Short Dialysis Schedules (SDS)—Finally Ready to Become a Routine?

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Summary

One hundred and one patients were treated for up to two years for three hours every other day (10.5 hr/week), or four hours thrice-weekly with conventional disposable 1m² dialysers have been investigated. Rigorous control of water balance and the maintenance of predialysis serum K and PO₄ within normal limits were the main criteria for judging the adequacy of the treatment. The results regarding blood pressure, phosphate problems, haematocrit, peripheral nerve status, pericarditis and range of rehabilitation are discussed.

Introduction

The importance attributed in recent years to the retention of small or middle molecular-weight solutes, as important factors in the genesis of uraemic toxicity, have given rise to several clinical trials. Experimentally, however, a simplified approach to the problem of uraemic toxicity is required. The removal of a toxic factor cannot be investigated without knowing its degree of binding with other molecules (Farrel et al, 1972), the generation rate, the presence of inhibiting factors, the distribution space, and possibly intestinal or renal removal (Kjellstrand et al, 1972; Milutinovic et al, 1973). Different dialysis schedules with conventional disposable 1m² dialysers set up in order to reduce the removal of small molecules (low-flow dialysis) (Christopher et al, 1971; Cambi et al, 1972) or small and middle molecules (short dialysis) (Cambi et al, 1972) have not yielded any proof as to the toxicity of these solutes within a very broad range of blood concentrations.

The relationship between dialyser efficiency and solute removal appears incomplete, and can only be described in terms of its efficiency with reference to a theoretical molecule.

The uncertainties inherent in such a model are further complicated by the circumstances of clinical experimentation. For example, patients who undergo
a single trial are limited in number, are not homogeneous, and are treated for a very short period of time. It is also well known that the number of clinical variables of a single patient are very often far from being quantified by presently available biochemical parameters.

Attempts made by our group in these last three years in order to modify the ‘ideal’ removal of these so-called small and middle molecules (Cambi et al., 1972) have not been associated with any change in the patients clinical condition. In particular, the reduction of the weekly dialysis time to 10–12 hr was not associated with clinical neuropathy. A blood flow up to 250–300 ml/min was clearly beneficial in allowing a normal control of potassium and phosphates although control of the latter required aluminium hydroxide. The routine long-term feasibility of short-dialysis schedules (SDS) has been inquired into without considering the theoretical retention of unknown toxic factors of different molecular weight.

**POPULATION STUDIED AND METHODS**

The 101 patients are being treated by either 4-hr thrice-weekly dialysis or for three hours on alternate days. They represent a reasonably homogeneous, unselected adult population, mostly taken from an area of 500,000 inhabitants and treated in the same dialysis unit.

The mean age is 40-5 ± 5-2 (range 17–74), mean body weight 61-0 ± 4-7 kg (range 46–87); 10% of the patients are aged 60 or older.

Of the total, 53 patients have been treated exclusively with SDS for periods of 3 to 24 months. Eight patients were previously treated with traditional dialysis (Kii Standard for 10 hr, thrice weekly) and, later, after 12 months with low-flow dialysis ($Q_B$ 150–200 ml/min, $Q_D$ 100 ml/min), were transferred to short dialysis treatment.

The remaining 40 patients began dialysis with thrice-weekly Kii Standard. Gradually their schedules were changed to five hours on alternate days with 1m² coils (1971), and subsequently to four-hour alternate-day treatment (1971–1972). Since November 1972, all patients have been treated with SDS.

Either 1m² coils or disposable parallel-flow dialysers, and for a short period of time a coil of 1·5m² and a capillary kidney of 1·3m² have been used.

Blood flow was 250 ml/min or more, and dialysate flow 400–600 ml/min. Dialysate composition (in mEq/l) was: Na 137, K - 2, Cl 103·5 ±1, Ca 4, Mg 1·5, acetate 40. The serum samples for biochemical and haematocrit estimations were always taken immediately before dialysis and 40 to 48 hr from the end of the previous treatment.

