

CLINICAL STUDY ON THE CAUSES OF DEATH IN UREMIC PATIENTS ON MAINTENANCE HEMODIALYSIS

Pei-Yuan Chen, Chi-Jen Tsai, Tze-Che Wang

Abstract

During the period from July 1978 to December 1982, thirty patients on maintenance hemodialysis, died in Taipei Medical College Hospital, were studied. There were 20 males and 10 females, ranging in age from 18 to 76 years. Cardiovascular disease (56.7%), consisting of cardiac disease (30%) and cerebral disease (26.7%), was the most common causes of death. Patients died in a mean duration of 13.3 months after starting hemodialysis. The mortality rate was 53% in patients aged 50 or over and was 34% in patients aged under 50. The overall mortality rate for all age was 41.7%. 11 (73%) of 15 deaths in patients aged 50 or over were due to cardiovascular disease, while only 6 (40%) of the 15 deaths in patients aged under 50 were due to cardiovascular disease. 70% of all deaths occurred between July 1978 and December 1980, and only 30% of all deaths occurred in the subsequent two years. In conclusion, patients aged 50 or over had higher mortality rate and higher incidence of cardiovascular death.

Keywords: Maintenance Hemodialysis, Uremia, Cardiovascular disease

Maintenance hemodialysis was introduced by Scribner and his colleagues in 1960 and has become an accepted therapy for uremic patients. There are a considerable number of complications reported in patients on maintenance hemodialysis, cardiovascular disease and infection are the two most common causes of death.⁽¹⁻⁸⁾

Here, we describe our experience in thirty uremic patients died on maintenance hemodialysis between July 1978 and December 1982.

Materials and methods

Thirty patients with chronic renal failure on maintenance hemodialysis, died

between July 1978 and December 1982 in Taipei medical college hospital, were studied. Each patient was hemodialyzed for 5-6 hours each time and two times weekly on a coil or hollow fiber dialyzer. Heparin was used as the anticoagulant. The dialysate flow rate was 500 ml per minute and the blood flow rate was 150-250 ml per minute. All patients were taking a 60 gm protein diet and received folic acid supplement and aluminum hydroxide tablets for phosphate binding. Antihypertensive drugs were given if patients had hypertension.

Result:

Department of Internal Medicine, Taipei Medical College Hospital.

Received for Publication: May 25, 1983.

Age and sex distribution

As shown in table 1, there were 20 males and 10 females ranging in age from 18 to 76 years. The mean age was 47.6 years for all patients and was 47.3 years and 48 years for male and female patients respectively.

Causes of uremia

As shown in table 2, 13 of the 30 patients had chronic glomerulonephritis; 4, chronic pyelonephritis; 3, hypertensive nephrosclerosis; 3, obstructive uropathy; 2, diabetic nephropathy; 2, uncertain causes; 1 each, polycystic kidneys, gouty nephropathy and lupus nephritis respectively.

Causes of death

As shown in table 3, cardiovascular disease (56.7%), consisting of cardiac disease (30%) and cerebral disease (26.7%), and infection (20%) were the most common causes of all deaths. Of 8 patients with cerebral death, 5 died of cerebral hemorrhage; 2, cerebral thrombosis; 1, hypertensive encephalopathy. Of 9 patients with cardiac death, 5 had left ventricular failure with pulmonary edema; 2, acute myocardial infarction; 2, pericardial tamponade. Of 6 patients died of infection, 3 had pneumonia; 2, urinary tract infection; 1, biliary tree infection. In the remaining 7 patients, 2 died of hyperkalemia; 1, hepatoma; 1, cachexia; 1, upper GI bleeding and 2 with uncertain causes.

