

Effect of Dialysis on Bleeding Time in Chronic Renal Failure

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SUMMARY

Renal failure is associated with severe hemorrhagic complications. Platelets play an important role in coagulation and their dysfunction may be responsible for the bleeding tendency in these patients. 60 patients with advanced renal failure were investigated for bleeding tendency due to platelet dysfunction. The pre-dialysis platelet count was 46 to 325×10⁹/L (mean 166×10⁹/L). Pos-dialysis platelet count was 60 to 310×10⁹/L (mean 172×10⁹/L). Pre-dialysis mean bleeding time (BT) was 4.95±0.27 minutes (range 1.30 to 20 minutes). Thirty three patients (55%) had prolonged BT before dialysis. Mean BT in all patients after dialysis was 2.46±0.24 minutes (range 1.15 to 10 minutes). BT was corrected in 27 (81.8 %) out of 33 patients with prolonged BT before dialysis. In 6 patients (10 %) it remained prolonged. This improvement in BT after dialysis was statistically significant (p value < 0.001). Both peritoneal and hemodialysis resulted in significant improvement in bleeding time.

INTRODUCTION

Severe hemorrhagic complications in the course of uremia due to renal failure have long been reported¹. The advent of dialysis has definitely lowered the incidence of the most severe hemorrhagic event, but bleeding still remains a major problem for uremic patients especially while undergoing surgery or invasive procedures^{2,3}.

Quantitative and qualitative defects of platelets were suggested on the basis of prolonged bleeding time and other investigations. Bleeding time is the test that provides an overall measure of the primary hemostatic plug formation and is now generally accepted as the best laboratory parameter of clinical bleeding.

This study was designed to find out the incidence of prolonged bleeding time in patients with chronic renal failure, the effect of dialysis on prolonged bleeding time and to compare the effect of two methods of dialysis.

MATERIALS AND METHODS

A total of sixty (60) patients were included in the study irrespective of age, sex or ethnic group. All

these patients were suffering from advanced renal failure. Half of them underwent acute peritoneal dialysis and the other half were getting regular hemodialysis. The diagnosis of advanced renal failure was confirmed by clinical and laboratory parameters. Platelet counts and bleeding time were done before the dialysis was started and 6 hours after the dialysis was stopped to allow time for disappearance of action of heparin given during dialysis. Bleeding time was done by Duke's method. Normal range by this method is 1-3½ minutes. Value of 04 minutes or above was considered abnormal.

RESULTS

Total sixty patients are included in this study. Forty four patients were male and 16 were females. Their age varied from 15 to 68 years. Table 1 shows causes of renal failure in these patients. Hypertension, diabetes mellitus and chronic glomerulonephritis were leading causes of renal failure.

The incidence of bleeding from different sites in these patients is depicted in Table 2. Hematuria and epistaxis were seen most commonly. Each of these symptoms was present in 11 patients. Other

symptoms related to bleeding diathesis were bleeding from gums in 7, rectal bleeding in 3, hemoptysis in 2, hematemesis in 2 and skin bleeding in one patient. Hematuria could have been due to underlying primary renal pathology in some patients.

Table 1:

Diagnosis	Patients number	Percentage
Hypertension	16	26.7
Diabetes Mellitus	13	21.7
Chronic Glomerulonephritis	08	13.3
Obstructive Nephropathy	05	08.3
Toxic Nephropathy	04	06.7
Polycystic Kidneys	02	03.3
Amyloidosis	02	03.3
Toxic Nephropathy	01	01.7
Kidney transplant rejection	01	01.7
Unknown Etiology	08	13.3

Table 2:

Symptom	No. of patients	Percentage
Epistaxis	11	18.3
Hematuria	11	18.3
Gum bleeding	07	11.7
Rectal bleeding	03	05.0
Hemoptysis	02	03.3
Hematemesis	02	03.3
Purpura	01	01.7

Pre-dialysis platelet count was 46 to $325 \times 10^9/L$ (mean $166 \times 10^9/L$). Post-dialysis count was 60 to $360 \times 10^9/L$ (mean $172 \times 10^9/L$) which was not statistically different from pre-dialysis count.

