Short-term outcome of diabetic patients in renal replacement therapy

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Abstract

Background. Diabetic nephropathy or diabetes-related nephropathies represents one of the most relevant causes of renal failure in recent years. This complex pathological picture becomes particularly severe as time elapses and after starting renal replacement therapy (RRT).

Methods. In an attempt to investigate the evolution of the major clinical features, a retrospective study was carried out on a cohort of 76 diabetic patients on RRT. Sixty-five have been treated by haemodialysis (HD) and 11 by peritoneal dialysis (CAPD), for at least 1 year. In these patients change in modality of treatment, metabolic control, cardiovascular, and ophthalmological complications, peripheral neuropathy, state of vascular access, and intradialytic complications were surveyed at initiation and after 1 year of treatment. A modified Karnofski’s score was utilized, to evaluate the degree of rehabilitation. The comparison of prevalence was evaluated, using Student’s t-test for paired samples.

Results. After 1 year, 11 patients on CAPD remained on the same type of treatment. Out of 65 patients on standard bicarbonate HD, 11 were moved to acetate free biofiltration, two to paired filtration dialysis and one to haemofiltration. A worsening in arrhythmias was recorded with an increased prevalence from 25.0 to 35.0% (n.s.), and one more patient (15 vs 16 and 19 vs 20 respectively) experienced ischaemic cardiomyopathy and cerebrovascular insufficiency. Hypertension showed a significant improvement (72 vs 42, P <0.01). Nausea and vomiting, hypotensive episodes, and muscular cramps were more frequently observed. A worsening in patient’s welfare was also recorded but without statistical significance.

Conclusions. This clinical evaluation even if retrospective and lasting 1 year, may suggest that RRT does not per se represent a cause of the development and progression of the major complications related to diabetic disease.

Key words: cardiovascular complications, chronic renal failure, diabetes complications, diabetes mellitus, dialytic treatment, renal replacement therapy

Introduction

Over the last decades diabetic patients with chronic renal failure have progressively become the largest cohort among subjects requiring renal replacement therapy (RRT) in Western countries. The figure is at its highest in the USA, where diabetic uraemic patients account for more than one-third of the whole population of patients on regular dialytic treatment (37.4% of incidence reported by USRDS in 1997) [1]. The reasons for this increase are multiple and involve epidemiological and socio-economic aspects, such as lifestyle and genetic background [2,3]. Moreover these patients are drawn to the attention of nephrologists and diabetologists because of the severity of clinical complications which are related to metabolic disease.

In Italy the incidence of uraemia associated with diabetes has not shown the same increase as in other Western countries. According to the last EDTA Report [4], it is possible to divide Europe into two, Northern and Southern countries with higher and lower incidence of diabetes and chronic renal failure respectively. The recent reports estimated by Italian regional registries (Piemonte, Veneto, Lombardia and Calabria) show only a slight increase in incidence (10.8% Veneto, 17.1% Piemonte) [5], not dissimilar to that detected by Catalano et al. in 1990 [6]. In spite of this lower incidence this population represents an emerging problem due to the severity of clinical complications associated with higher morbidity and mortality [7]. For these reasons some authors suggest an early or better defined ‘pre-emptive’ kidney or kidney–pancreas transplantation in order to overcome the complications related to dialytic treatment. From this point of view, RRT could contribute per se to the progression of several morbidity or co-morbidity factors such as:

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— increase of insulin requirement due to glucose load in peritoneal dialysis solutions [8];
— hyperlipaemia related to glucose load during peritoneal dialysis [9];
— metabolic disorders promoted by haemodialysis-linked malnutrition [10];
— haemodialysis unphysiology with mineral and electrolyte metabolic disorders [11];
— amino acid and oligoelement imbalance in haemodialytic treatment [12];
— insulin resistance in patients on haemodialysis or peritoneal dialysis—particularly in type II diabetic patients [13].

**Aim of study**

In order to verify a single-centre experience on some aspects of this important issue a group of uraemic diabetic patients undergoing RRT from 1989 up until 1997 was examined.

The aim of the study was to evaluate retrospectively out of the cohort of patients, those who survived at least 1 year, in an attempt to detect the development and/or progression of the main complications related to diabetes, such as cardiovascular complications, state of vascular access, complications occurring during dialysis and other co-morbidity factors.

