

Effect of dialysis on bleeding diathesis in uraemic patients

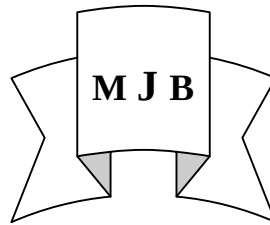
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**Abstract**

To compare the improvement in platelet count, bleeding time and clotting time immediately after and 24 hours after haemodialysis and peritoneal dialysis .

The effect of haemodialysis and peritoneal dialysis was studied in 50 patients with renal failure admitted to Merjan teaching Hospital between June 2004 to October 2004 ,platelet count , bleeding time and clotting time were studied before dialysis , immediately after and 24 hr. after dialysis .

A total number of 50 patients were studied , 29 patients treated with peritoneal dialysis and 21 patients treated with haemodialysis .

Mean percentage of improvement in platelet count in peritoneal dialysis was 2.1% immediately post dialysis and became 7.4 % 24 hr. post dialysis while the percentage of improvement in platelet count in haemodialysis was 7.1 % immediately post dialysis and became 25.4 % 24 hr. later.

Mean percentage of improvement in bleeding time immediately after peritoneal dialysis was 11.5 % and became 20.9% 24 hr. later, while the percentage of improvement in bleeding time immediately after haemodialysis was 13.1 % and became 30.6 % 24 hr. later .

Mean percentage of improvement in clotting time immediately after peritoneal dialysis was 9% and became 17% 24hr. later, while the percentage of improvement in clotting time immediately after haemodialysis was 11.6% and 24.3% 24 hr. later .

This improvement in platelet count, bleeding time and clotting time immediatly after and 24hr. after both peritoneal dialysis and haemodialysis was statistically significant but the results of haemodialysis were more significant when compared with the results of peritoneal dialysis .

الخلاصة

لمقارنة التحسن في عدد الأقرص الدموية وزمن النزف وزمن التخثر مباشرة بعد الديليزة وبعد 24 ساعة من الديليزة الدموية والبريتونية تأثير الديليزة الدموية والبريتونية قد درست على خمسين مريضا مصابين بعجز الكلى في مستشفى مرجان ادخلوا للفترة من الشهر السادس إلى الشهر العاشر سنة 2004 .

عدد الأقرص الدموية وزمن النزف وزمن التخثر قد درست قبل الديليزة ومباشرة بعد الديليزة و24 ساعة بعد الديليزة ولقد تمت الدراسة على خمسين مريضا منهم 29 مريضا عولجوا بالديليزة البريتونية و21 مريضا عولجوا بالديليزة الدموية

نسبة التحسن في عدد الأقرص الدموية للديليزة البريتونية كان 2,1 % مباشرة بعد الديليزة البريتونية واصبحت 7,4 % بعد 24 ساعة من الديليزة فيما كانت نسبة التحسن في عدد الأقرص الدموية للديليزة الدموية 7,1 % مباشرة بعد الديليزة واصبحت 25,4 % بعد 24 ساعة من الديليزة .

نسبة التحسن في زمن النزف للديليزة البريتونية كان 11,5 % مباشرة بعد الديليزة واصبحت 20,9 % بعد 24 ساعة من الديليزة بينما كانت نسبة التحسن في زمن النزف للديليزة الدموية 31,1 % مباشرة بعد الديليزة و 30,6 % بعد 24 ساعة من الديليزة

نسبة التحسن في زمن التخثر للديليزة البريتونية كان 9 % مباشرة بعد الديليزة واصبحت 17 % بعد 24 ساعة من الديليزة فيما كانت نسبة التحسن في زمن التخثر للديليزة الدموية 11,6 % مباشرة بعد الديليزة وأصبحت 24,3 % بعد 24 ساعة من الديليزة.

نسبة التحسن في عدد الأقرص الدموية وزمن النزف وزمن التخثر كان أفضل للديليزة الدموية منه للديليزة البريتونية كما إن نسبة التحسن كانت أفضل بعد 24 ساعة من الديليزة

Introduction

Chronic renal failure refers to an irreversible deterioration in renal function which classically develops over a period of years. Initially, it is manifested only as a biochemical abnormality, eventually loss of the excretory, metabolic and endocrine functions of the kidney leads to the development of the clinical symptoms and signs of renal failure which are referred to as uraemia[1].

