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Original article

Electrocardiographic monitoring in children with chronic renal failure

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Abstract. Continuous electrocardiographic (ECG) monitoring was performed over 24 h in 44 children at various stages of chronic renal failure in order to determine the incidence and nature of cardiac dysrhythmias. In addition the ECG was followed during haemodialysis sessions and during dialysate exchanges in continuous ambulatory peritoneal dialysis (CAPD) patients. In contrast to adult patients on haemodialysis life-threatening dysrhythmias were not observed. The proportion of children with premature ventricular complexes (41%) was at the upper limit of that in healthy children. A relatively high heart rate was found in children on CAPD, which varied during the exchange procedure. In 57% of all patients a transient marked prolongation of the QT interval up to 40% greater than normal was observed without obvious changes in the serum electrolyte levels. Continuous ECG monitoring is a useful tool for detecting alterations of cardiac rhythm and conduction in at-risk children with renal failure.

Key words: Cardiac dysrhythmias – Chronic renal failure – Dialysis – Electrocardiography – Potassium – Transplantation – Uraemic heart disease

Introduction

Uraemic heart disease is a common and potentially lethal complication of children with chronic renal failure (CRF) [1, 2]. The European Dialysis and Transplant Association (EDTA) reported that out of 326 paediatric patients who died on renal replacement therapy during 1981–1985, 50% had a cardiovascular cause of death, which was specified as "cardiac arrest" and "hyperkalaemia" in 14% each [3]. The current methods of cardiological monitoring, such as chest X-rays, standard electrocardiography (ECG) and echocardiography do not adequately reflect the cardiac state because they usually assess only changes observed at rest and neglect spontaneous variations of cardiac function, reactions to stress, exercise or to therapeutic procedures. Using long-term (Holter) ECG monitoring [4] we have tried to obtain more information on cardiac function in children with CRF. We were particularly interested to know (1) the incidence and nature of potentially dangerous cardiac dysrhythmias and (2) the changes of cardiac conduction and repolarisation during the course of different forms of dialysis. The study followed similar investigations which have applied long-term ECG recording to adult patients on haemodialysis treatment [5–13].

Patients and methods

ECG monitoring was performed over 24 h in 44 children with CRF who were clinically stable and were subdivided into four groups according to the mode of treatment: (1) conservative therapy, i.e. preterminal CRF (CT); (2) maintainance haemodialysis (HD); (3) continuous ambulatory peritoneal dialysis (CAPD); and (4) successful transplantation (TP) (Table 1). Patients in the HD group underwent ECG monitoring on a day of dialysis and in 6 cases again on a day without dialysis. Drug treatment included vitamin D, aluminium hydroxide, calcium carbonate, sodium (Na) bicarbonate and various antihypertensive drugs: propranolol (19), hydralazine (14), nifedipine (5), captopril (2), prazosin (1). The mean blood pressure at the time of ECG monitoring was 129/88 mmHg in patients on CT, 123/70 mmHg (predialysis) on HD, 108/73 mmHg on CAPD and 120/85 mmHg after TP. No patient received digitalis.

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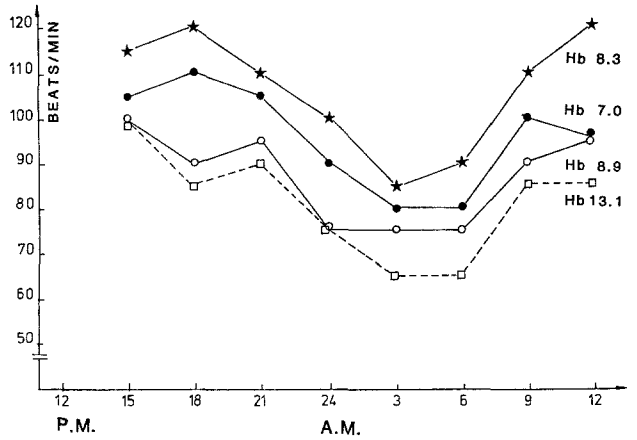

Fig. 1. Heart rate measured at 3-h intervals in children with chronic renal insufficiency on conservative treatment (*CT* –○–), haemodialysis (*HD* –●–), continuous ambulatory peritoneal dialysis (*CAPD* –*–) and after transplantation (*TP*– –□– –). *Hb:* mean haemoglobin levels

Patients on HD were dialysed three times per week for an average of 4.2 ± 0.5 h, usually with capillary dialysers using cuprophane membranes. The dialysate contained Na 140 mmol/l, potassium (K) 2.0–2.5 mmol/l, calcium (Ca) 1.5–1.75 mmol/l, magnesisum 0.5–0.75 mmol/l, glucose 1.1 g/l, and acetate 36 mmol/l. The mean duration of HD treatment was 13 (2–23) months. Patients on CAPD were slightly younger than those on HD (NS). They generally had four exchanges a day with a filling volume of 400–1500 ml per exchange. Mean duration of HD and CAPD treatment was 3 (2–23) and 6 (1–18) months, respectively. The mean survival of TP patients after a successful graft was 21 (4–39) months.