33 patient out of 60 (66.7%) showed abnormally prolonged bleeding time before dialysis. 20 out of 30 who underwent peritoneal dialysis and 13 out of 30 (43.2 %) who had hemodialysis showed prolonged BT. After dialysis BT improved. Only 6 (10 %) showed prolonged BT (Table 3). 16 out of 20 (80%) patients in peritoneal dialysis group and 11 out of 13 (84.6 %) patients with prolonged BT in hemodialysis group showed improvement in BT after dialysis (P value < 0.001). Mean BT was 4.95 ± 0.27 before dialysis. Post-dialysis BT improved to 2.46 ± 0.24 minutes (P value < 0.001). Effect of two types of dialysis on BT are shown in table 4. In peritoneal dialysis group pre and post-dialysis mean BT was

5.78 ± 0.81 and 2.43 ± 0.18 respectively (P < 0.001). Similarly in hemodialysis group pre and post-dialysis mean BT was 4.12 ± 0.39 and $2.5 \pm$ respectively (P < 0.001). Pre-dialysis BT was lower in the hemodialysis group as these patients were getting regular hemodialysis and were not severely uremic. On the other hand patients in peritoneal dialysis group had dialysis first time and they were more uremic at the time of dialysis.

Table 3: Incidence of Prolonged bleeding time before and after dialysis.

Method of Dialysis	Pre-dialysis		Post-dialysis		P Value
	Patients	Percent	Patients	Percent	
Peritoneal Dialysis (n=30)	20	66.7	4	13.3	< 0.01
Hemodialysis (n=30)	13	43.3	2	06.7	< 0.01
Total (60)	33	55.0	6	10.0	< 0.01

Table 4: Effect of dialysis on mean bleeding time and comparison of two methods.

Method	Pre-dialysis		Post-dialysis		P Value
	Mean	SEM	Mean	SEM	
Peritoneal Dialysis (n=30)	5.78	0.81	2.43	0.18	< 0.001
Hemodialysis (n=30)	4.12	0.39	2.50	0.30	< 0.001
P Value	< 0.05	NS			

DISCUSSION

Prolonged bleeding time is a frequent finding in patients of chronic renal failure. In uremic patients there is impairment of platelet function which are based upon the availability of storage pool and the platelet phospholipid⁴.

Aggregation studies using various aggregating agents have demonstrated such defects in platelet aggregation⁵. There is evidence that impaired vessel wall and platelet interaction mediated by prostacyclin and Von Willibrand factor (VWF) is an important defect responsible for bleeding tendencies in uremic patients^{6,7}. Aggregation studies using various aggregating agents have demonstrated

defects in platelet aggregation⁵. Decreased sensitivity of platelets to the aggregating agents like adenosine phosphate, epinephrine and collagen has been confirmed in vitro⁸. Platelet factor-3 availability is also abnormal in chronic renal failure^{9,10}. Some dialyzable compounds like guanidino-succinic acid, phenol and several other hydroxy phenolacetic acids have been implicated in various hematological abnormalities in renal failure^{11,12}.

With frequent dialysis platelet abnormality can be corrected and normal hemostasis maintained, suggesting that the observed defects are due to inhibition of platelet function by retained metabolites

None of our patients had thrombocytopenia severe enough to cause hemorrhagic complications. Mild thrombocytopenia was noticed in 3 out of 12 patients (25 %) by Lewis et al¹, in 8 out of 33 patients by Cheney et al (1962)¹³ and in 3 out of 29 patients with uremia by Evans et al¹⁴. Nency et al (1979)⁵, Ivanovich et al (1983)¹⁵, Mannucci et al¹⁶ (1983)¹⁶ and Bloomm et al(1986)¹⁷ reported normal platelet count in uremic patients.

