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Original article

High lead content of deciduous teeth in chronic renal failure

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Abstract. Lead is suspected to contribute to the progression of kidney disease. Lead content of blood and deciduous teeth was determined in 22 children aged 5–14 years at different stages of chronic renal failure (CRF). In addition, individual lead exposure was estimated from histories. The results were compared with a control group of 20 siblings or neighbours of patients living in the same environment (C1), and to a group of children known to be free of excessive lead exposure (C2). The mean blood lead concentration of patients was normal (mean 2.9 μg/dl, range 1.1.–10.1). Mean dental lead content was 2.8, 1.7 and 1.4 μg/g in CRF, C1 and C2, respectively. It always exceeded that of healthy peers. Increased dental lead content was associated with a high risk of exposure. It is suggested that both an increased lead uptake and renal dysfunction may contribute to the increased lead burden in children with CRF.

Key words: Lead – Chronic renal failure – Dialysis – Toxic nephropathy – Teeth

Introduction

Lead is a well-known nephrotoxic agent. Prolonged exposure in adults or children has been associated with a slowly progressive "lead nephropathy" characterized by renal scarring, minor urinary abnormality and frequent association with gout and hypertension [1–4]. The rather non-specific kidney lesions initially consist of tubular atrophy, interstitial fibrosis and vascular changes [5].

Recently it was postulated that adult patients with chronic renal failure (CRF) may have an increased lead burden in the absence of an obvious excessive exposure to lead [4]. This view is supported by: (1) increased bone lead before and after the start of dialysis treatment [6–8]; (2) high blood levels of lead (PbB), especially when corrected for the anaemia [9–11]; (3) excessive urinary lead excretion following the infusion of $CaNa_2EDTA$ [2, 6, 12], especially in CRF patients with some lead exposure but without obvious plumbism [10].

The possibility that occult plumbism may be a risk factor for progression of chronic renal disease has been raised for adults [4], but this issue has not been evaluated in children. In general, children are at a higher risk of developing adverse health effects from lead exposure than adults [13–15]. Earlier investigations suggested that prolonged lead poisoning in childhood may be a risk factor for later development of renal damage [1, 2], although this view was challenged by later studies [16]. The increased lead burden reported for adult CRF patients led us to investigate whether uraemic children exhibit a similar accumulation of lead. Besides blood, teeth were examined because, similar to bone, they represent the slow exchange pool of lead. Lead concentration in deciduous teeth (PbT) is an appropriate marker of past lead exposure [14, 15, 17, 18], although some lead deposited before the age of 18 months can be lost through exchange [19]. With that caveat, PbT reflects lead exposure, starting from the late prenatal period up to the loss of deciduous teeth between the ages of 6 and 12 years, since dental development starts during the 4th month of gestation and there is no placental barrier for lead.

Patients and methods

From January 1988 to April 1989 we examined 22 children (14 boys, 8 girls) with CRF aged 5.7–14.2 (median 9.8) years at the time of the loss of the first examined tooth. The patients originated from a large geographical area covering southwest Germany, but were mainly from rural areas. Sixteen patients had a congenital and 6 an acquired kidney disorder. The first increase in serum creatinine levels (SCR) above the age-related standards was observed at an age of less than 1 year in 12, between 1 and 5 years in 5 and between 5 and 11 years in 5 patients. At the time of tooth collection, 11 children were on conservative treatment [(CT) mean SCR 2.0 mg/dl, range 1.0–4.0]; 8 were being treated by dialysis (D), either by haemodialysis (HD) ($n = 2$) or continuous ambula-

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Table 1. Deciduous teeth examined

Group	No. of probands	No. of teeth examined		Age at loss (years)
		incisors	cuspids + molars	
CRF	22	22	9	8.8 (5.7–14.2)
Controls 1: healthy siblings or neighbours	20	20	9	8.7 (6.0–14.4)
Controls 2: healthy children with low lead exposure	16	12	7	8.0 (6.0–12.0)

CRF, Chronic renal failure

Table 2. Blood lead levels (PbB) in children with CRF

Treatment group	PbB (μg/dl)		
	n	Mean ± SD	Range
Conservative treatment	11	3.0±1.7	1.1– 6.1
Dialysis	8	2.5±2.0	1.3–10.1
Transplantation	3	4.9±1.5	3.7– 6.4
All patients with CRF	22	2.9±1.8	1.1–10.1
Healthy children in non-polluted area (Borken, 1988) aged 6–7 years (Brockhaus et al., unpublished work)	238	4.7±1.3	2.2–10.6

tory peritoneal dialysis (n = 6) for 2–38 (mean 12) months and 3 successful transplants (TP). The terminal stage of CRF (first D) was reached at the age of 4.7–10.8 (mean 7.0) years (n = 11).

For comparison we examined two control groups of similar age (Table 1): (1) a group of 10 healthy siblings and 10 healthy neighbours of the patients, all residing in the same geographical area and assumed to be subjected to similar specific lead exposure (group C1); (2) 16 unrelated healthy children living in an environment with low lead exposure as indicated by a risk factor of zero (see below, group C2).