Maximum motor nerve conduction velocity (max. MNCV) was measured in our laboratory by a dual-channel Hewlett-Packard 1510 Electromyograph with
a variable-persistence storage scope and camera. Recordings were obtained by means of supramaximal stimuli from the peroneal nerve between the head of the fibula and the ankle.

Pick-up was always a bipolar needle electrode. In our laboratory, normal values of max. MNCV in the peroneal nerve are 49.04 ± 3.31 m/sec. For considerations about temperature control the reader is referred to other papers (Savazzi et al, 1974). The needle electrode inserted in different depths of the extensor digitorum brevis muscle gave us EMG patterns during maximum muscular contraction (recruitment).

RESULTS

Blood Pressure

A total of 84% of patients had post-dialysis values of diastolic blood pressure under 95 mm Hg. Four patients were nephrectomised, two because of malignant hypertension and two because of infected polycystic kidney disease. Some of the patients (15%) were treated with guanethidine (10 mg) or propanolol (40–80 mg) or both.

Haematocrit

The present pre-dialysis haematocrit excluding nephrectomised patients and children is 28.1 ± 5.7% in males and 26.4 ± 6.9% in females (Figure 1). Five percent of the patients (generally elderly patients at the beginning of the treatment) receive androgens (Sustanon 250 mg/week) for one to two months. Blood transfusions have been abolished since January 1971. All the patients receive 2 to 3 g of intravenous iron per year.

The most impressive change in the haematocrit was noticed after the change from conservative treatment to short dialysis: after a short period of three to seven months, the haematocrit in 45 consecutive patients rose from 21.0 ± 5.1% to 26.9 ± 5.5% (p < 0.001).

Bone Related Aspects

The mean pre-dialysis serum phosphate is 5.4 ± 1.7 mg.%. No fractures have been recorded in the last two years. Two patients have been parathyroidectomized. Whilst 30% of patients have never been treated with aluminium hydroxide, 70% receive an average of 3.5 g/day of aluminium hydroxide with individual ranges up to 7 g. In 47 consecutive patients, treated for at least 9 months and evaluated for two years, pseudo-gout attacks appeared in one case out of 32 in the group with pre-dialysis phosphates higher than 6 mg.%(x² = 5.875, p < 0.01) (Cambi
Figure 1. Pre-dialysis haematocrit, excluding nephrectomised patients and children. Five per cent of the patients receive androgens.

et al, 1974). Table I summarizes the X-ray pictures in our population treated for at least nine months with SDS.

Peripheral Nerve

A subclinical change of the functional status of the peripheral nerve is not detected by maximum motor nerve conduction velocity alone; consequently an analysis of the electromyographic indices, in particular recruitment, has been
started. Figure 2 shows the qualitative modifications of the recruitment in patient CV from a poor to a reduced pattern after 11 months of short dialysis; in this patient, in spite of a definite change of recruitment, no modification of peroneal MNCV(931–32 m sec) was observed.

<table>
<thead>
<tr>
<th>TABLE I. Predialysis Serum Phosphates and Evidence of Bone Disease in Patients Treated with Short-Dialysis Schedule (75 Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P &lt; 6 $ mg% (51 patients)</td>
</tr>
<tr>
<td>11 (21.5%)</td>
</tr>
<tr>
<td>2 (3.9%)</td>
</tr>
<tr>
<td>4 (7.8%)</td>
</tr>
<tr>
<td>34 (66.6%)</td>
</tr>
</tbody>
</table>

Patients in dialysis for at least 9 months.

Figure 2. Qualitative modifications of the recruitment of nerve velocity after 11 months of dialysis. The traces shown were taken (left) in November 1973 in conservative treatment, and (right) October 1974 (after 11 months of short dialysis) and are for the extensor digitorum brevis muscle during maximum muscular contraction. Calibration, 20 msec, 1 mV per division.

