Eighteen Months’ Experience with Haemodialysis in Children

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Since January 1969 a paediatric haemodialysis unit in the Hôpital des Enfants Malades (Paris) has taken care of children with end-stage renal insufficiency. Nineteen children and adolescents aged from twenty months to twenty years have been treated for two to twenty-one months with a view to cadaver kidney transplantation. Age, sex, initial disease and duration of regular haemodialysis are given in Table I.

Table I. Age, sex, initial disease and duration of regular haemodialysis

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Initial disease</th>
<th>Duration of regular haemodialysis (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 PIN</td>
<td>17- 4/12</td>
<td>M</td>
<td>Membranoproliferative GN</td>
<td>13</td>
</tr>
<tr>
<td>2 CAU</td>
<td>20- 1/12</td>
<td>M</td>
<td>Primary nephrotic syndrome</td>
<td>21</td>
</tr>
<tr>
<td>3 BEP</td>
<td>9- 9/12</td>
<td>F</td>
<td>Rapidly progressive GN</td>
<td>11/2</td>
</tr>
<tr>
<td>4 GOE</td>
<td>13- 4/12</td>
<td>F</td>
<td>Nephronphritis</td>
<td>17</td>
</tr>
<tr>
<td>5 GRA</td>
<td>12- 7/12</td>
<td>M</td>
<td>Proliferative GN</td>
<td>15</td>
</tr>
<tr>
<td>6 DEM</td>
<td>13-10/12</td>
<td>M</td>
<td>Hypoplasia with dysplasia</td>
<td>14</td>
</tr>
<tr>
<td>7 ADA</td>
<td>9- 5/12</td>
<td>F</td>
<td>Haemolytic uraemic syndrome</td>
<td>14</td>
</tr>
<tr>
<td>8 AND</td>
<td>14-10/12</td>
<td>F</td>
<td>Segmental renal hypoplasia</td>
<td>14</td>
</tr>
<tr>
<td>9 TOU</td>
<td>17-10/12</td>
<td>M</td>
<td>Primary nephrotic syndrome</td>
<td>20</td>
</tr>
<tr>
<td>10 LET</td>
<td>9- 8/12</td>
<td>F</td>
<td>Renal hypoplasia</td>
<td>13</td>
</tr>
<tr>
<td>11 BOU</td>
<td>14- 4/12</td>
<td>M</td>
<td>Unknown</td>
<td>13</td>
</tr>
<tr>
<td>12 PER</td>
<td>1- 8/12</td>
<td>F</td>
<td>Haemolytic uraemic syndrome</td>
<td>11</td>
</tr>
<tr>
<td>13 SEN</td>
<td>13- 1/12</td>
<td>M</td>
<td>Schönlein Henoch purpura</td>
<td>10</td>
</tr>
<tr>
<td>14 HAP</td>
<td>13- 6/12</td>
<td>F</td>
<td>Urinary tract abnormalities</td>
<td>9</td>
</tr>
<tr>
<td>15 COL</td>
<td>15- 4/12</td>
<td>M</td>
<td>Alport's syndrome</td>
<td>6</td>
</tr>
<tr>
<td>16 ALL</td>
<td>11- 9/12</td>
<td>F</td>
<td>Renal hypoplasia</td>
<td>3</td>
</tr>
<tr>
<td>17 GUI</td>
<td>14</td>
<td>M</td>
<td>Focal glomerular hyalinosis</td>
<td>2</td>
</tr>
<tr>
<td>18 MOT</td>
<td>11- 9/12</td>
<td>F</td>
<td>Proliferative GN</td>
<td>2</td>
</tr>
<tr>
<td>19 MIM</td>
<td>3- 1/12</td>
<td>M</td>
<td>Chronic interstitial nephritis</td>
<td>2</td>
</tr>
</tbody>
</table>
The decision to begin a haemodialysis-transplantation programme was taken in each case in accord with the stated wish of the family. The main clinical criterion considered was a glomerular filtration rate under 5ml/min/1.73 m² with or without uraemic complications.

Within the same period only two other children died of terminal uraemia, a boy with vesical extrophy and a girl whose parents were opposed to extended haemodialysis.

Thus, twenty-one children and adolescents with end-stage uraemia have been referred to our unit since January 1969. Half of them came from the Paris area whose population is about ten million.