Bleeding diathesis is important complication of advanced uraemia and has been considered more significant during recent years. The frequency of haemorrhagic disorder in renal failure appears to be related to the degree of uraemia, although the haemostatic defect in uraemia is often complex and may include thrombocytopenia and minor coagulation abnormalities, it is possible that platelet dysfunction is most consistent and a clinically important feature [2].

Disorder of coagulation and fibrinolysis have also aroused interest. There's decreased fibrinolytic activity and increased content of inhibitor of plasminogen activator were found to be common in conservatively treated patient with chronic uraemia [3].

As early as 1861; chemists applied the technique of dialysis to remove solute from the solution, indeed; the first solution used for dialysis in 1800s. was urine, from which urea could be extracted [4].

There are two types of dialysis peritoneal dialysis and haemodialysis. Patients selection for these two different forms of treatment is usually decided by special needs of the patient and the nephrologists clinical judgement of which treatment will be best tolerated, many patients who start peritoneal dialysis switch to haemodialysis before they finish a year of treatment [4].

The dialysis procedure is based on two scientific principles diffusion and ultrafiltration. Dialysis by diffusion depends on the membrane (it's pore number and size), the time that solution is exposed to the membrane and the concentration of the particles in the solution. Ultrafiltration depends on pressure to move particles or water across a membrane, the pressure is either hydrostatic or osmotic in nature [4].

The objective of this study is to delineate the bleeding diathesis in uraemic patients and to compare the effect of haemodialysis and peritoneal dialysis on platelet count, bleeding time

and clotting time immediately after and 24 hr. after dialysis.

Patients and Method

A total number of 50 patients with renal failure of both sexes were studied over a period of 4 months (from June 2004 to October 2004) In Merjan teaching Hospital. Patients whom already had haematological disease were excluded from the study.

Clinical details of each patient including details of renal disease, drug therapy and bleeding tendency were taken.

Peritoneal dialysis was done for 29 patients (duration of peritoneal dialysis was 48 sets for 48 hrs.), haemodialysis was done for 21 patients (duration 3 hrs. twice weekly). Platelet count, bleeding time and clotting time were done for each patient prior to dialysis, immediately after and 24 hr. post dialysis.

Blood was collected by venepuncture and then transferred to EDTA tube, the platelet counted by direct visual method using the light microscope and counting chamber [Haemocytometer] [5], improved double neubaur ruling chamber was used with a depth of 0.100 mm, the problem of platelet aggregation was solved by using tubes with EDTA (ethylene-diamine-tetra-acetic acid) which don't affect the cell number or size and inhibit platelet clumping [5], tripotassium EDTA K3 was used, plastic syringes were used, venous blood was obtained without delay, the solution for dilution used was aqueous ammonium oxalate, the dilution was (1 – 20), five groups of 16 small squares in the central area of the chamber (0.02 μ L) were counted.

Total platelet counted according to the formula:

Total platelet count = Number of cells counted in 5 small squares X 1/0.02 X 20 (dilution) [5]

To reduce the coefficient of variation at least 100 cells were counted [5].

Bleeding time was estimated by punching of the pinna of the ear by lancet and filter paper was applied every 10 seconds till the bleeding stopped and after that record the time using stop watch [6].

While clotting time had been done by pricking the thumb by lancet using blue capillary (without anticoagulant) and the time was estimated by stop watch when the blood clotted [5].