In a previous communication (Cambi et al., 1973) it was demonstrated that maxMNCV carried out as a routine test in the same patient, treated with different dialysis schedules for prolonged periods, failed to demonstrate the superiority of any one dialysis treatment. Nevertheless all patients attained a satisfactory clinical condition. It appears, consequently, that maximum MNCV alone does not reveal subclinical changes in the motor-neurone in haemodialysis.
patients. Various EMG indices show the true condition of the peripheral nerve more precisely (Savazzi et al, 1974).

Table II shows the modifications of recruitment during maximum muscular contraction in the extensor digitorum brevis muscle from conservative treatment to short-dialysis schedule. In this experiment the analysis of the recruitment of the different motor units alone versus maxMNCV shows that no patients had a normal interference pattern at the beginning of the dialysis treatment, whereas five cases in 24 still had normal conduction values. After 3–24 months of short dialysis 12 patients (50%) showed improvement of varying degrees towards normality. In only four patients (16%) did recruitment become normal.

**TABLE II. Changes of Recruitment and max.MNCV (peroneal) from Conservative Treatment to Short-Haemodialysis Schedule (24 consecutive patients)**

<table>
<thead>
<tr>
<th>Results recruitment</th>
<th>Changes recruitment</th>
<th>Number of cases</th>
<th>max.MNCV (m/sec)</th>
<th>Before haemodialysis</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>improved 50%</td>
<td>poor normal</td>
<td>2</td>
<td></td>
<td>40.0 ± 5.8</td>
<td>41.2 ± 4.4</td>
</tr>
<tr>
<td></td>
<td>poor reduced</td>
<td>8</td>
<td></td>
<td>not significant</td>
<td></td>
</tr>
<tr>
<td></td>
<td>reduced normal</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>not improved 50%</td>
<td>reduced</td>
<td>5</td>
<td></td>
<td>39.9 ± 7.2</td>
<td>40.8 ± 9.4</td>
</tr>
<tr>
<td></td>
<td>poor</td>
<td>7</td>
<td></td>
<td>not significant</td>
<td></td>
</tr>
</tbody>
</table>

worsened none

**Pericarditis**

(A) Four cases of pericarditis appeared during conservative treatment and recovered after the beginning of SDS, one being treated with pericardiotomy.

(B) Three cases of pericarditis appeared during the course of SDS November 1972 – November 1974). One had lupus erythematosus and died of miliary disseminated tuberculosis with tubercle bacilli in the pericardial fluid.

**DISCUSSION**

As the only dialysis unit in a province of some 500,000 inhabitants, it was decided two years ago to accept all adult patients coming from this area. The actual number of new candidates is 25–30 per year, corresponding to about 60 patients per million per year. Of these, 40% of the patients are receiving SDS
as a home programme. Our present two-year survival is over 90%.

Rehabilitation (EDTA parameters): I degree 60%, II degree 16%, III degree 15%, IV degree 7%, V degree 2%.

This long-term study concerning a continuously growing number of patients obliged us to select very few and easily reproducible clinical parameters. The examination of the peripheral nerve has been followed with great attention because a relationship between dialysis time and peripheral neuropathy has always been suspected.

We found no clear correlation between recruitment and maxMNCV because the physiopathological mechanism of an abnormal MNCV and of recruitment are not quite the same. Considering the results obtained, the changes of recruitment from conservative treatment to dialysis treatment offer an adequate index of recovery in those patients whose MNCV does not give a definite answer.

With regard to bone disease, a combination of a slightly positive calcium balance (obtained by the use of 4 mEq/l of calcium in the dialysate for a limited number of hours) and a rigorous control of phosphate level is very important in avoiding the incidence of the clinical complications described in the literature (Moorhead, 1974).

In conclusion SDS can be considered a routine treatment since it is easily possible to maintain correct water balance and pre-dialysis PO₄ and K within normal limits. The higher blood flow needed to keep the pre-dialysis values of such small molecules within the normal range requires very careful attention to the technicalities of dialysis treatment, especially with regard to routine maintenance of a high blood flow through the A–V fistula. However, the number of advantages obtained by SDS (Cambi et al, 1973) justifies a larger extension of such treatment.

