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LETTER TO THE EDITOR

PLATELET AGGREGATION PATTERNS IN NORMOTENSIVE AND HYPERTENSIVE SUBJECTS

Sir,

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There is considerable evidence from animal experiments and clinical observations that platelets have an important influence on the atherosclerotic and thrombotic complications associated with hypertension (1). Although there have been few reports on platelet hyperactivity in hypertension (2), data on Indian population is lacking. Therefore, the present study was planned to investigate platelet aggregation patterns in normotensives and untreated hypertensives.

The study was conducted in the Departments of Pharmacology and Medicine, Lady Hardinge Medical College and associated Hospitals and Department of Biochemistry, GB Pant Hospital, New Delhi. Group A comprised of 25 normotensives (blood pressure, BP<140/90 mm Hg). Group B comprised of 25 patients attending the medical OPD who were freshly diagnosed as suffering from primary hypertension (BP ≥ 140/90 mm Hg) according to WHO guidelines 1999 (3). Both groups comprised of male and female subjects in the age group of 30–60 years. Written, informed and valid consent was taken from each subject. Exclusion criteria were bleeding disorders, liver disease, renal disease, patients on oral anticoagulants and non-steroidal anti-inflammatory drugs (NSAIDs), diabetes mellitus, chronic diarrhoea, malabsorption syndrome, chronic alcoholism, smoking, pregnancy, women on oral contraceptives, severe hypertension (BP > 180/110 mm Hg), coronary artery disease, history of myocardial infarction, cerebrovascular accident. The study was approved by the institutional ethical committee.

Following baseline investigations were performed in all subjects: Fasting blood glucose, liver function tests, kidney function tests, complete blood counts and electrocardiogram (standard 12 leads). BP was measured in supine position by mercury sphygmomanometer after making the subject rest for 15 minutes. Mean BP was calculated as diastolic BP plus one-third of the pulse pressure.

Platelet aggregability was determined on a chronolog automatic platelet aggregometer (Model 560–CA, Chronolog Corporation, Havertown, USA). Platelet aggregation test was carried out following Born's method (4). After an overnight fast, 4.5 ml of venous blood was collected from the antecubital vein with minimal venous occlusion and mixed with 0.5 ml of 3.8% trisodium citrate in a plastic tube. Platelet rich plasma (PRP) was prepared by centrifuging this citrated sample at 200 g for 10 min at room temperature. The PRP was carefully removed and the remaining blood was centrifuged at 2000 g for 10 min to obtain platelet poor plasma (PPP). The transmittance of incident light in PRP, relative to PPP (blank) was

recorded. The aggregation was recorded with 2 standard agonists : adenosine diphosphate (ADP)-10 µM (Sigma Chemical Co., USA) and epinephrine-2 µM (Sigma Chemical Co., USA). On adding the agonist to PRP, the formation of increasingly large platelet aggregates resulted in a decrease in absorbance of light. The percentage fall in absorbance was measured upto 5 min after the addition of an agonist. This change in transmittance was recorded as an index of platelet aggregation. Results are presented as mean ± standard error. Student's *t*-test (unpaired) was used for comparison of data. P value <0.05 was regarded as statistically significant.

Table I shows the biophysical characteristics, BP and platelet function status of the 2 study groups. The systolic, diastolic and mean BP in the hypertensive group ranged from 146–180, 96–110 and 114–137.33 mm Hg respectively. Platelet aggregability was significantly higher in group B as compared to group A (P<0.001). The mean ADP induced aggregation was 63.42% in hypertensive group and 46.05% in normotensive group while epinephrine induced aggregation was 59.42% in the hypertensive group and 40.08% in the normotensive group.

The above observations suggest a significant difference in platelet aggregation between normotensives and hypertensives indicating that patients with hypertension have a state of platelet hyperactivity as compared to normal subjects. Our findings are in concordance with studies that have demonstrated hyperfunction of platelets in established essential hypertension with or without vascular complications. Craveri and co-workers (2) showed a significant difference between the aggregation curves of the hypertensive and the healthy subject with excessive platelet aggregation in those suffering from uncomplicated arterial hypertension.

TABLE I: Biophysical characteristics, BP and platelet function status of the 2 study groups.

Parameter	*Normotensives (n = 25) Mean ± SEM*	*Hypertensives (n = 25) Mean ± SEM*
Age (years)	48.2±2.1	49.4±1.8
Sex (Males/Females)	15/10	13/12
Haemoglobin (g%)	14.6±0.8	13.9±0.9
TLC (per cu. mm)	$7.1\pm1.2\times10^3$	$6.6\pm1.8\times10^3$
Heart rate (per minute)	80±1.2	78±2.2
Blood Pressure (mmHg)		
Systolic BP	118.2±1.4	154.8±1.7
Diastolic BP	78.4±1.1	102.8±1.1
Mean BP	91.6±1.2	120.0±1.2
Platelet count (per cu. mm)	$280\pm15\times10^3$	$243\pm19\times10^3$
Percentage platelet aggregation		
ADP (10 µM)	46.05±1.6	63.4±1.8***
Epinephrine (2 µM)	40.08±1.40	59.4±1.12***

***P value <0.001 (unpaired Student's *t* test), ADP-adenosine diphosphate

Increased platelet aggregation is attributed to impaired endothelial function in hypertension. It has been suggested that disturbed endothelial function could be present early in arterial hypertension. The endothelium is in a strategic position within the blood vessel wall, located between the circulating blood and vascular smooth muscles. It plays a protective role against raised BP by basal formation of nitric oxide (NO) and prostacyclin (5). NO possesses antiatherogenic and thrombo-resistant properties by preventing platelet aggregation and adhesion. Plasma levels of NO are reduced in patients with essential hypertension (6). Biosynthesis of prostacyclin, which is a vasodilator, a natriuretic and a potent inhibitor of platelet aggregation, is also impaired in hypertensives (7).

Drugs that reduce platelet aggregation such as aspirin, has a significant protective effect in secondary prevention of cardiovascular diseases. It is now established that antiplatelet therapy reduces the risk of vascular death by about one-sixth and risk of non-fatal myocardial infarction and stroke by one-third (8). Antiplatelet therapy with low-dose aspirin reduced primary cardiovascular events in patients with essential hypertension as demonstrated in Hypertension Optimal Treatment (HOT) study (9).

The results of our study show that there is a state of platelet hyperaggregability in hypertensive patients in Indian population. Thus, it may be concluded that in addition to good control BP, therapeutic approaches to decrease the tendency of platelets to aggregate may ultimately improve the prognosis in hypertensive patients. Therefore, the goal of antihypertensive therapy should be not only to decrease the elevated BP but also to bring down the hyper-aggregable state of platelets to a normal state. Further, it is also suggested that antiplatelet action of existing antihypertensive drugs should be investigated and those agents which decrease platelet hyper-aggregation should be preferred over others to avoid thrombotic complications.

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