METHODS

Under local or (more frequently) general anaesthesia cannulation of vessels was always possible with standard Silastic-Teflon Quinton cannulae. Generally the smallest tips (No.18) were used. In children over twenty kg body weight cannulae were inserted into the radial artery and a superficial vein. Under twenty kg body weight, cannulae were inserted into the brachial artery and the cephalic or a deep vein. In three subjects of more than thirty kg an arterio-venous fistula was created.

Dialysate was provided at a rate of 500 ml/min by an individual proportionating system and the final formula was: Na 132 mEq/l, K 2 mEq/l, Cl 100.5 mEq/l, acetate 38 mEq/l, Ca 6 mg/100 ml, Mg 1.5 mEq/l.

Three types of dialysers were used: a standard Kiil dialyser (Barnas-Lyon, France), a paediatric modified Kiil dialyser (Barnas-Lyon, France), and the Rhone-Poulenc disposable dialyser.

If preserved blood is not to be used for priming, extracorporeal blood volume becomes critical in paediatric haemodialysis. The eight-layer Rhone-Poulenc dialyser offers a flexible solution to the problem of extracorporeal volume (Figure 1), and the use of special connection tubing may decrease this volume further.

Measurements of dialysance were carried out with the three types of dialyser mentioned above (Figures 2 and 3). It is clear that for an equal extracorporeal volume the best results are given with the Rhone-Poulenc dialyser, and that the paediatric Kiil model gives better results than the standard Kiil.

Each child was dialysed twice a week (twenty to thirty hours per week). The dialyser and the number of layers were chosen according to weight; the upper limit of extracorporeal volume tolerance is between 10 and 15 ml/kg, depending on the haematocrit and the state of hydration. Layers are successively opened to the blood stream. Arterial pressure, pulse and weight were checked regularly during dialysis to adjust ultrafiltration. Except for patients with arteriovenous fistula no pump was used.
A limited diet was prescribed in every case: 1 to 2 mEq/kg/day of sodium and potassium, depending on the urinary output, 1 to 3 g/kg/day of proteins according to age, with 50 to 70% of protein being of animal origin. Vitamins, calcium and iron were added regularly (as Kayexalate and Aluminium hydroxide) according to the plasma potassium and phosphorus concentrations.

![Figure 1. Theoretical extracorporeal volume of blood with three types of dialyser](image)

![Figure 2. Urea dialysance compared to the volume of blood in the layers of three types of dialyser](image)
RESULTS AND DISCUSSION

After starting regular haemodialysis, a general improvement was observed as is usual (Fine et al, 1968, 1969). In three cases with pericarditis, symptoms disappeared within two to three weeks. Ten to thirty days after the first haemodialysis, children regained good physical activity and could be sent home. All children above six, except one, now attend school normally.

More or less severe anaemia persists. Transfusions are required in some children in order to maintain the haematocrit above 15%.

Arterial pressure promptly returned to normal except in four cases; in two of these, hypertension was well controlled with hypotensive drugs; in two others with malignant hypertension nephrectomy had to be performed; in both these cases the initial disease was the haemolytic-uraemic syndrome.

CANNULA LONGEVITY

Cannula problems have been numerous and varied: clotting, infection of exit sites, eczema, skin necrosis, secondary angulation of the tip, vein sclerosis and intussusception of the tip in a deep vein. Some of these accidents have been transient, some necessitated reinsertion of one or both cannulae at another site. During 171 patient-months experience we observed one failure of arterial cannula per 1.2 years and one failure of venous cannula per 0.8 years; the global failure rate is 1.9 per cannula-year.
COMPICATIONS

Other complications are rare:

One patient with pericarditis (Case No. 7) improved rapidly with increasing haemodialysis.

Four episodes of transient pulmonary oedema responded promptly to adequate ultrafiltration.

Seizures were observed in two cases in relation to dialysis; both had electroencephalographic abnormalities persistent between haemodialysis. Case No.12 responded well to phenobarbitone.

One case (No.11) developed staphylococcal septicaemia from an infected shunt; recovery was obtained after reinsertion of the cannulae in the other arm.

A transient icteric hepatitis with Australian antigen in the blood was observed in one case (No.4). Two others exhibited only mild biochemical abnormalities.

RENAL OSTEODYSTROPHY

Renal osteodystrophy and hyperparathyroidism were obvious in two children with a long-standing renal failure.