Holter monitoring. Two bipolar leads were recorded continuously during 24 h on an ambulatory basis. High-speed analysis was performed using a Pathfinder II system (Reynolds). The data were analysed during continuous operator control [14]. In order to follow diurnal ECG changes short tracings were analysed at random every 3 h. As ECG references we used the data given by Davignon et al. [15] for heart rate (HR) and by Gutheil [16] for the other parameters. QT intervals were assessed at 3-h intervals and calculated as QTc according to Bazett's formula [17]. They were regarded as normal if their HR-related values were within −5% to +10% of the standard.

Additional investigations. Blood pressure was recorded at least once. Blood samples were taken in the morning for analysis of haemoglobin (Hb), urea, creatinine (CR) and electrolytes. In the HD group blood pressure and blood chemistry were assessed at the start and at the end of the session. Further methodological details have been described elsewhere [18].

Results

Heart rate

The mean HR was 125000 ± 23500 beats 24/h in CT, 135000 ± 73400 in HD, 146000 ± 23700 in CAPD and 117000 ± 17400 in TP patients (NS). The 24-h HR did not correlate with Hb. The HR data analysed at 3-h intervals showed a physiological decrease during the night [15] in all treatment groups (Fig. 1). Again HR was highest in the CAPD patients followed by the HD patients. Six age-matched patients (mean age 14 years) in each of these two groups who were not treated with beta blocking agents were selected for comparison. Despite higher Hb values in CAPD patients, HR was significantly higher in this group compared with HD patients at midnight, 3 a.m. and 6 a.m. ($P < 0.05$). During HD the HR increased by 30% (−20% to +55%), followed by a decrease after fluid replacement (150 ml of 0.9% NaCl). Usually the patient's preparation for returning home induced a further period of sinus tachycar-

Table 1. Clinical and biochemical data in 44 paediatric patients undergoing 24-h ECG monitoring

Patient group	*n*	Age (years)	Sex (m/f)	Weight (kg)	Height (cm)	Blood urea (mg/dl)	SCR (mg/dl)	Hb (g/dl)	K (mmol/l)	Ca (mmol/l)	*n* with beta-blockers
1. Preterminal CRF	13	13.1±4.7 (3.1–18.2)	5/8	35.6±17	140±27	143±28	4.7±2.1	8.9±1.6 (4.8–10.1)	4.5±0.6 (3.5–5.2)	2.1±0.4 (1.0–2.4)	8
2. Haemodialysis	11	14.5±2.4 (11.5–19.4)	8/3	37.4± 9	149±14	185±28 B	11.5±2.3 B	7.0±1.4 B (5.5–10.2)	5.0±0.7 B (3.9–6.3)	2.4±0.4 B (1.9–3.4)	2
						142±200 A	5.3±2.0 A	8.3±2.5 A	3.6±0.2 A (3.2–4.0)	3.0±0.3 A (2.6–3.8)	
3. CAPD	10	10.1±6.2 (2.1–17.3)	3/7	30.6±20	121±32	124±26	6.7±4.3	8.3±0.6 (7.5–9.5)	4.2±0.5 (3.5–4.8)	2.4±0.3 (2.0–2.8)	2
4. Transplantation	11	14.8±3.9 (4.5–20.5)	6/5	44.0±18	142±24	40±15	1.6±0.9	13.1±1.6 (10.5–16.1)	4.0±0.4 (2.8–4.4)	2.4±0.1 (2.2–2.6)	7
Total	44[a]										

Means ± SD are given; B = before dialysis; A = after dialysis; BUN = blood urea nitrogen; SCR = serum creatinine