Relationship between duration on hemodialysis and mortality

For male patients, the mean duration on hemodialysis for those aged 50 or over was 13.3 months and 15.2 months for those aged

under 50. For female patients the mean duration were 10.9 months and 14.1 months for those aged 50 or over and aged under 50 respectively. The mean duration for all age was 13.3 months, ranging from 22 days to 43 months. 16 (53.3%) of 30 patients died between the 6th month and 43th month. 8 patients (26.7%) died within 6 months, 6 of them were aged 50 or over. (Table 4)

Incidence of cardiovascular death and mortality

As shown in Table 5, of 44 patients aged under 50, 15 (34%) of them died, of 28 patients aged 50 or over, 15 (53%) of them died. The overall mortality rate for all age was 41.6%. 11 (73%) of 15 deaths in patients aged 50 or over were due to cardiovascular disease, while 6 (40%) of 15 deaths in patients aged under 50 were due to cardiovascular disease.

Annual incidence of death

As shown in Table 6, of 30 deaths, 4 (13.3%) were between July and December 1978; 9 (30%) in 1979; 8 (26.7%) in 1980; 5 (16.7%) in 1981 and 4 (13.3%) in 1982.

Discussion

In our series, cardiovascular deaths account for 56.7% of all deaths. This result is comparable with 50 - 60% reported in Europe and USA. (1,5,6,8) Cardiac failure is common in patients with uremia on maintenance hemodialysis. Various factors such as anemia, hypertension, ischemic heart disease, fluid overload, electrolyte disturbance and possibly uremic toxins may be contributory to the development of cardiac failure. (2,3,4,9) A specific uremic cardiomyopathy has also been suggested (4)

Five of our patients died of left ventricular failure with pulmonary edema. Two of the patients using digitalis died of ventricular arrhythmia, one during hemodialysis and the other one after hemodialysis. Patients using digitalis with left ventricular failure have an unexpected high incidence of occult, potentially dangerous ventricular arrhythmia during and after dialysis.^(9,10,11) A low potassium bath concentration may be responsible.^(9,10) In our hospital, the concentration of potassium in the dialysate is about 2.6 meq/L and the concentration can not be changed due to the use of automatic proportionate pump for the mixing of water and concentrated dialysate. Morrison et al suggest that the use of a 3.5 meq/L potassium dialysate plus a 400 mg dose of quinidine sulfate orally 45 minutes before hemodialysis was successful in reducing ventricular ectopic frequency.⁽¹⁰⁾ Two patients died of acute myocardial infarction, one had diabetes mellitus the other had underlying ischemic heart disease. Rostand et al reported that the incidence of ischemic heart disease during dialysis was not different from similarly matched nondialysis subjects and coronary artery disease only affected long-term survival of patients with preexisting disease.⁽⁹⁾ Two patients died of pericardial tamponade, one during hemodialysis and the other one during cardiocentesis. Cardiac tamponade has been reported with increasing frequency in uremic patients since initial report by Goodner and Brown in 1956.⁽¹³⁾ Comty et al reported that uremic pericarditis occurred in 25 of 152 patients on maintenance dialysis. 4 of the 25 patients had pericardial tamponade.⁽¹⁴⁾

Fever, anterior chest pain and

pericardial friction rub are the most frequent manifestations.⁽¹⁴⁾ Disappearance of pericardial friction rub during hemodialysis may herald a life threatening pericardial tamponade.^(14,15,16) Treatment for pericarditis includes indomethacin, steroid and intensive hemodialysis with regional heparinization. Treatment for pericardial tamponade requires cardiocentesis and/or pericardiectomy.^(14,16,17,18)

Eight of our patient died of cerebral disease, all of them had poor hypertension control. It has been reported in many series that hypertension is one of the most important risk factors for cerebrovascular disease and ischemic heart disease.^(16,19,20,21) In uremic patients blood pressure should be controlled as near normal as possible to reduced the incidence of cardiovascular death.

