EFFECT OF FREQUENCY OF DIALYSIS ON PLATELET AGGREGATION

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BY

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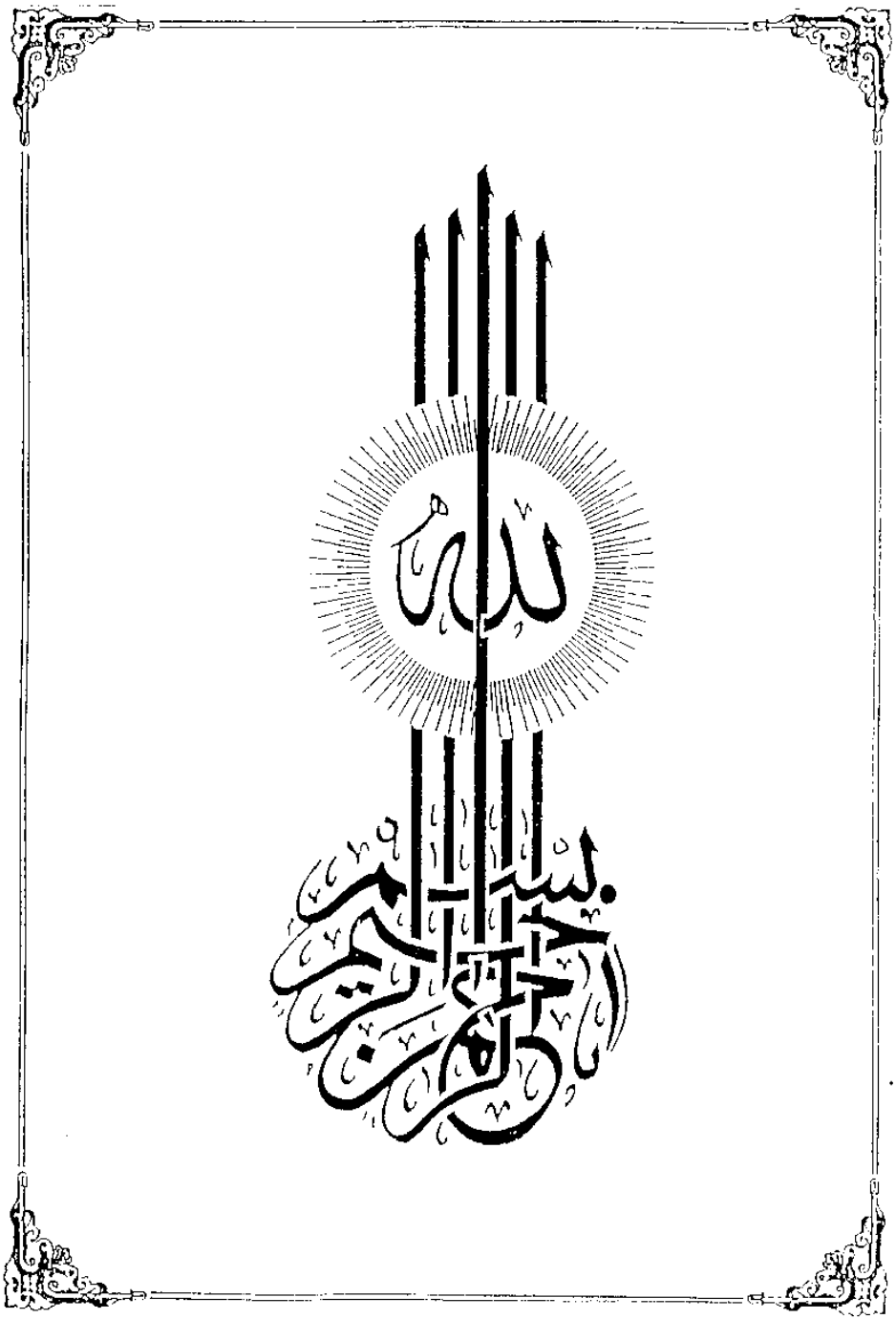

TO MY WIFE

ACKNOWLEDGMENT

THANKS TO GOD

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INTRODUCTION

AND

AIM OF THE WORK

INTRODUCTION AND AIM OF THE WORK

* *Introduction :*

Bleeding frequently complicates chronic renal failure, it can be reduced or aggravated by dialysis (Jubelirer, 1985).

The usual frequency of hemodialysis sessions abroad is thrice weekly; each dialysis lasting 4 hours. It is thought by some physicians in Egypt that a predominatly twice weekly dialysis regimen, each dialysis lasting 6 hours would be almost equally good and save money.

However several problems resulting from inadequate dialysis were observed among patients on twice weekly dialysis. Platelet functions are known to be affected badly in uremia; and this usually leads to bleeding tendency among uremic patients.

Recent report showed that the improvement of platelet functions is complete with adequate dialysis; and only partial with inadequate dialysis (Lindsay et al., 1978).

* *Aim of the work :*

To study the effect of the optimum frequency of dialysis (thrice weekly); versus the effect of twice weekly dialysis on platelet aggregation and bleeding tendency.

REVIEW OF LITRATURE

BLEEDING TENDENCIES AND PLATELET DYSFUNCTIONS IN UREMIA

Bleeding frequently complicates chronic renal failure : it can be reduced or aggravated by dialysis. The most common abnormalities are defective platelet aggregation, decreased platelet adhesiveness, decreased platelet factor-3 availability, and prolongation of the bleeding time. Among the above platelet function tests, the bleeding time is the single test that most closely correlates with clinical bleeding (Jubelirer, 1985).

