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Physiology

PLATELET MORPHOLOGY IN DIABETICS & NORMAL HEALTHY ELDERLY INDIVIDUALS

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ABSTRACT

BACKGROUND: Diabetic mellitus is considered to be a prothrombotic state with chronic platelet activation, activation of the coagulation system & decreased fibrinolytic potential. A number of studies performed during the past decades have documented several different platelet function alternations in patients with DM.

OBJECTIVE: This study is performed to assess the platelets morphology in control & diabetics.

MATERIALS & METHODS: This study is performed in Alluri Sita Rama Raju academy of medical sciences (ASRAM), Eluru. Platelet count was performed by REES-ECKER method in dept of physiology, ASRAM. Platelet morphology is performed through Thyrocare. Height and weight were measured with the subject in light clothes without shoes and body mass index (BMI) (kg/m2) was calculated. Statistical analysis was done by Microsoft office 2010. Predefined inclusion and exclusion criteria were set for selection of the study group.

RESULTS: We evaluated totally of 60 male persons. The average considered is between 50-60years. We obtained statistically significant results. There is a significant increase in fasting blood glucose, platelet distribution width, mean platelet volume & platelet count in study group people as compared with control.

CONCLUSION: Factors that contribute directly to greater platelet reactivity include metabolic abnormalities such as hyperglycemia and hyperlipidemia, both insulin resistance (relative insulin deficiency) and absolute insulin deficiency, as well as associated conditions such as oxidative stress, inflammation, and endothelial dysfunction. Change in platelet structure & volume is observed in diabetes mellitus people. Platelet structure & volume should be monitored frequently & proper care should be taken.

KEYWORDS : Fasting Blood Glucose (FBG), Platelet Distribution Width (PDW), Mean Platelet Volume (MPV), Platelet Count (PC), Diabetis mellitus (DM).

INTRODUCTION:

Hyperglycemia is the diagnostic hallmark finding in diabetes mellitus and is associated with macrovascular disease even in the prediabetic stage. Hyperglycemia, particularly postprandial, plays a significant role in the DM-associated development of cardiovascular disease as well as the DM prothrombotic state[1-2] Exposure of platelets to hyperosmolar solutions also causes increased reactivity, suggesting that hyperglycemia may have a direct osmotic effect[3]. Both chronic and acute hyperglycemia causes in vivo activation of protein kinase C (PKC), a transduction pathway mediator for many pro-aggregatory platelet agonists[4].

Advanced glycation end products (AGEs) cause externalization of platelet membrane phosphatidylserine that leads to surface clotting factor activation and so directly enhance the thrombogenic state[5]. Similarly, the platelets of patients with diabetes have increased glycation levels of surface membrane proteins which cause decreased membrane fluidity and increased platelet sensitivity to agonists[6-7]. Insulin can directly regulate platelet function via a functional insulin receptor (IR) found on human platelets[8]. The effects of hyperinsulinemia on platelets, however, are complex and disparate between normal individuals and patients with insulin resistance. In vitro experiments using platelets from healthy nonobese individuals reveal that binding of insulin to its receptor causes magnesium to translocate into the platelet and is associated with decreased thrombin-induced platelet aggregation and reduced production of proaggregatory thromboxane B2[9]. Binding of insulin to the IR leads to activation of the insulin receptor substrate 1 (IRS-1) through tyrosine phosphorylation which initiates association with the $G_i\alpha$-subunit. The result is reduced $G_i$activity that impairs tonic cAMP suppression, and thus leads to increased cAMP intraplatelet levels, blunting of P2Y12 signaling and reduced platelet activity[10-11].

MATERIALS & METHODS:

This study was conducted at ASRAM Hospital, Eluru in Central Lab. 30 persons were considered in each group. Totally, study was conducted on 60 males and having age 50–60 years.

In this study we compared serum blood glucose levels at early morning before breakfast in control & study group men. Mean platelet volume, platelet distribution width & platelet count tests were performed in study & control group men.

We excluded diabetic, obese and any chronic disordered women. Height and weight were with the subject in light clothes without shoes and Body Mass Index (BMI) was calculated kg/m2.

The considered subjects were interviewed and basic history was taken into consideration. The subjects were given proper precautions and self-consent form was taken before drawing blood.