Infection has been noted as the second most common causes of death in patients on maintenance hemodialysis.^(1,5,23,24) Factors including reduced resistance to infection due to compromised immune system and need for frequent vascular access, may be responsible. Infection accounted for 6.9 - 25% of all death in patients on maintenance hemodialysis in different reports.^(1,5,7,16,22) Respiratory infection, urinary tract infection and vascular access infection are most common. In our series, 6 (20%) of the 30 patients died of infection, 3 had pneumonia, 2, due to urinary tract infection and one due to biliary tree infection. It is reasonable to start antibiotic therapy early at the evidence of infection to reduce infectious complications. Hemodialysis patients are also prone to cytomegalus virus, hepatitis B

virus and tuberculous infection. (16,23,24)
Fortunately none of our patients died of these infection.

Two patients died of hyperkalemia due to excessive intake of potassium-rich fruits and foods. Hypercatabolism due to starvation or poor intake, and mismatch dialysate may also cause hyperkalemia in uremic patients on maintenance dialysis. (26) Hyperkalemia is a life threatening condition. Every uremic patients presents with chest discomfort, short of breath, and irregular heart beat together with history of excessive intake or starvation, hyperkalemia must be considered. (24,26) Treatment includes administration of calcium gluconate to antagonize the membrane effect of hyperkalemia, sodium bicarbonate and/or glucose and insulin to shift potassium into cells, kayexalate and hemodialysis to remove the excessive potassium. (25) It should be noted that a patient with an extreme high serum potassium level probably should not be dialyzed initially with very low dialysate potassium concentration, especially in patients with ischemic heart disease or in patients with cardiac failure taking digitalis. (4,10,11,16) A preferable approach to such patients is multiple bath exchanges with graded lowering of potassium concentration of the dialysate. (16)

The mean interval between the starting of hemodialysis and death was 13.3 months which was comparable with 13.8 months reported by Burton et al. (1) In our series, patients aged 50 or over have shorter mean duration of survival than

those of under aged 50. (table 5). The overall mortality rate (41.6%) in our series was slightly higher than 28.1% and 32.9% observed by Parson et al and Bryan et al respectively, but comparable with 41% reported by Su et al. and lower than 58.9% reported by Linder et al. (1,3,5,27) Patients aged 50 or over have higher mortality (53% versus 34%) and higher incidence of cardiovascular death (75% versus 40%) than those aged under 50. The finding of increasing mortality rate with increasing age is similar to the results of Lewis et al, Cameron et al and Gross et al. (6,28,29) Most of our deaths (70%) occurred between July 1978 and December 1980, and death decreased significantly in the subsequent two years, 16.7% and 13.3% in 1981 and 1982 respectively. The reasons for decreasing incidence of death in the last two years are not clear. Various factors, such as health status at the entry of hemodialysis, control of hypertension, the attitude of the patient's family to the therapy, cooperation between patients and hemodialysis staffs, experience in the management of complications of hemodialysis, may be responsible. (7,23,24)

In conclusion, our study revealed that cardiovascular death was the most common cause of death and patients aged 50 or over had higher mortality rate and higher incidence of cardiovascular death. We suggest that patients complicated with cardiovascular disease should be treated carefully and observed closely during hemodialysis.

Table 1. Age and Sex Distribution

sex Age	Male	Female	Total
< 20	0	1	1
20-29	0	1	1
30-39	7	0	7
40-49	4	2	6
50-59	7	5	12
60-69	1	0	1
> 70	1	1	2
Total	20	10	30
Mean age	47.3	48.0	47.6

Table 2. Causes of uremia

Cause of uremia	no. of case
Chronic glomerulonephritis	13
Chronic pyelonephritis	4
Hypertensive nephrosclerosis	3
Obstrutive uropathy	3
Diabetic nephropathy	2
Polycystic kidneys	1
Gouty nephropathy	1
Lupus nephritis	1
Uncertain	2

Table 3. Causes of death

Cause of death	no. of case	% of total
Cerebral	8	26.7
cerebral hemorrhage	5	
cerebral thrombosis	2	
hypertensive encephalopathy	1	
Cardiac	9	30
acute myocardial infarction	2	
left ventricular failure with		
pulmonary edema	5	
pericardial tamponade	2	
Infection	6	20
pneumonia	3	
urinary tract infection	2	
biliary tree infection	1	
Hyperkalemia	2	6.7
Hepatoma	1	3.3
Cachexia	1	3.3
Upper GI bleeding	1	3.3
Uncertain	2	6.7
Total	30	100

