation in response to ADP as compared to Wistar-Kyoto (WKY) rats.

CONCLUSION

- Because the exaggerated platelets reactivity is not found, endothelial dysfunction may not occur yet in our human model of prehypertension, i.e. normotensive subjects with family history of hypertension.
- However, the temporary conclusion inducted by this preliminary study needs further investigation.
  - Platelets aggregation in normotensives subjects with a family history of hypertension can be measured after endothelial cells are activated or stimulated.
  - Different platelets agonists can be used, such as ADP, thrombin, thromboxane, and epinephrine, which act through G protein-coupled receptors (GPCR), and collagen, which acts through tyrosine kinase [12].

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