The parameters that were studied for coagulation data with their normal values are listed below :

1. bleeding time (BT)/ (2-5 minutes) [6]
2. clotting time (CT)/ (2-8 minutes) [5]
3. platelet count / (150- 400 x10⁹) [5]

Chi square was used for statistical analysis and the result considered significant when P value < 0.05

Results

50 patients were studied “32 males & 18 females” aged (2 – 85 y.) , mean (46.92 $\pm$ 9.02) , Divided into two groups:

1. Those who were treated with peritoneal dialysis 29 patients; 17 males & 12 females; mean age (52.1 $\pm$ 3.41)
2. Those who were treated with haemodialysis, 21 patients; 15 males & 6 females ; mean age of them (39.6 $\pm$ 14.1)

Platelet count:

The mean platelet count in patients treated with peritoneal dialysis was 233.6 x10⁹ (ranged 150- 340 x 10⁹)

before dialysis, immediately after dialysis it was 238.4 (155-350 x10⁹) then it became 250.2 x10⁹ (160-365 x 10⁹) 24 hr. after dialysis (table I).

19 out of 29 patients (65.5%) improved immediately after peritoneal dialysis, then they became 25 patients out of 29 (86%) who were improved 24 hr. after dialysis, the last 4 patients out of 29 (14%) the platelet count remain in the same level but within normal range.

The mean percentage of improvement in platelet count was 2.1% immediately after peritoneal dialysis and 7.4% 24 hr. after dialysis (table II), (fig.I). P value < 0.05 and < 0.01 respectively.

The mean platelet count before haemodialysis was (206.9x10⁹) (80 – 320 x 10⁹) then it was (219x10⁹) (100 – 320) immediately after dialysis and then it became 250.9 x10⁹ (150 – 350 x 10⁹) 24 hr. later (table III).

18 out of 21 patients (85.5%) improved immediately after haemodialysis and then they became 20 of 21 patients (95%) who were improved 24 hr. after haemodialysis, while 1 patient (5%) didn't improve but his platelet count was within normal range.

The mean percentage of improvement in platelet count in patients treated with haemodialysis was 7.1% immediately after dialysis and 25.4% 24hr. later (table IV), (fig.I1). P value < 0.01, 0.001 respectively.

Bleeding time:

The mean bleeding time in peritoneal dialysis improved from 4.39 minutes (ranged 2.25 – 7 m.) before peritoneal dialysis to 3.7 m. (2 – 6 m.) immediately after peritoneal dialysis then to 3.2 m. (2 – 5.15m.) 24hr. after peritoneal dialysis (table I). The mean percentage of improvement in bleeding time was 11.5 % immediately after

peritoneal dialysis and 20.9% 24 hr. after peritoneal dialysis (table II), (fig.I), P value < 0.5, 0.01 respectively.

11 of 29 patients (37%) who were undergone peritoneal dialysis had bleeding time above normal before dialysis, 4 out of 11 patients (36%) returned to normal bleeding time immediately after dialysis, becoming 7 of 11 (63 %) returned to normal 24 hr. later, while the rest “4 of 11 patients (36%)” got improvement but didn't return to normal bleeding time.

21 patients who were undergone haemodialysis their mean bleeding time was 5.85 m (2.4 – 16.30m) before haemodialysis then became 5 (2.25 – 15 m.) immediately after haemodialysis and became 3.7 m. (2 – 8.15 m.) 24 hr. later (table III).

10 patients out of 21 (47%) had prolonged bleeding time 5 of them (50%) returned to normal immediately after haemodialysis while 8 out of 10 (80 %) returned to normal 24 hr. after haemodialysis, the rest 2 patients (20%) got improvement but didn't return to normal.

The mean percentage of improvement in bleeding time was 13.1% immediately after haemodialysis and 30.6% 24 hr. later (table IV), (fig. I1). P value < 0.01, 0.001 respectively.

Clotting time:

The mean clotting time in peritoneal dialysis improved from 4.57m. (3 – 7.20 m.) before peritoneal dialysis to 4 m. (2.20–5.35) immediately after peritoneal dialysis then to 3.50m.(2 – 5m.) 24 hr. later (table I).

The mean percentage of improvement in clotting time was 9% immediately after peritoneal dialysis then it was 17% 24 hr. later (table II), (fig. I).

Those treated with haemodialysis their clotting time improved from 6.9 m. (3.20 – 17.15 m.) before haemodialysis to 6.1m. (3 – 13 .30 m.) immediately after haemodialysis then became 5.3 m. (2 – 8.35 m.) 24hr. later (table III) .