For each patient a careful history of the renal disease was taken. The specific exposure to lead was estimated from six risk factors comprising: (1) the father's employment in the lead-processing industry [20]; (2) smoking habits of parents (>10 cigarettes/day or smoking of mother during pregnancy and 1st year of patient's life); (3) living in a lead-polluted environment, e.g. near highways or lead-processing industries; (4) persistence of lead pipelines in the plumbing system of the house of residence (year of construction before 1940) [18]; (5) location of the family's garden less than 10 m from a highway; (6) regular visit to a playground at a similar distance from a highway.

In all patients, but not in controls, blood was drawn for determination of PbB, with EDTA as an anticoagulant, taking precautions to avoid any contamination. Blood was stored at –80° C until analysis, and the lead concentration was determined after deproteinization using electrothermal atomic absorption spectrophotometry [15].

Non-carious deciduous teeth were analysed within a few weeks to months after falling out. The location of the shed teeth was similar in patients and in control groups, with incisors making up the largest proportion followed by cuspids and molars (Table 1). The distribution of the different position of teeth was similar in the three groups. The mean weight of the teeth was also very similar in patients and C1, although individual variations were large.

PbT was determined after washing, weighing and dissolving the teeth in concentrated nitric acid by using L'vov platform graphite furnace atomic absorption spectrophotometry [15, 21]. All measurements were performed in duplicate; if more than one tooth was available for analysis the mean PbT was taken for evaluation. Further details have been reported by Veits [22].

Statistical analysis. Student's t-test and linear regression analysis were used for statistical analysis.

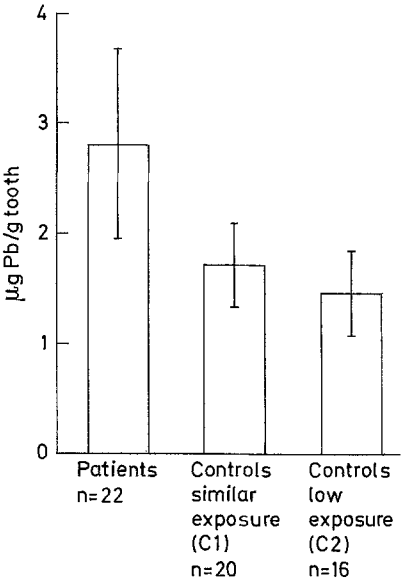

Fig. 1. Lead (*Pb*) concentration in deciduous teeth of children with chronic renal failure (n = 22) and of two control groups (C1, n = 20; C2, n = 16). Values are means ± SD

Results

Blood lead levels

PbB are shown in Table 2. In the patients the geometric mean PbB was 2.9 μg/dl, i.e. somewhat lower than in a large group of normal children of similar age living in a non-polluted area of northwestern Germany and examined in the same laboratory [15] (difference not significant). Only 4 patients had PbB greater than 5 μg/dl. PbB of CT and HD patients was similar. Girls had a slightly higher PbB than boys (not significant).

Lead concentration in deciduous teeth

Mean PbT was significantly (P <0.05) higher in the patients (2.81±0.87 μg/g tooth, range 1.4–5.4) than in C1 (1.72±0.33 μg/g, range 1.1–2.5) and in C2 (1.45±0.39 μg/g, range 0.8–2.2) (P <0.05, Fig. 1). C1 in turn had higher PbT than C2 who were known to have a low lead exposure (P <0.05). When 3.0 μg/g tooth was taken as the upper normal limit, corresponding to the 90th

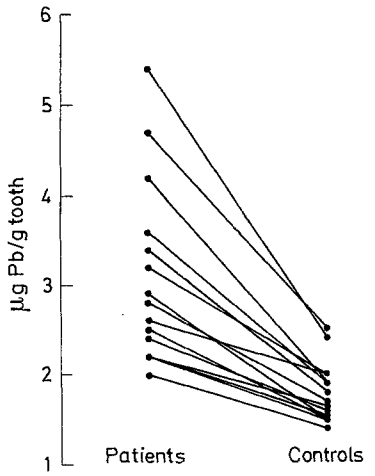

Fig. 2. Dental lead concentration (*PbT*) in 15 patients with chronic renal failure compared with 15 siblings or neighbours living in similar environmental conditions (group C1). Only those pairs are shown who provided teeth from a similar position

centile calculated for incisors in a large series of normal children living in a non-polluted area (Borken, 1986) of West Germany [15], 7 of 31 teeth of patients, but only one of 20 teeth of C1, exceeded this level. No difference was found between the mean PbT values in the three treatment groups: CT (range 2.0–4.2 µg/g), D (range 1.4–5.4 µg/g) and TP (range 2.3–3.6 µg/g). The figures in boys and girls were almost identical. Patients with congenital nephropathies had a slightly higher mean PbT (2.93 µg/g) than those with acquired disease (2.53 µg/g, NS).