Table 4. Interval between the starting of hemodialysis and death

Interval	male		female		Total (%)
	≥50	<50	≥50	<50	
< 1 mon.	0	0	1	1	2(6.7)
1-3 mon.	1	1	1	0	3(10)
3-6 mon.	2	0	1	0	3(10)
6-12 mon.	2	6	1	2	11(36.6)
12-24 mon.	1	3	1	0	5(16.7)
24-36 mon.	2	1	1	0	4(13.3)
> 36 mon.	1	0	0	1	2(6.7)
Total	9	11	6	4	30(100.0)
Mean	13.1	15.2	10.9	14.1	13.3

Table 5. Incidence of cardiovascular death and mortality according to age at beginning HD

	age		Total
	≥50	<50	
Total no. entering HD	28	42	72
Total no. of death	15	15	30
Cardiovascular death	11	6	17

Table 6. Annual incidence of death

Year	no. of death	%
1978*	4	13.3
1979	9	30.0
1980	8	26.7
1981	5	16.7
1982	4	13.3
Total	30	100.0

*July to December only

References

1. Burton Bt, Krueger KK, Bryan Fa: National registry of long-term dialysis patients. *JAMA* 218: 718-722, 1971.
2. Montague TJ, Macdonald RR, Boutier FE et al. Cardiac function in end stage renal failure: *Chest*. 82: 441-446, 1982.
3. Lazarus JM, Lowrie EG, Hampers CL et al. Cardiovascular disease in uremic patients on hemodialysis. *Kidney Int.* 7 (suppl. 2) 167-175, 1975.
4. Hung J, Harris PJ, Uren RF et al. Uremic cardiomyopathy effect of hemodialysis on left ventricular function in end stage renal failure. *N. Engl. J. Med.* 302: 547-551, 1980.
5. Gurland HT, Brunner FP, Dehn HV et al. Combined report on regular dialysis and transplantation in Europe III, 1971 in *proc. Eur. Dialysis Transplant. Assoc.* 1972 Vol 9, p. 3.
6. Lewis EJ, Foster DM, Dela Puente J et al. Survival data for patients undergoing intermittent hemodialysis. *Ann. Intern. Med.* 70: 311-315, 1969.
7. Jimmy RL, Analysis and outcome of 1063 patients trained for home hemodialysis. *Kidney Int.* 9: 363-374 1976.
8. Lowrie EG, Lazarus JM, Mocelin AJ et al; Survival of patients undergoing chronic hemodialysis and renal transplantation, *N. Engl. J. Med.*: 288, 863-867, 1973.
9. Rostand SG, Gretes TC, Kirk KA: Ischemic heart disease in patients with uremia undergoing maintenance hemodialysis, *Kidney Int.* 16: 606-611, 1979.
10. Morrison G, Michelson EL, Brown S et al: Mechanism and prevention of cardiac arrhythmia in chronic dialysis patients. *Kidney Int.* Vol. 17: 811-819.
11. Fisch C, Relation of electrolyte disturbance to cardiac arrhythmia, *Circulation*: 408-417, 1973.
12. King W, Masler DS, Brown DC: Hemodialysis in diabetic patients with chronic renal failure, *Ann. Int. Med.* 83, 215-217, 1975.
13. Goodner CJ, Brown H: Report of cases of cardiac tamponade in uremic pericarditis, *JAMA*, 162: 1459-1461, 1956.
14. Comty CM, Cohen SL, Shapiro FL: Pericarditis in chronic uremia and its sequels, *Ann. Int. Med.* 75, 173-183, 1971.
15. Hager EB,: Clinical observation of five patients with uremic pericardial tamponade, *N. Engl. J. Med.* 273: 304-307, 1965.
16. Lazarus ML: Complications in hemodialysis: An overview *Kidney Int.* 18: 783-796, 1980.
17. Sing NS, Newmark K, Ishikawa et al: Pericardiectomy in uremia, the treatment of choice for cardiac tamponade in chronic renal failure, *JAMA* 228: 1132-1135, 1974.
18. Wray TM, Humphreys J, Perry JM: Pericardiectomy for treatment of uremic pericarditis, *Circulation* 50 (suppl. II) 268-270, 1974.
19. Kannel WB, Gordont, Schwartz MJ: Systolic versus diastolic blood pressure and risk of coronary heart disease, *The Framingham Study. Am. J. Med.* 27: 335-346, 1971.
20. Hutchinson TA, Tomas DC, Macgibbon B. et al: predicting survival in adults with end stage renal disease, An age equivalence index. *Ann. Int. Med.* 96; 417-423, 1982.