The percentage of improvement in clotting time was 11.6% immediately after haemodialysis and 24.3% 24hr. later (table IV), (fig. I1) ,P value < 0.01 in immediately after haemodialysis and < 0.001 in 24 hr. after haemodialysis .

4 patients out of 21 (19%) had prolonged clotting time before haemodialysis, 1 patient of 4 (25%) returned to normal clotting time

immediately after haemodialysis, then became 3 patients of 4 (75%) who were returned to normal clotting time 24 hr. after haemodialysis while the last one got improvement in clotting time but didn't return to normal.

When the results of bleeding time, clotting time and platelet count in peritoneal dialysis and haemodialysis were compared with each other the results showed that haemodialysis was more effective in improvement than peritoneal dialysis (figures III, 1V, V) , P value < 0.001 .

Table I Result of mean platelet, bleeding time, clotting time in peritoneal dialysis.

	before P.D	Immediatly after P.D	24 hr. after P.D
Platelet	233.6x10 ⁹ (150 – 340 x10 ⁹)	238.4x10 ⁹ (155 – 350 x10 ⁹)	250.2x10 ⁹ (165 – 365x10 ⁹)
B.T	4.39 m. (2.25 – 7 m.)	3.7 m.(2 – 6 m.)	3.2 m. (2 – 5.15 m.)
C.T	4.57 m. (3 – 7.2 m.)	4 m. (2.20 – 5.35 m.)	3.50 m. (2 – 5 m.)

Table II P value and mean percentage of improvement in platelet count, bleeding time, clotting time in peritoneal dialysis.

	mean % of improvement and P value in immed. After P.D	mean %of improvement and P value 24 hr. after P.D
platelet P value	2.1 % <0.05	7.4 % <0.01
B.T Pvalue	11.5 % <0.05	20.9 % <0.01
C.T P value	9 % <0.05	17 % <0.01