The nature of platelet defect in uremia is still not well understood the pathophysiologic mechanisms which have been implicated include platelet inhibition by plasma metabolites, e.g. urea, phenolic acid, guanidinosuccinic acid, increased vessel wall prostacyclin, abnormal platelet arachidonic acid metabolism, increased level of parathyroid Hormone (P.T.H), defective binding of Factor VIII complex to platelet or defective binding of platelets to vessel wall subendothelium by Factor VIII complex, decreased platelet vessel wall interaction due to severe anemia, platelet storage pool deficiency, and/or defective fibrinogen binding to platelets (Jubelirer, 1985).

* *Uremic Toxins and Platelets :*

The abnormal biochemical environments of renal failure could be one of the causes of defective platelet quality which is responsible for bleeding disorder in uremia (Castaldi, P.A., et al., 1966).

It was found that many dialyzable toxins are responsible for altering the function of normal platelets as urea, creatinine, methyl guanidine, phenol and phenolic acid and guanidino succinic acid (Herbert, I. Horowitz, 1970).

The average guanidino succinic acid in the serum of uremic patients was found to be 2.53 mgm% at this high level, it accounts for a number of the in vitro abnormalities of uremic platelet function and A.D.P. induced aggregation (Herbert, I. Horowitz, 1970).

Also in a study of human platelet aggregation induced by ADP after incubation with urea, methyl guanidine, creatinine and oxalic acid, oxalic acid significantly inhibits human platelet aggregation (Camici-M, et al., 1986), urea, it-self, affects platelet aggregation and energy metabolism and may contribute directly to platelet abnormality (Johnson et al., 1975).

Although urea may adversely affect platelet function alone, it cannot be responsible for the platelet abnormality in uremia. Also, creatinine, methyl guandine, quanidino

succinic acid, phenols, and phenolic acids in the abnormal concentrations present in patients with uremia can affect platelet function by different mechanisms (Rabiner, 1972).

The impaired glucose utilization caused by there uremic toxins may contribute to the pathogenesis of bleeding in chronic renal failure by affecting platelet function (Tison et al., 1981).

In uremia, the platelet do not function properly, there is reduction of platelet adhesiveness and retention in glass bead columns and also both platelet aggregation and disaggregation with ADP and thrombin are slower and less complete than normal (Evans et al., 1972).

Biochemically, this inhibition of platelet aggregation is related to increased cellular cyclic A.M.P. levels which is due to increased adenyl cyclase levels in the platelets with renal insufficiency. This implies that the toxins activate adenyl cyclase directly, as there toxins appear to be peptide hormones, or perhaps in conjugation with one or more hormones as modulators which include prostaglandin E_1 and prostaglandin E_2, thus, stimulating the production of cyclic A.M.P. within the cell (Volchoyannis and Schoeppe, 1982).

To further define the effect of uremic toxins on platelets leading to platelet abnormality responsible for

uremic bleeding, it is found that uremic patients had considerable inhibition in several peaks of middle molecular range but that finding was inconsistant and not clearly related to the degree of uremia.

Thus, it is impossible to identify accurately the many possible uremic retention products or uremic toxins that could cause uremic bleeding (Basiliniski N. et al., 1985).

* *Platelet Factor 3 in Uremia :*

Platelet factor 3 is a lipoprotein component of the platelet membrane which becomes available to the coagulant enzymes and Co. factors of plasma following platelet aggregation or platelet Trauma. The active component is the phospholipid mostly which catalyst (Marcus et al., 1966).

Platelet factor 3 is essential for the conversion of prothrombin to thrombin by the intrinsic mechanism of blood coagulation (Rabiner, 1972). It is found that some metabolites in uremic plasma inactivate platelet factor 3 of the circulating platelets.

Thus, the uremic platelets had reduced platelet factor 3 activity, there should be some relationship between the severity of uremia and platelet thromboplastic factor deficiency. The exact cause of this abnormality is not well known (Rabiner, 1972).

As regards coagulation factors in chronic uremia, it has

been found in patients with conservatively treated chronic uremia that there is insignificantly abnormal concentrations of factor XIII and significantly lower values of plasminogen activators. This could be another good reason for abnormal haemostasis in chronic uremia (Panicucei-F et al., 1983).

* *Blood Vessel and Platelets in Uremia :*

It was also found that the subendothelial surface covered by platelets was significantly decreased in experiments with uremic whole blood when compared to normal control. The interaction of platelets with subendothelium was also decreased when perfusions were carried out with platelet-plasma mixtures contains either normal washed platelets or uremic washed platelets. This shows an impaired platelet adhesion caused by platelet and plasmatic abnormality (Castillo-R et al., 1985).

So,there is a defective platelet adhesion to subendothelium in uremic patients, caused by platelet and plasmatic alterations that are influenced by low hematocrit (Castillo-R et al., 1986).

Another factor related to vessel wall endothelium is prostacyclin ($PG-I_2$), a recently discovered hormone, which is generated from prostaglandin endoperoxides by vessel wall endothelium, particularly in the lungs, and also in the kidneys. It is the most potent inhibitor of platelet aggregation so described (Yalikorkala et al., 1982).