Evaluation of survival rate was not the aim of the present investigation.

**Methods**

From 1989 to 1997, 92 patients in the Padova city area, of about 696 000 inhabitants, including the southern part of its province and surrounding territories received RRT. Out of these patients, 16 were excluded because their survival was less than 1 year. Seventy-six subjects were studied, 41 males (53.9%) and 35 (46.1%) females. Twenty-eight of these (36.8%) were affected by type I and 48 (63.2%) by type II diabetes. The mean age at diagnosis was 42.8 ± 17.6 years (ranging from 3–71 years), mean age at start of dialytic treatment 64.3 ± 11.3 years (range 33–74 years), plasma creatinine at start of treatment was 9.5 ± 1.4 mg (range 6.3–12.4 mg/dl). The patients underwent the following initial treatment: 11 (14.5%) peritoneal dialysis (CAPD) and 65 (85.5%) standard bicarbonate dialysis (HD). The following parameters were evaluated retrospectively at initiation of RRT and after 1 year: Modality of RRT, type and condition of vascular access, changes in ophthalmological examination, cardiovascular complications, peripheral neuropathy by means of electromyographic modifications. Furthermore, the major intradialytic problems were examined at 12 consecutive dialytic sessions, at the start of haemodialytic therapy and at the seventh month of treatment. The condition of vascular access was also compared with that of a gender- and age-matched non-diabetic uraemic population. The degree of rehabilitation was evaluated using the modified Karnofski's scale [14,15]. The prevalence was compared using the Student’s t-test for paired samples. For data collection and processing a Microsoft Excel Program was utilized. P values ≤0.05 were considered statistically significant.

**Results**

After 1 year of RRT the modality of treatment of uraemic diabetic patients was as follows: 11 subjects remained on peritoneal dialysis (CAPD) following the same type of treatment utilized at the start. Out of the 65 patients treated by standard bicarbonate haemodialysis at the start, 51 (78.4%) remained on the same treatment, whereas the remaining 14 were moved after 1 year to the following haemodialytic modalities: 11 (16.9%) to acetate free biofiltration (AFB), two (3%) to paired filtration dialysis (PFD) and one to haemofiltration. The changes in dialytic treatment are given in Table 1.

The following changes were noted with regard to the treatment of metabolic disease. Out of the total of patients who survived 1 year, the 11 on CAPD increased their insulin dosage as follows: for five patients a twofold increase and for six a threefold increase in amount of insulin was needed. Out the 65 patients on haemodialytic treatment, six subjects were moved to dietary treatment whereas two patients, treated by diet only, were moved to insulin treatment. One patient treated with oral antidiabetic drugs was able to maintain metabolic control with diet management and one on bicarbonate dialysis was moved from oral antidiabetic drugs to insulin therapy. One patient had insulin withdrawn and only oral antidiabetic (Glybenclamide) and dietary treatment was given. Finally three patients experienced a decrease in insulin requirement. Mean glycated haemoglobin was 9.3 ± 1.1% at the start and 8.9 ± 0.9% after 1 year.

One of the most relevant problems in these patients is the difficulty in performing and maintaining efficient vascular access. The retrospective observation pointed out that in contrast to non-diabetic patients, the most common vascular access was a proximal artero-venous fistula (43 out 65 patients = 66.1%). In one patient a synthetic vascular graft (PTFE) was implanted. Two patients had a permanent central venous catheter and the cumulative number of surgical procedures/year was 1.83, significantly greater (P < 0.05) than that recorded in gender- and age matched non-diabetic patients, who accounted for 1.24 procedures/year.