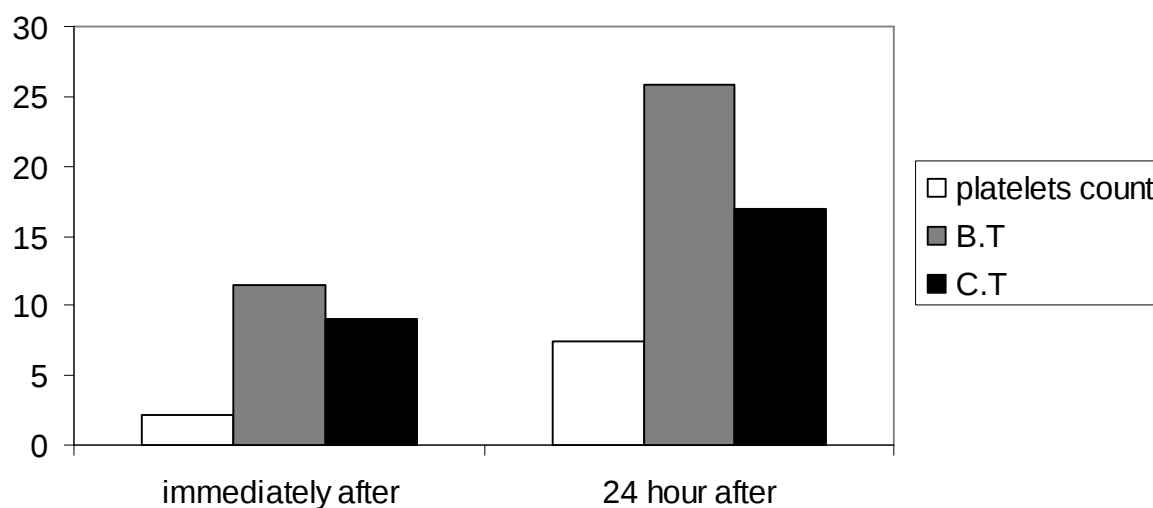
mean % value

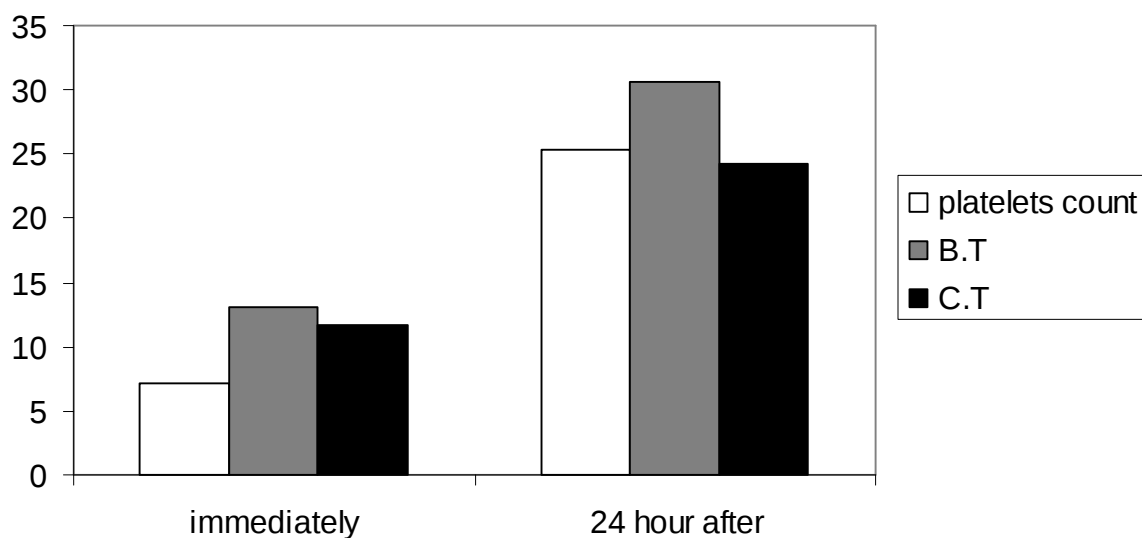
Fig. I Mean percentage of improvement in platelet count, bleeding time, clotting time in peritoneal dialysis.

Table III Result of mean platelet, bleeding time, clotting time in haemodialysis.

	before H.D	Immediatly after H.D	24 hr. after H.D
Platelet	206×10^9 ($80 - 320 \times 10^9$)	219×10^9 ($100 - 320 \times 10^9$)	250.9×10^9 ($150 - 350 \times 10^9$)
B.T	5.85m. (2.4 – 16.30 m.)	5 m.(2.25 – 15 m.)	3.7 m. (2 – 8.15 m.)
C.T	6.9m. (3.2 – 17.15 m.)	6.1 m. (3 – 13.30 m.)	5.30 m. (2 – 8.35 m.)

Table IV P value and mean Percentage of improvement of platelet count, bleeding time, clotting time in haemodialysis.

	mean % of improvement and P value in immed. After H.D	mean %of improvement and P value 24 hr. after H.D
Platelet P value	7.1 % <0.01	25.4 % <0.001
B.T Pvalue	13.1 % <0.01	30.6 % <0.001
C.T P value	11.6 % <0.01	24.3 % <0.001

mean % values**Fig. II** Mean Percentage of improvement of platelet count, bleeding time, clotting time in haemodialysis .