[a] One patient was examined both in group 1 and in group 3

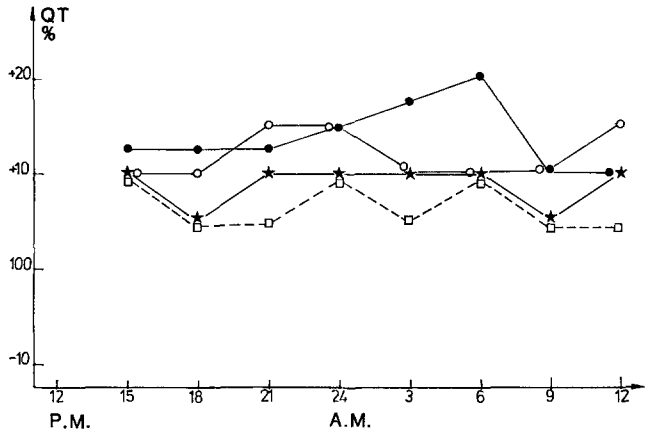

Fig. 2. QT intervals measured at 3-h intervals. Abbreviations as in Fig. 1

dia. In 3 CAPD patients HR increased during refilling by 20–50 beats/min, while in another 3 it decreased and in 4 it was unchanged. Periods of sinus tachycardia (163–190 beats/min) occurred in 17 of 44 patients (Table 2), mainly during exercise and in HD patients mainly following the dialysis session.

PQ and QRS intervals

The PQ time analysed at 3-h intervals showed a similar pattern in all groups with a slight (physiological) increase at night. Individual mean values remained between 0.13 and 0.16 s. A first-degree heart block with PQ intervals exceeding the upper limit of normal [15] was noted in 4 children (1 taking a beta blocker) at night (Table 2). This is similar to the frequency observed in healthy children. A single CT child was observed with an intermittent second heart block (Wenckebach type) while receiving small doses of propranolol and nifedipine. An atrioventricular rhythm was observed in only 3 children (7%) for a maximum of 5 min compared to 21–45% in healthy children [19, 20]. QRS intervals were within normal limits in all except 2 cases; a CT and a TP patient had an increase to a maximum of 0.14 s and 0.12 s at night, respectively.

QT interval

The QTc interval varied greatly during the testing period. It was clearly increased (⩾20% above QTc) at least once in 25 of the 44 children (57%). Individual mean QTc was persistently high (+10%) in the CT patients and reached even higher values in the HD patients at night (Fig. 2). In the CT patients alarming levels of +20% up to +40% were seen in 4 of 7 patients with a serum CR less than 5 mg/dl, and in 5 of 6 patients with a serum CR greater than 5 mg/dl. Prolongation of QTc was noted in 4 of 9 CT patients despite the absence of hypocalcaemia (<2.25 mmol/l). Mean serum K was 4.5 (3.5–5.1) mmol/l and was not related to the QT interval.

QTc values greater than 20% above the standard were found in 8 of 11 HD patients at least once during the 24-h period. when QTc was analysed at 15- to 30-min intervals during the Hd session the mean values increased slightly but significantly from +10% immediately before HD to +15% of normal after 3 h of HD, followed by a slight drop. In 1 case it reached +30% during dialysis. The mean changes of serum Ca and K levels during HD are listed in Table 1. Changes of serum electrolyte levels and changes of QT intervals varied independently of each other during HD sessions. In the CAPD patients the mean QTc was lower than in the HD patients (NS) but individual values of +20% were reached in 5 of 10 children. During a dialysate exchange QTc intervals

Table 2. Changes of heart rhythm in 44 paediatric patients with chronic renal insufficiency

	CT	HD	CAPD	TP	Total
Number of patients	13	11	10	11	44[a]
Sinus tachycardia (>60 beats/min)	4	7	5	1	17
Supraventricular extrasystoles	2	2	–	2	6 (15%)
Ventricular extrasystoles	3	6	3	6	18 (41%)
>10/24 h	–	–	1	2	3
Artrioventricular block					
First degree	1	1	1	1	4
Second degree	1	–	–	–	1

CT = Conservative treatment; HD = intermittent haemodialysis; CAPD = continuous ambulatory peritoneal doalysis; TP = transplantation

[a] One patient was examined both in group 1 and in group 3

changed only slightly. A prolonged QTc (+20 to 35%) was observed in 3 of 11 TP patients.

Dysrhythmias

Isolated supraventricular premature beats (extrasystoles) were noted in 6 of 44 children (15%) with a frequency of 1–3/24 h. Premature ventricular complexes (PVC) were observed in 18 of 44 patients (41%). They all were monomorphic, occurred mainly at night (as found in normal children) and were not related to exercise. We observed less than 10 PVC/24 h in 15 patients, in 1 patient as a bigeminal rhythm. In one CAPD patient we found 97 PVC/24 h, in a TP child 22 PVC in the form of couplets, and in a 17-year-old adolescent TP patient with cystinosis 458 PVC/24 h associated with a varying coupling interval. During exchanges in CAPD patients cardiac dysrhythmias were never noted.