In every patient the PbT was higher than in the corresponding healthy sibling or neighbour (group C1) (Fig. 2). A high correlation was found between PbT of patients and that of their healthy peers in group C1 with comparable exposure ($r = 0.85$, $P < 0.0001$). A significant correlation existed between PbB and PbT in the patients with CRF ($P < 0.0006$, $r = 0.45$). PbT was not influenced by the duration of renal disease calculated from the first increase of SCR above 1.2 mg/dl to the age at the loss of the first examined tooth, nor to the age at first D ($n = 11$).

Lead exposure

With a few exceptions it was possible to obtain complete histories on the individual lead exposure conditions in patients, as well as in the reference groups C1 and C2. Table 3 gives the number of risk factors and the corresponding PbT. At least one risk factor was present in 15 patients, and at least 3 risk factors were found in 5 patients. The risk factors in C1 were similar to the patients, except for 4 unrelated cases where it differed by one point only. The most frequent risk factor encountered in the patients was parental smoking (10 cases) followed by living in a lead-polluted environment (6 cases). As shown in Table 3 the group means of PbT and PbB increased in the patients with an increasing number of risk factors. A similar trend was noted with regard to PbT in C1.

Table 3. Lead exposure, expressed as the number of risk factors present in individual children, compared with dental lead level (PbT) and PbB in 22 patients with CRF and 20 controls (group C1)

No. of risk factors	Patients			Controls	
	n	PbT (µg/g) mean (range)	PbB (µg/dl) mean (range)	*n*	PbT (µg/g) mean (range)
0	7	2.0 (1.4–2.6)	2.7 (1.3– 6.4)	5	1.5 (1.1–2.0)
1	8	2.4 (2.0–2.9)	2.6 (1.1– 3.9)	8	1.6 (1.4–1.7)
2	2	3.3 (3.2–3.4)	4.1 (4.0– 4.3)	3	2.1 (1.8–2.4)
3–4	5	4.4 (3.6–5.4)	5.6 (1.4–10.1)	4	2.0 (1.8–2.5)

Discussion

The higher PbT of children with CRF compared with those of healthy children living in the same environment supports the view derived from studies of adult patients that reduced renal function per se is associated with an increased accumulation of lead [8, 11]. The high correlation between PbT in the patients and their healthy siblings or neighbours (Fig. 2) and between PbT and previous lead exposure (Table 3) suggest that the increase in PbT observed in CRF correlates with increased lead exposure. In adult patients with CRF, high lead excretion after mobilization with EDTA also tended to correlate with a history of high lead exposure [10]. In CRF patients with low-level exposure, the PbT is approximately 30% greater than in similarly exposed healthy subjects and increases to as much as 100% greater with greater exposure (Fig. 2). The major factor responsible for the increased lead burden in CRF is probably reduced urinary loss (the main route of lead excretion). Other factors such as increased lead absorption from the gut and lung due to the greater solubility of lead at low pH, and absorption from dialysate [11] may also play a role.

Although obvious lead intoxication in children has become rare in parallel with a falling lead burden in the normal population over the last 10 years [18], low-level lead exposure remains a potential health hazard [13–15], particularly in infants. Infants with umbilical PbB of 10–15 µg/dl have an increased risk of retarded cognitive development [23]. The developing kidney also appears to be more susceptible to damage by lead. Non-nephrectomized rats undergoing lead exposure from the 3rd–9th weeks of life developed CRF with impaired kidney growth and hypertension [24], whereas unilaterally nephrectomized adult rats show only fibrotic interstitial lesions [25]. It has been proposed that in adults with CRF, the increased lead burden may aggravate the basic lesion by predisposing to hypertension [9], a frequent and early complication of lead nephropathy, or by producing hyperuricaemia with or without gout [2, 6, 10]. To determine whether these and other factors are applicable to children with CRF, a longitudinal investigation would be required to correlate the extent of the increasing lead burden with the manifestations of CRF and the rate of deterioration. Such a study could also determine the impact of the lead burden on vitamin D metabolism [12, 26], and on brain function [13].

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Literature abstract

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Metabolic disturbance as a cause of recurrent hematuria in children

Heloisa Cattini Perrone, Horacio Ajzen, Julio Toporovski, and Nestor Schor

To evaluate metabolic disturbance as a cause of hematuria, 250 children, aged eight months to fourteen years, with recurrent hematuria were studied. In the present series, metabolic disturbance was mainly due to idiopathic hypercalciuria (IH), the most common etiology of hematuria without proteinuria in childhood. Sixty-seven (27%) of the children had IH, ten children (4%) had hyperuricosuria, and 27 (11%) had nephrolithiasis. To better characterize the IH into renal (RH) or absorptive hypercalciuria (AH) subtypes, 45 of the 67 children (ranging age from six to twelve years) were further submitted to an oral calcium load test. Eighteen patients (40%) had AH, 7 (15.5%) RH and 20 (44.4%) could not be classified as having AH or RH [indeterminant (ID) idiopathic hypercalciuria group]. Intravenous pyelography or ultrasound were normal in all children. The oral calcium load test may be useful in characterizing the subtype of IH in some children; however, a great number of the IH children were characterized as indeterminant. Also hyperuricosuria, recently described as another metabolic disturbance associated with hematuria, may be an important cause of recurrent hematuria in children.