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Follow up study of renal tubular dysfunction and mortality in residents of an area polluted with cadmium

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Abstract

A retrospective cohort study was conducted to investigate the association between cadmium induced renal tubular dysfunction and mortality. A total of 230 subjects aged 40 or older and living in a cadmium polluted area in Kosaka Town, Akita Prefecture, Japan, were studied at least once between 1975 and 1977 and again in 1990. Urinary β_2-microglobulin and total amino nitrogen concentrations were significantly related to mortality from all causes in women. The finding supports the idea that cadmium induced kidney damage is a factor associated with mortality in a general population exposed to environmental cadmium.

The effect of exposure to cadmium on mortality has recently been a major concern of researchers in Japan. Arguments differ as to whether exposure to environmental cadmium increases or decreases mortality in the general population.[1–3]

In previous papers[4,5] we reported that kidney damage induced by cadmium was significantly related to all cause mortality among residents of Sasu, an area polluted with cadmium in Nagasaki Prefecture, Japan. To assess whether the results are applicable in general we carried out a follow up study in another cadmium polluted area in Akita Prefecture.

Methods

The target area of this study consisted of nine districts: Hosogoe, Fujiwara, Tokito, Torigoe, Kamikosaka, Nakakosaka, Shimokosaka, Ushiumanagane, and Nigorikawa, which were located in Kosaka Town, Akita Prefecture. The soil of these districts had been contaminated by an exhaust containing cadmium from a copper refinery. The geometric mean of cadmium excretion in faeces from Kosaka residents was 146 μg/day in the mid 1970s, a value roughly 3·6 times as high as that of the control residents (Ikawa Town, 41 μg/day).[6]

Epidemiological health surveys were conducted on 115 residents in the Hosogoe district (aged 40 or older) from 1975 to 1977, and on 115 residents in the other eight districts (aged 70 to 79) in 1975. Some of the results have been reported by Saito *et al.*[7] The participants included roughly 80% of all residents belonging to the target age group at that time. Urinary β_2-microglobulin (β_2-m) concentration was determined by radioimmunoassay with Phadebas β_2-microtests (Pharmacia/Shionogi, Osaka), and urinary total amino nitrogen concentration by the trinitrobenzene sulphonic acid method.

In August 1990, we checked vital status of the 230 participants in the health surveys. The observation period was from the date of the initial examination to the date of death or transfer or 1 August 1990. Of 230 subjects in the cohort, 88 had died and three had moved out of the study area. The total number of observation person-years was 2700·7.

Results and discussion

The mean age of the study population at the time of initial examination was 61·9 (standard deviation (SD) 11·8) for men and 63·5 (SD 12·7) for women. The geometric mean of urinary β_2-m concentration at the initial examination was 418·3 (SD 4·88) μg/g creatinine for men and 642·2 (SD 6·41) μg/g creatinine for women. The geometric mean urinary total amino nitrogen concentration was 14·1 (SD 1·48) mmol/g creatinine for men and 16·7 (SD 1·51) mmol/g creatinine for women.

All subjects were dichotomised according to their urinary β_2-m concentration. Table 1 shows the numbers of subjects, deaths, and transfers for each group. Analysis using the Cox proportional hazards

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Table 1 Number of subjects, deaths, and transfer by sex, age, and urinary β_2-microglobulin concentration

Sex	Age‡ (y)	Urinary β_2-m < 1000 μg/g creatinine*			Urinary β_2-m ≥ 1000 μg/g creatinine†		
		No	D	T	No	D	T
Men:	40–49	13	1	0	4	0	0
	50–59	23	6	0	1	0	0
	60–69	14	6	0	7	4	0
	70–79	22	19	2	6	5	0
	80–99	2	2	0	3	3	0
Total		74	34	2	21	12	0
Women:	40–49	21	1	0	1	0	0
	50–59	26	1	0	10	1	0
	60–69	9	2	0	9	2	0
	70–79	28	11	1	20	15	0
	80–99	2	2	0	9	7	0
Total		86	17	1	49	25	0

‡Age at the first examination.
D = subjects who died; T = subjects who transferred to other towns.

Table 2 Relation between renal tubular function and mortality, adjusted for age (proportional hazards model)

Sex	Factors	β	SE	χ^2	p Value
Men:	Urinary β_2-m* (μg/g creat)	0·0838	0·1899	0·19	0·6590
	Urinary total amino N* (mmol/g creat)	−0·1643	0·7947	0·04	0·8362
Women:	Urinary β_2-m (μg/g creat)	0·3645	0·1766	4·26	0·0390
	Urinary total amino N (mmol/g creat)	1·6616	0·8375	3·94	0·0473

*Data were used after logarithmic transformation; creat = creatinine.

model[8] showed that urinary β_2-m and total amino nitrogen concentration in women were significantly associated with mortality independent of age (table 2). In women, the hazard ratio corresponding to a 10-fold rise in urinary β_2-m was estimated to be 1·44 (95% confidence interval 1·02–2·04).

Although analysis of mortality was limited to within the cadmium polluted area in this study, the result is consistent with those of earlier studies in two other cadmium polluted areas in Japan,[2 4 5] and supports the idea that renal tubular dysfunction is a factor associated with mortality in a general population exposed to cadmium. Shigematsu *et al*[1] have reported that the mortality in cadmium polluted areas along the Jinzu river of Toyama Prefecture, where Itai itai disease occurs endemically, was lower than that in reference areas. One possible explanation for their results may be that low exposure to cadmium reduces mortality[5]; however, it should be pointed out that many residents in the Jinzu river basin have renal damage induced by cadmium. Re-evaluation of the relation between renal tubular dysfunction—for example increased urinary β_2-m excretion—and mortality may help to clarify the effect of exposure to cadmium on mortality in people living in the Jinzu river basin of Toyama Prefecture.

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