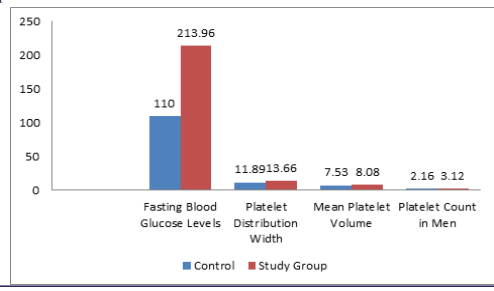
RESULTS

We evaluated totally of 60 male persons. The average considered is between 50-60 years. We obtained statistically significant results. In control, the fasting blood sugar levels are within normal limits. We considered study group people based on their fasting blood sugar levels. If the fasting blood sugar levels exceed 250mg/dl, we excluded them. There is a significant increase in fasting blood glucose levels, platelet distribution width, mean platelet volume & platelet count in study group people as compared with control.

Table- 1

S. NO	VARIABLE	Control MEAN±STDEV	Study Group MEAN±STDEV	"p" VALUE
1	Fasting Blood Glucose Levels	110±5.65*	213.96±41.33*	0.05*
2	Platelet Distribution Width	11.89±0.53*	13.66±1.38*	0.05*
3	Mean Platelet Volume	7.53±0.34*	8.08±0.43*	0.05*
4	Platelet Count in Men	2.16±0.22*	3.21±0.41*	0.05*

Graph -1



DISCUSSION

Platelets from subjects with diabetes exhibit increased reactivity. Diabetes is associated with systemic inflammation and oxidative stress that may contribute to increased platelet reactivity. Superoxide has been shown to increase platelet reactivity[12]. Insulin antagonizes the effect of platelet agonists such as collagen, ADP, epinephrine, and platelet-activating factor[13]. This antagonism is mediated by activation of an inhibitory G protein by insulin receptor substrate (IRS)-1[14]. Hyperglycemia can increase platelet reactivity by inducing nonenzymatic glycation of proteins on the surface of the platelet. Such glycation decreases membrane fluidity and increases the propensity of platelets to activate[15]. Osmotic effect of glucose is a second mechanism by which hyperglycemia can increase platelet reactivity[16]. We found that brief exposure of platelets in vitro to hyperglycemia or a similar concentration of mannitol increased their reactivity. Activation of protein kinase C is a third mechanism by which hyperglycemia can increase platelet reactivity. Protein kinase C is an essential mediator of platelet activation[17].

A large body of evidence from animal models and patient studies indicates that redox stress plays a major role in the pathogenesis of vascular complications of diabetes. There is convincing evidence linking decreased vascular NO production coupled with the overproduction of reactive oxygen species (ROS) and the generation of potent oxidants such as peroxynitrite ($ONOO^-$) to altered platelet function. Although the regulation of a platelet NOS is currently controversial, insulin-induced cyclic GMP production in platelets from subjects with diabetes is reported to be attenuated, and agonist-induced platelet aggregation becomes insensitive to NOS inhibitors[18]. The generation of ROS in diabetes may either lead to or result from platelet activation, suggesting that oxidative stress and platelet activation may be closely interrelated. Indeed, superoxide anions and hydrogen peroxide, which are both reported to play an important role in platelet activation, are continuously produced in these cells, and diabetes is associated with reduced platelet antioxidant levels[19]. High concentration of ROS can modify platelet function in different ways; e.g., hydrogen peroxide elevates protein tyrosine phosphorylation by activating Bruton's tyrosine kinase, the Janus kinases, and the SRC family tyrosine kinases[20-21]. The results of a recent clinical study revealed that platelet responsiveness to the nitrovasodilator sodium nitroprusside was increased by insulin administration to patients with acute coronary syndrome, which is an insulin-resistant state[22]. Despite the proven benefits of insulin, optimal protection against the cardiovascular complications of diabetes has been obtained when insulin was used in combination with oral antidiabetes drugs, such as the thiazolidinediones and biguanides[23].

CONCLUSION

Diabetes is associated with increased platelet reactivity. Factors that contribute directly to greater platelet reactivity include metabolic abnormalities such as hyperglycemia and hyperlipidemia, both insulin resistance (relative insulin deficiency) and absolute insulin deficiency, as well as associated conditions such as oxidative stress, inflammation, and endothelial dysfunction. Although antiplatelet therapy is necessary to suppress increased platelet reactivity, control of hyperglycemia with regimens that decrease insulin resistance and prevent apoptosis of pancreatic β-cells should decrease platelet reactivity and enhance the efficacy of antiplatelet therapy by addressing root causes of increased reactivity. Change in platelet structure & volume is observed in diabetes mellitus people. Platelet structure & volume should be monitored frequently & proper care should be taken.

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