References


Open Discussion

R KKLUTHE (GFR) You found relatively high haematocrit values in your patients and we know there may be histidine deficiency in patients on dialysis treatment. Did you measure histidine in your patients?

CAMBI No, we never measured histidine.

H MANN (GFR) Did you measure the blood loss from cannulation sites?

CAMBI No, we didn’t measure blood losses.

MIGONE May I suggest that short dialysis may lead to minimal trauma of blood in the dialyser and a consequent beneficial effect on haematocrit.

S SHALDON (France) Could you tell us how much blood you take per month for laboratory tests, and do your patients receive iron supplements routinely?

CAMBI We take blood samples once a month, of about 30 to 40 ml, and they receive 2 to 3 g of iron per year unless there is much blood loss, when we give them more.

J HOELTZENBEIN (GFR) In judging the efficiency of dialysis, chemically, we should look at the absolute amounts of any chosen reference substance removed, rather than looking at blood levels. Proportionating machines for dialysate preparation make this impossible where tank systems, especially those with recirculation, lend themselves more readily to the quantitative determination of the wastes removed.

F BRUNNER (Switzerland) I would like to provoke some comments by our British colleagues. Dr Cambi has shown us that, apparently, short dialysis is as good as long dialysis. In Britain, it is usual to dialyse 24 to 30 hr per week with quite efficient dialysers, like the Meltec multi-point. British colleagues tell me that the patients feel better with longer dialysis. What do the British say?

CAMBI Maybe I’ll ask one of the many distinguished British colleagues to discuss this point.

D OLIVER (UK) The Oxford experience using multi-point dialysers, 15-18 hr/week in three treatment sessions, is not in agreement with this paper. We have found that in three-quarters of our patients plasma phosphate has risen to very high levels with saturation of the calcium phosphate product but not to the extent of obvious metastatic classifications. This occurs when we optimize dialysis by obtaining blood flows up to 300 ml/min. Are you phosphate depleting your patients, and are you protein restricting them as well?
CAMBI I agree that the limiting factor of short dialysis is the pre-dialysis level of phosphate. We give a mean of 3.5 g of aluminum hydroxide to 70% of the patients, but individual doses can reach 7 g a day. Thirty per cent of the patients don’t receive aluminium hydroxide. The protein intake of all the patients is about 1.2 g/kg.

B I CHAZAN (UK) Just recently we finished a one-year comparison between long- and short-term dialysis. For the long-term we used the Kiil (6–9 hr), and for the short-term the coil (3 hr). We dialysed three times a week. The blood creatinines before and after were much the same in both. As a result the hours the unit has operated have decreased from 465 to 240 per month. The technicians have been decreased from 13 to 11, and yet the number of dialyses per month has increased from 280 to 310. Thus in the short-term at least the changeover to SDS has been worthwhile.

CAMBI I can add that as far as our experience in reducing dialysis time in 1971, with twelve nurses, we were performing 254 dialyses per month; in August 1974, with twelve nurses, we were performing 750 per month.

J L FUNCK-BRENTANO (France) I am in favour of short dialysis, but before comparing different methods we need to know the residual clearance of the kidney. The second limiting factor is phosphate concentration. I would like to ask you how many patients you have been obliged to remove from the programme because it didn’t work for them?

CAMBI The residual function of the patients is less than 2 ml/min and several patients are totally anuric. Recently we have been dialysing a group of ten patients, with a residual renal function of about 5–7 ml/min. Some of these patients have been treated for over a year, with no more than 6 to 9 hr/week, with a urine output of about 2000 ml/day. Everybody agrees that phosphates are a limiting factor in short dialysis, but the majority of patients on aluminum have a pre-dialysis phosphate of less than 6 mg/100 ml. According to recent literature, inhibition of PTH is obtained when the phosphate is about 5.0 mg/100 ml. Finally, no patients were removed from the programme.