Ophthalmological examination gave the following

### Table 1. Modality of treatment in 76 diabetic uraemic patients at initiation and after 1 year of RRT

<table>
<thead>
<tr>
<th></th>
<th>At start</th>
<th>After 1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peritoneal dialysis</td>
<td>11 (14.5%)</td>
<td>11 (14.5%)</td>
</tr>
<tr>
<td>CAPD</td>
<td>11 (100%)</td>
<td>11 (100%)</td>
</tr>
<tr>
<td>Haemodialysis</td>
<td>65 (85.5%)</td>
<td>51 (78.4%)</td>
</tr>
<tr>
<td>Bicarbonate dialysis</td>
<td>65 (100%)</td>
<td>11 (16.9%)</td>
</tr>
<tr>
<td>Haemofiltration</td>
<td>1 (1.5%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIC HD</td>
<td>51 (78.4%)</td>
<td></td>
</tr>
<tr>
<td>AFB</td>
<td>11 (16.9%)</td>
<td></td>
</tr>
<tr>
<td>PFD</td>
<td>2 (3.0%)</td>
<td></td>
</tr>
</tbody>
</table>

Changes in type of treatment at initiation and after 1 year of RRT: BIC HD, standard bicarbonate haemodialysis; AFB, acetate-free biofiltration, PFD, paired filtration dialysis.
results: a proliferative retinopathy was observed in 36 patients (47.3%) at the beginning and was detected in a further patient 1 year after (37 patients = 48.8%). Symptomatic peripheral neuropathy, prevalence was unchanged at the start and after 1 year of RRT (15 patients = 19.7%).

With regard to cardiovascular complications a progression in microangiopathy was observed, represented by peripheral vascular disease, principally located at the inferior extremities. This feature was seen in four patients (5.2%) at initiation of RRT and after 1 year was present in six (7.8%). Arrhythmias were present in 19 patients (25%), at the start and significantly increased \( (P < 0.05) \) in 26 (34.2%) after 1 year. Cerebrovascular diseases such as cerebrovascular accidents, transient ischaemic attacks, or stroke were evident in 19 patients (25%) and occurred in one more patient after 1 year (20 subjects, 26.3%). No change was seen in coronary artery disease or cardiomyopathy which remained evident in 15 patients (19.7%). Hypertension, evident in 72 patients (94.7%), decreased significantly \( (P < 0.05) \), being detected in 42 (55.2%) of uraemic subjects on RRT after 1 year. (Table 2).

Intra-dialytic complications are obviously restricted to the cohort of 65 diabetic patients on RRT, treated with extracorporeal haemodialysis. The most frequent complication occurring during dialytic treatment was hypotension, which maintained a similar prevalence at initiation and after 1 year (35 patients, 53.8% vs 37 patients, 56.9%). During the course of dialytic sessions arrhythmias occurred in 32 patients (49.2%) at the beginning of treatment and were evident in 35 (53.8%) after 1 year. No significant difference was noticed in headache, nausea, and vomiting, but hypoglycaemia, present in 26 (40%) patients during the first month of treatment, occurred in 20 (30.7%), showing an evident, albeit not statistically significant, reduction. Cramps occurred persistently in six patients (9.2%) at initiation and in eight (12.3%) after 1 year (Table 3). Patients rehabilitation state was regarded good in 43 (56.5%) vs 41 (53.9%), acceptable in 11 (14.4%) vs 13 (17.1%) and remained poor in 22 (28.9%).

**Discussion**

In Italy the increase in the number of diabetic patients, requiring RRT was less evident in comparison to the recent increase in the diabetic dialytic population of North Europe (EDTA Registry, 1998) [4]. Nevertheless, as our data confirm, this population does not represent a negligible problem. These diabetic patients, in fact, show a greater incidence of clinical complications than the non-diabetic population, mainly related to the progression of metabolic disease. Complications occur in spite of more appropriate metabolic control [16]. These complications explain the high morbidity and mortality rate of these patients. As already reported, the survival rate was not considered in the present investigation, owing to the heterogeneity of the cohort and the lengthy time interval (9 years) of the retrospective analysis of patients. Among the clinical features seen in our series cardiovascular complications were prevalent. These results are similar to those reported by Ritz [17] in diabetic patients on RRT.

Hypertension can be regarded as crucial in uraemic or non-uraemic diabetic patients [18–20]. At the start of RRT this complication is detected in almost all the subjects examined, but after 1 year 39.3% of uraemic patients showed a normalization in blood pressure, reducing to about one-half the number of hypertensive patients on RRT. This phenomenon was observed regardless of the modality of treatment, both in extracorporeal haemodialysis and in CAPD. However there was an evident increase in arrhythmia. This clinical feature can be related to diabetic cardiomyopathy [21,22], which can be worsened by other factors such as: dysaemia [23]; anaemia [24]; haemetic hyperviscosity [25]; and autonomic neuropathy [26]. Our investigation, though limited, was able to detect a greater but not significant prevalence of arrhythmia vs the non-diabetic population. This occurrence, can in part be explained by methodological problems. Recently, Holter continuous ECG monitoring [27,28] has been used to investigate these phenomena more accurately. Unfortunately, this method was not available to our retrospective study which examined only routine ECG evaluations of uraemic patients.