Bleeding time was prolonged in 55 % of our patients and was corrected with hemodialysis in 81.8 % and in 80 % with peritoneal dialysis. Our findings are in agreement with most of the reports in literature^{7,13,11,18,19}

CONCLUSION

- The study shows that the incidence of prolonged bleeding time in chronic renal failure is 55 %.
- Significant decrease was observed in the bleeding time after dialysis.
- Statistical analysis shows that both techniques of dialysis i.e hemodialysis and peritoneal dialysis have nearly the same efficacy.

REFERENCES

1. **Eknoyan G, Wacksman SJ, Glueck HI, Will JJ.** Platelet dysfunction in renal failure. *N Engl J Med* 1969; **280**: 677-81.
2. **Janson PA, Jubelirer SJ, Weinstein MJ, Deykin D.** Treatment of the bleeding tendency in uraemia with cryoprecipitate. *N Engl J Med* 1980; **303**: 1318-22.
3. **Smith MC, Dunn MJ.** IMPaired platelet thromboxane production in renal failure. *Nephron* 1981; **29**: 133-7
4. **Lewis JH, Zucker MB, Ferguson JH.** Bleeding tendency in uraemia. *Blood* 1956; **11**: 1073-6.
5. **Nenci GG, Berrettini M, Agnelli G, Paise P, Buoncrisiani U, Ballatori E.** Effect of peritoneal

- dialysis, hemodialysis and kidney transplantation on platelet function. *Nephron* 1979; **23**: 287-92.
6. **Kazatchkine M, Sultan Y, Caen JP, Bariety J.** Bleeding in renal failure: a possible cause. *Br Med J* 1976; **2**: 612-5
7. **Remuzzi G, Cavenaghi AE, Mecca G, Donati MB, Gaetano GD.** Prostacyclin like activity and bleeding in renal failure. *Lancet* 1977; **2**: 1195-7
8. **Minno GD, Martinez J, Makean ML, Rosa JD, Burke JF.** Platelet dysfunction in uraemia: multifaceted defect partially corrected by dialysis. *Am J Med* 1985; **79**: 552-9.
9. **Rabiner SF, Hrodec J.** Platelet factor-3 in normal subjects and patients with renal failure. *J Clin Invest* 1968; **47**: 901-12.
10. **Tison P, Kubisz P, Cernacek P, Dzuri KR.** Influence of inhibitor of glucose utilization on the platelet dysfunction. *Nephron* 1983; **33**: 253-6.
11. **Horowitz HI, Stein IM, Cohen BD, White JG.** Further studies on platelet inhibitory effect of guanidinosuccinic acid and its role in uraemic bleeding. *Am J Med* 1970; **49**: 336-15.
12. **Rabiner SF.** Bleeding abnormalities. In Massery SG, Sellers AL, Clinical aspects of uraemia and dialysis. Springfield: Charles C Thomas publisher, 1976; 179-84.
13. **Cheney K, Bonnin JA.** Haemorrhage, platelet dysfunction and other coagulation defects in uraemia. *Br J Haematol* 1962; **8**: 215-22.
14. **Evans EP, Branch RA, Bloom AL.** A clinical and experimental study of platelet function in chronic renal failure. *J Clin Pathol* 1972; **25**: 745-53.
15. **Ivanovich P, Kwaan CGX, Hathiwalla S.** Studies of coagulation and platelet function in heparin free hemodialysis. *Nephron* 1983; **33**: 116-20.
16. **Mannucci PM, Remuzzi G, Pusineri F, et al.** Deamino-8-D-arginine vasopressin shortens the bleeding time in uraemia. *N Engl J Med* 1983; **308**: 8-11.
17. **Bloom A, Greaves M, Preston FE, Brown B.** Evidence against a platelet cyclooxygenase defect in uraemic subjects on chronic hemodialysis. *Br J Haematol* 1986; **62**: 143-9.
18. **Hutton RA, Shea MJO.** Haemostatic mechanism in uraemia. *J Clin Pathol* 1968; **21**: 406-11.
19. **Harker LA, Slighter SJ.** The bleeding time as a screening test for evaluation of platelet function. *N Engl J Med* 1972; **287**: 155-59.

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