Discussion

In adult patients with CRF Holter monitoring has been mainly applied to detect potentially dangerous dysrhythmias during dialysis treatment, with contradictory results [5–13]. Earlier studies underlined the high frequency and serious nature of ventricular dysrhythmias in dialysed patients [5, 6, 8]. Recent reports have shown a lower incidence [9–11]. The variable findings could be explained by differences in patient's age, pre-existing heart disease, medication, electrolyte composition of the dialysate or by variable definitions. The pathogenesis of ventricular dysrhythmias in CRF is still debated. From two large studies in adult patients on HD it was concluded that preexisting left ventricular dysfunction was the most important predictor of severe ventricular dysrhythmias [12, 13].

In our study we compared the findings of 24-h ECG monitoring in four groups of paediatric patients with CRF. Except for a slightly younger age in the CAPD patients the groups had comparable clinical characteristics. The unexpected finding of this study is the complete absence of cardiac dysrhythmias when compared with representative investigations in healthy children of similar age [19–23]. The incidence of supraventricular premature beats was 15% in all our patients compared with 6–44% in normal children followed by Holter monitoring. The proportion of children presenting with PVC was at the upper limit (41%) of that found in healthy children of similar age (16–41%), but lower than in young adults [24]. The rare monomorphic appearance of PVC at night suggests that their clinical significance is low. Only 3 of our patients had more than 20 PVC/24 h, 1 on CAPD and 2 TP patients; one associated with couplets and one with a changing coupling interval. None of our HD patients showed abnormal ventricular dysrhythmias. This is in contrast to a similar series of nine children on HD followed by Holter monitoring reported by Germain et al. [25]; two of them showed above 30 PVC/h.

The relatively high resting HR found in our HD and CAPD patients contrasts with a lower resting HR in the CT and TP groups. Unexpectedly, a correlation between HR and the degree of renal anaemia was not noted. The rise in HR due to volume depletion during HD is a well-known feature in children [26] and adults [11, 12]. The normal circadian pattern of HR with a fall during night was preserved in all treatment groups, which is similar to adult patients on HD [11, 12]. In a selected group of age-matched children who received no beta blocking therapy we found the circadian pattern to be more pronounced on HD than on CAPD, probably as a result of an HD-induced rise in HR during day-time dialysis.

The reason for the higher HR in CAPD- compared with HD-treated children is not clear. It is known that various vagal stimuli are associated with peritoneal dialysis (insertion of catheter, distention of abdomen, peritonitis) and may lead to bradyarrhythmias [27]. Monitoring of HR during the dialysate exchange of our CAPD patients showed inconsistent findings. There is, however, no doubt that dysfunction of the autonomous nervous system plays an important role in the changes of HR observed in patients with CRF [28].

A prolonged QT interval, which may be associated with an increased risk for life-threatening dysrhythmias, is a well-known alteration found in the ECG of adult HD patients [11, 12, 29]. In a series of 64 children with preterminal CRF (serum CR >5 mg%) investigated in our centre by a standard ECG, 13% had a prolonged QT interval in the presence of hyperkalaemia and hypocalcaemia [30]. In the present series investigated over 24 h we were surprised by the high proportion (57%) of children with transient prolongation of the QT interval, which was sometimes alarming, especially during the first hours after HD. This finding might be explained by a K shift from the intracellular to the extracellular space immediately after dialysis, since it is known that the intracellular K concentration is an important determinant of the QT interval. We demonstrated earlier that whole body K, representing mainly intracellular K, is significantly reduced in children

with CRF [31]. A prolonged QT interval might also be ascribed to hypocalcaemia; however, a strong correlation between the length of QT interval and serum Ca levels was not observed. QT prolongation in our patients might therefore be interpreted as a sign of imbalance in the cardiac sympathetic innervation [32] or of cellular electrolyte shift [33].

In conclusion, 24-h monitoring of the ECG in children with CRF disclosed almost no serious alterations of heart rhythm but a transient prolongation of the QT interval in more than half of the patients, which remains unexplained. Since the QT changes may persist after TP together with other alterations of heart function [34], they may indicate irreversible cardiac damage.

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