mean platelet count

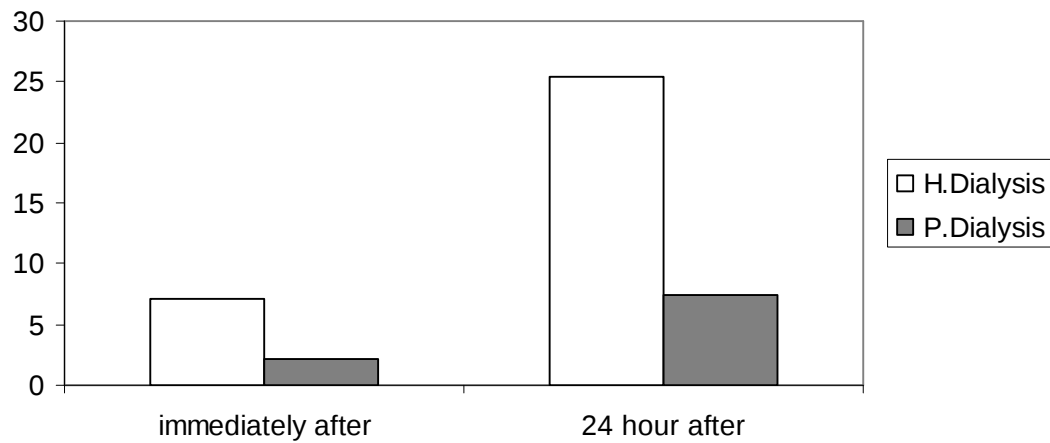


Fig. III Comparison in mean percentage of platelet count in haemodialysis and peritoneal dialysis (immediately after and 24 hr. later).

B.T

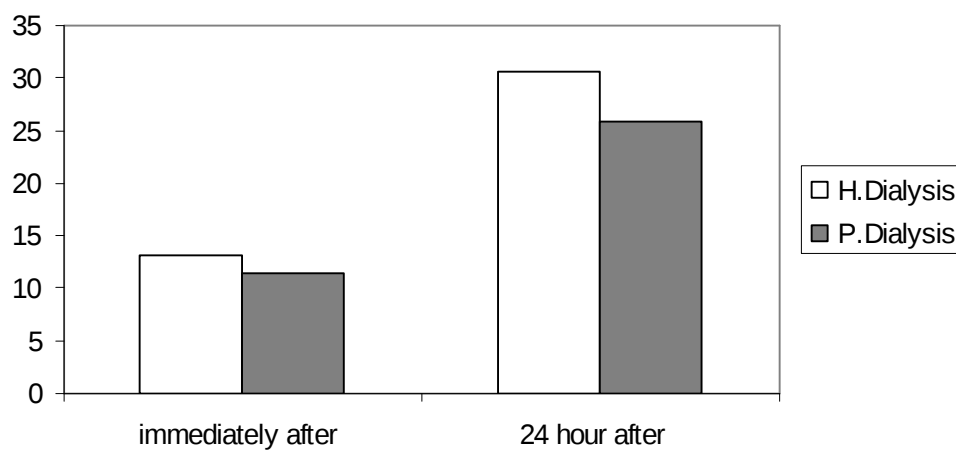


Fig.IV Comparison in mean percentage of bleeding time in haemodialysis and peritonealdialysis.

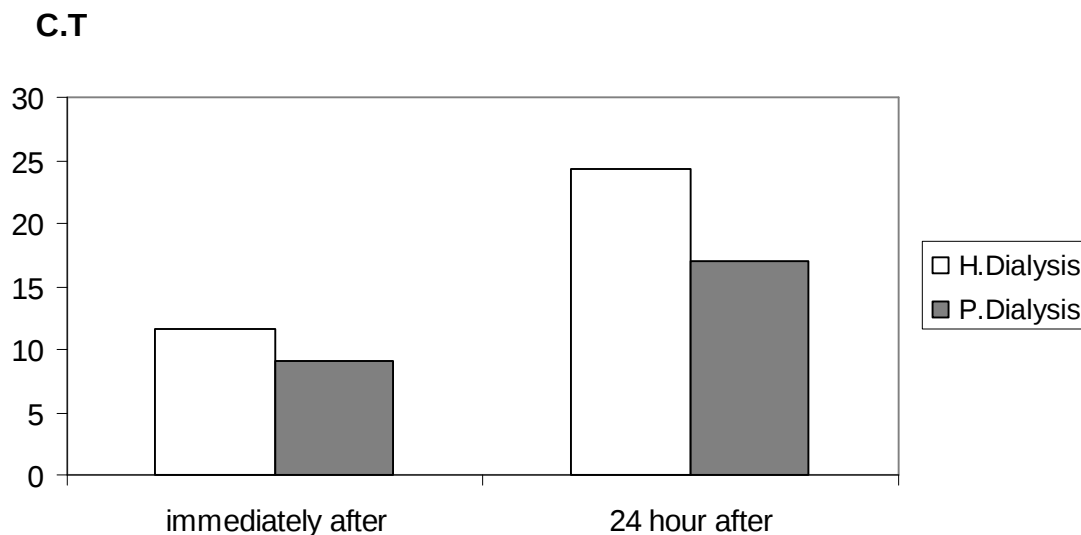


Fig. V : Comparison in mean percentage of clotting time in haemodialysis and peritonealdialysis (immediately after and 24 hr. later).