21. Rabkin SW, Mathewson, Tate RB: Predicting risk factor of ischemic heart disease and cerebrovascular disease from systolic and diastolic blood pressure. *Ann. Int. Med.* 88; 342-345, 1978.
22. Montogomerie JZ, Kalmanson GM, Guez LB: Renal failure and infection, *Medicine* 47, 1-32, 1968.
23. Paul J, Johanna Z: Results and limitation of longterm dialysis treatment. In *Neprology* (Haburger J, Crosnier J, Grunfeld JP) Paris, Flammarion Medecine - Sciences, 1255-1260.
24. Henderson LW: Hemodialysis in: Disease of the Kidney. (Earley LE, Gottschalk CW.) New York, Little, Brown and Co., I, 427-467, 1979.
25. Tannen RL, The patients with hypokalemia or hyperkalemia. In: *Manual of Nephrology* (Schrier RW.) New York, Little, Brown and Co. 42-46, 1981.
26. Su YH, Lai YH, Tsai JH et al: Acute hyperkalemic episodes on long term hemodialysis patients (Abstract) *J. Formosan Med. Assoc.*; 76, 760-761, 1977.
27. Su YW, Lai YH, Chi CY et al. Eight years cumulative survival rate of maintenance hemodialysis patients in Kaohsiung Medical College (Abstract), *J. Formosan Med. Assoc.* 81, 1250, 1982.
28. Cameron JS, Ellis FG, Ogg CS: A comparison of mortality and rehabilitation in regular dialysis and transplantation in *Proc. Eur Dialysis Transplant Assoc.* 1970, Vol. 7, p. 25-32.
29. Gross JB, Keane WF, McDonald AK: Survival and rehabilitation of patients on home dialysis, *Ann Int. Med.* 78; 341-346, 1973.

血液透析病人死因之臨床研究

陳培源 蔡啓仁 王子哲

摘要

民國六十七年七月至七十一年十二月間，在本院內科接受血液透析治療的病人中有卅人死亡。其中包括男廿人，女十人。年齡從十八歲至七十六歲。其死因如下：心臟病血管疾病（56.7%）包括心臟疾病（30%）及腦疾病（26.7%）、感染症（20%）、高血鉀症（6.7%）、肝癌（3.3%）、惡液質（3.3%）、上消化道出血（3.3%）及原因不明（6.7%）。病人由開始接受血液透析至死亡的時間平均是13.3個月。平均死亡率是41.6%，五十歲以上的病人死亡率為53%，五十歲以下的病人死亡率為34%。死亡的病人中，五十歲以上的病人十五人中有十一人（73%）死於心臟血管疾病。五十歲以下的病人十五人中有六人（40%）死於心臟血管疾病。有廿一人（70%）死於六十七年七月至六十九年十二月的二年半間，其後二年只有九人（30%）死亡。這些結果顯示在本院接受血液透析治療的病人，最常見的死因是心臟血管疾病。年齡五十歲以上的病人死亡率較高且較常死於心臟血管疾病。

台北醫學院附設醫院內科

民國七十二年五月二十五日受理