In order to overcome this problem and the dialytic intolerance, due to cardiovascular instability, our

<table>
<thead>
<tr>
<th>Complications occurring during dialysis</th>
<th>Absent</th>
<th>Rare</th>
<th>Frequent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting (%)</td>
<td>88.2</td>
<td>10.9</td>
<td>1.9</td>
</tr>
<tr>
<td>After 1 year</td>
<td>86.1</td>
<td>12.4</td>
<td>1.5</td>
</tr>
<tr>
<td>Cramps (%)</td>
<td>64.6</td>
<td>27.6</td>
<td>7.8</td>
</tr>
<tr>
<td>After 1 year</td>
<td>56.9</td>
<td>30.7</td>
<td>12.4</td>
</tr>
<tr>
<td>Hypoglycaemia (%)</td>
<td>63.3</td>
<td>23.5</td>
<td>14.2</td>
</tr>
<tr>
<td>( (P &lt; 0.05) )</td>
<td>68.1</td>
<td>24.6</td>
<td>7.3</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>58.4</td>
<td>18.4</td>
<td>23.2</td>
</tr>
<tr>
<td>After 1 year</td>
<td>64.6</td>
<td>16.9</td>
<td>18.5</td>
</tr>
</tbody>
</table>

\*\( P < 0.05 \). Occurrence of hypertension (number of patients with hypertension) was significantly lower after 1 year of RRT.

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**Table 2. Retrospective evaluation of cardiovascular complications in 76 diabetic patients at initiation and after 1 year of RRT**

<table>
<thead>
<tr>
<th>Complication</th>
<th>At start</th>
<th>After 1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>72 (94.7%)</td>
<td>42 (55.0%)*</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>19 (25.0%)</td>
<td>26 (35.0%)*</td>
</tr>
<tr>
<td>Ischaemic cardiopathy</td>
<td>15 (19.7%)</td>
<td>16 (21.05%)*</td>
</tr>
<tr>
<td>Cerebrovascular insufficiency</td>
<td>19 (25.0%)</td>
<td>20 (26.3%)*</td>
</tr>
<tr>
<td>Distal angiopathy</td>
<td>4 (5.2%)</td>
<td>6 (7.8%)</td>
</tr>
</tbody>
</table>
patients were moved to other modalities such as AFB and PFD. The relevance of this problem has also arisen recently and was pointed out in a recent multicentre study [29] by Verzetti et al. who demonstrated that AFB appears to be better tolerated than other techniques of extracorporeal treatment. Hypotension also behaves in a similar way and its prevalence did not show significant changes at initiation and after 1 year of RRT. This complication, more frequently observed during haemodialytic treatment, is more strongly related to volume depletion [30,31], decreased cardiac output [32] and autonomic dysfunction [33]. It should be emphasized that, in spite of a detectable reduction, the degree of rehabilitation after 1 year remains as a similar score to that at initiation.

Conclusions

Diabetic patients with chronic renal failure still represent the most important high risk cohort of uremic patients requiring RRT. Cardiovascular disease, micro and macroangiopathy, as well as cerebrovascular accidents remain the major problems and affect the morbidity and mortality rates of these patients. In spite of the high prevalence of severe complications, a positive message can be called from the data concerning hypertension. In fact, the implementation of new dialysis techniques [29], associated to more accurate personalization of treatment modality as well as to the use of new pharmacological agents, can reduce the prevalence of hypertension in these patients. This clinical examination, even if retrospective and limited to 1 year, was able to demonstrate a slight worsening in degree of rehabilitation which was not significant. Important clinical and technical implications are related to performing and maintaining efficient vascular access. The observation of these patients after 1 year of treatment suggests that dialytic treatment cannot be regarded per se—at least throughout 1 year—as an important factor influencing the progression of the complications which are related to the evolution of metabolic disease.

References