Discussion

The precise cause of bleeding in uraemia still remain ill-understood and probably varies from person to person.

In this study **platelet count** among patients who were under gone peritoneal dialysis was within normal range before dialysis, while the platelet count was slightly lower among the patients who were under gone haemodialysis, and this is consistent with other studies in which the platelet count is usually within normal range or slightly lower in patients with uraemia[4], the lower number of platelets in patients on haemodialysis is probably because the patients who were under gone haemodialysis had longer duration of uraemia than patients on peritoneal dialysis .

This study showed that the percentage of improvement in haemodialysis was more than peritoneal dialysis, but both haemodialysis and

peritoneal dialysis resulted in significant improvement in platelets count[7], so thrombocytopenia has been incriminated as an important cause of haemorrhagic diathesis in uraemia, however; this was not found to be significantly so by Chenny & Bonnin[8].

Regarding the **bleeding time** 47% of patient with haemodialysis had bleeding time above normal range before dialysis while 37% of patient with peritoneal dialysis had bleeding time above normal before dialysis and this is consistent with the study of willoughby & Crouch[9], who found that the bleeding time to be prolonged in uraemic patients, contrary to the findings of a normal bleeding time as reported by Castaldi et al[10].

50% of patients who had prolonged bleeding time before haemodialysis returned to normal immediately after haemodialysis and then became 80% who were returned to

normal bleeding time 24hr. later, two patients (20%) improved but didn't return to normal, while 36% of patients who had prolonged bleeding time before peritoneal dialysis returned immediately after, and became 64% who were returned 24hr. after peritoneal dialysis, the last four patients (36%) who were under gone peritoneal dialysis got improvement but didn't return to normal bleeding time.

Other studies showed that haemodialysis corrects prolonged bleeding time in only 30% to 50% of the cases [11], so dialysis transiently improve or even completely correct prolonged bleeding time and the clinical bleeding tendency[12].

Also this study showed that the percentage of improvement in bleeding time in haemodialysis was more than peritoneal dialysis which was statistically significant, but both peritoneal dialysis and haemodialysis resulted in significant improvement in bleeding time[7].

In this study the **clotting time** in patients who were under gone peritoneal dialysis was within normal range, while in haemodialysis 4 patients out of 21 (19%) had prolonged clotting time and this is consistent with other studies in which there is normal or near normal clotting times were obtained by Kuhlback[13] in his studies. While Guild & coworkers[14] & Larrain & Adelson[15] found prolonged clotting time in uraemic patients.

Also this study showed that the percentage of improvement of clotting time in haemodialysis was more than peritoneal dialysis.

This study showed that the percentage of improvement in haemodialysis was more than peritoneal dialysis and this goes with the results of other studies which proved that haemodialysis is considered more efficient than peritoneal dialysis, as it is allowing rapid change in abnormal serum values, while in peritoneal dialysis there is a slower clearance rate, also in peritoneal dialysis inadequate clearance may occur in patients with vasculitis, malignant hypertension, peritoneal fibrosis and in heavy patient (more than 70kg.) with no residual renal function[16].

Also this study showed that there was significant improvement in the results of platelets count obtained in 24hr. after dialysis when compared with the immediately after dialysis results and probably this is explained on the fact that dialysis remove toxins responsible for depression of bone marrow and destruction of already formed platelet and this requires time to increase. The same explanation can be applied to the improvement in bleeding time and clotting time either peritoneal dialysis or haemodialysis can reverse the haemostatic defect [4].

Conclusion

1. Both haemodialysis and peritoneal dialysis improve platelet count, bleeding time and clotting time.
2. Improvement in platelet count, bleeding time and clotting time is better after 24hr. than immediately after dialysis.
3. Haemodialysis is more effective than peritoneal dialysis in improving platelet count, bleeding time and clotting time.

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