In one case after ten months' treatment with vitamin D (16,000 units/day) there was no change in the radiological findings; two months after beginning treatment with 25-OH cholecalciferol (16,000 units/day) a dramatic improvement was noted (Figure 4).

Figure 4. Case 14. X-ray of hand before (right) and after (left) two months treatment by 25 OH-D3

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Symptoms of rickets were improving, and even the radiological signs of hyperparathyroidism were disappearing; however, severe hypercalcaemia compelled us to perform parathyroidectomy. Biopsy of the iliac crest before the 25-OH cholecalciferol treatment showed an excess of osteoid and resorption; three months later, just before parathyroidectomy a second biopsy showed a marked reduction of osteoid, but an increase of resorption. Thus, 25-OH cholecalciferol appears to be much more active than vitamin D₂ in the same dosage expressed in antirachitic units, and must be used with caution.

GROWTH

Little information is available on the growth of children undergoing haemodialysis; however, this is one of the most important points to be considered. Among children treated in our unit, eight have sufficient follow-up to allow growth studies. Measurements were always made in the morning, in a recumbent position and by the same physician. Two groups of patients must be distinguished (Figures 5a, b and c).

In the first group (2 cases) significant growth was noted:

A boy of thirteen (Case No.5) whose growth had been almost stationary during the previous year, started growing again whilst undergoing haemodialysis. He exhibited a catch-up curve in the first six months; afterwards, he went on growing more slowly. The gain of +7 cm obtained within 15 months equals the mean growth of boys having the same skeletal age.

A girl aged twenty months (Case No.12) when dialysis was started went on growing as before during the first months of dialysis; growth rate decreased thereafter, but she gained 6.5 cm within the ten months' dialysis period, the mean growth for her skeletal age being 8 cm for the same period.

In the second group, growth rate is slow:

Two children (cases 7 and 13) had normal stature when haemodialysis began. Growth rate progressively decreased and is now quite insignificant.

The others had long-standing renal failure.

Two of them (Cases Nos.10 and 14) were short, and are growing slowly; however, patient No.14 has grown 3 cm since parathyroidectomy was performed, three months ago.

A girl of fourteen (Case No.4) with sexual maturity did not grow more than other girls with the same skeletal age.

A boy of fourteen (Case No.11) gained only 2.5 cm in the year versus a mean of 6 cm for the same skeletal age.
Figures 5a, b and c. Growth curves of children on intermittent haemodialysis (mean and standard deviation according to Sempe and Masse, 1968)
To summarise, although generally impaired, growth is possible in children on extended haemodialysis; gain in stature seems greater during the first six months than later on. For the moment, there is no satisfactory explanation to account for the variable growth rate observed in children undergoing haemodialysis.

GROWTH HORMONE

Data concerning growth hormone secretion in adults with renal failure indicate normal or high fasting levels and possibly abnormal regulation of secretion.

In normal subjects, after glucose infusion, plasma growth hormone levels (IRGH) are rapidly suppressed and rise between the 2nd and 3rd hour. In haemodialysed uraemic patients, neither early suppression (Samaan & Freeman, 1970), nor late increase of IRGH (Lindsay et al, 1969) have been observed, however plasma IRGH rose when these patients were subjected to stress (Lindsay et al, 1969).

The following preliminary results were obtained in four children on extended haemodialysis. IRGH was measured according to the method of Rosse-lin et al (1965, 1968).

Table II. Plasma growth hormone after IV Tolbutamide (1g/1.73 m2)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Blood glucose mg/100 ml</th>
<th>IRGH ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Minimal Level</td>
</tr>
<tr>
<td>GR (No. 5)</td>
<td>85</td>
<td>35</td>
</tr>
<tr>
<td>GO (No. 4)</td>
<td>110</td>
<td>75</td>
</tr>
<tr>
<td>AD (No. 7)</td>
<td>70</td>
<td>35</td>
</tr>
<tr>
<td>LE (No.10)</td>
<td>100</td>
<td>40</td>
</tr>
</tbody>
</table>

Table III. Plasma growth hormone after IV Insulin (0.1 u/kg)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Blood glucose mg/100 ml</th>
<th>IRGH ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Minimal Level</td>
</tr>
<tr>
<td>GR (No. 5)</td>
<td>75</td>
<td>46</td>
</tr>
<tr>
<td>GO (No. 4)</td>
<td>95</td>
<td>40</td>
</tr>
<tr>
<td>AD (No. 7)</td>
<td>76</td>
<td>40</td>
</tr>
<tr>
<td>LE (No.10)</td>
<td>165</td>
<td>100</td>
</tr>
</tbody>
</table>
Response to hypoglycaemia

Two methods of stimulation were used: intravenous insulin (0.1 u/kg) and intravenous tolbutamide (1 g/1.73 m²). Results are given in Tables II and III. Three children (Cases Nos. 4, 5 and 7) had a normal response in one test; only one child (Case No. 10) had a poor increase of IRGH in both tests, but during the insulin test, the blood glucose decreased by less than 40% (Somogyi and Nelson method).

Nevertheless, in all four cases peak plasma IRGH was over 5 ng/ml, which is the minimal level reached in our laboratory by normal children and children with short stature without growth-hormone deficiency. In addition, no constant correlation could be found between GH secretion and growth rate. Boy 5 did grow and responded well to insulin (12 ng/ml). Girl 10 had a slow growth rate and responded weakly to insulin and tolbutamide (5.5 ng/ml) but girl 7 stopped growing in spite of a good response to hypoglycaemia (12.7 ng/ml).

Thus our data are in accordance with the hypothesis that normal growth hormone secretion in response to hypoglycaemia is not sufficient to allow normal growth rate.

Plasma IRGH was determined during haemodialysis

Dialysis was performed from 9 am to 7 pm against a dialysate without glucose; assays were done in arterial and venous blood at 9 am, 10 am, 2 pm, 7 pm. Meals were absorbed at 7 am, noon, and 5 pm. Control observations were made at the same times two or three days later.

![Graph](image)

Figure 6. Plasma growth hormones levels during haemodialysis in four children

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Plasma IRGH levels were lower during haemodialysis than during control periods (Figure 6). We have no explanation for this fact. The relationship with blood glucose levels is not clear; blood glucose rises slowly during dialysis in the four patients, though glucose was absent from the dialysate.

Passage through the dialyser reduced the plasma insulin significantly (IRI) (Figure 7) which may indicate destruction or adsorption. However, arterial IRI levels increased during dialysis. On the contrary IRGH was not altered by the passage through the dialyser in our four cases, but the low levels of growth hormone do not permit definite conclusions.

**PSYCHOLOGICAL FEATURES**

Most of the children were unknown to us prior to their admittance to the haemodialysis programme. Upon their arrival they displayed the classic 'uraemic syndrome' (depression, drowsiness, indifference etc). These symptoms have generally disappeared on the 2nd or 3rd dialysis. The time taken for adaptation to the restrictions imposed on them for the sake of the treatment has varied in length according to each child's personality before the onset of renal insufficiency — inasmuch as we can deduce it from the parents' interviews. The major psychological problems lie in the resolution
of the conflict between dependence and autonomy. This conflict which characterises any child’s personality development is enhanced by the dependence on the machine, the hospital, the doctors, and the fact that it is not possible to set a definite limit on the duration of the treatment. During this period of adaptation the family’s role is most important in that it can help the child to accept these restrictions and still keep on with his school and social activities, or, on the contrary it can hinder the child from leading a fairly normal life, by considering him as an invalid. Doctors and nurses may become deeply emotionally involved with these children whose lives they have saved, but whose survivals remain quite doubtful and, at times, quite painful. Longitudinal studies will be necessary to appreciate the repercussions of these new treatments on the psychological development of these children.

SUMMARY

Technical aspects of haemodialysis in children are not fundamentally different from those of adult dialysis; but the dialyser must be adapted to age, paying particular attention to extracorporeal blood volume.

Nineteen children and adolescents aged from twenty months to twenty years with end stage renal disease have been treated by haemodialysis, in a paediatric unit, for periods of two to twenty-one months.

Among eight with adequate follow up, only two grew well. There is no explanation to account for the variable growth rate.

Growth Hormone was measured in four cases after hypoglycaemic stimulation and levels over 5 ng/ml were reached in all. This is the response obtained in children without GH deficiency.

Complications were rare and there were no major psychological problems. Rehabilitation was good in virtually all the cases, allowing family life and normal school attendance. Thus, haemodialysis appears to be as feasible and valuable method in children, as in adults.

ACKNOWLEDGMENTS

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REFERENCES

Rosselin, G. and Dolais, J. (1968) Annales de biologie clinique, 26, 763