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ORIGINAL PAPER

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Selenium, iodine and fungal contamination in Yulin District (People's Republic of China) endemic for Kashin-Beck disease

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Abstract We studied the status of selenium, iodine and fungal contamination in 353 school children (age 5–14 years) from four rural villages in the District of Yulin. In three villages Kashin-Beck disease (KBD) was endemic, whereas there were no cases of KBD in the fourth village. Clinical, biological and radiological examinations (right hand) were performed and KBD was established by X-ray diagnosis. The prevalence rate of KBD was 30.2%, 44.2% and 45.3% in the three endemic villages. Mean hair selenium and urine iodine concentrations were lower in affected than in unaffected children and fungal contamination in cereal grains stored in families with KBD was more elevated than in families without KBD. Low hair selenium concentration and presence of fungal cereal contamination were significantly associated with an increased risk of KBD, but low urine iodine was not.

Résumé Nous avons étudié les statuts en sélénium, en iode et la contamination fongique auprès de 353 écoliers âgés de 5 à 14 ans habitant dans quatre villages ruraux dans le district de Yulin. Dans trois villages la maladie de KB ètait endemique et dans un village contrôle aucun enfant ne présentait la maladie. Des examens cliniques, biologiques et radiologiques ont été réalisés et le KBD a été diagnostiqué par examen radiologique. La prévalence de l'atteinte était de 30.2%, 44.2% et 45.3% dans les trois villages endémiques. La teneur moyenne en sélénium des cheveux et la concentration moyenne en iode urinaire étaient plus basses chez les enfants atteints que chez les contrôles et la contamination fongique des céréales était plus élevée au sein des familles avec la maladie qu'au sein des familles sans maladie. L'analyse statistique montre qu'une teneur basse en sélénium dans les cheveux et une contamination fongique des céréales sont des facteurs significativement associés à un risque accru de maladie, mais pas une concentration basse en iode urinaire.

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Introduction

Kashin-Beck disease (KBD) is mainly found in rural China [1, 5] and three causal factors have been suggested: selenium deficiency, mycotoxin toxicity and the presence of fulvic acid in drinking water [4, 11, 21]. The recent relationship between selenium and thyroid hormone metabolism and the severe iodine and selenium deficiencies found in areas of Tibet endemic for KBD [10] have favoured a study in Yulin District (Shaanxi Province) in order to determine the importance of these risk factors, i.e. selenium status (hair selenium concentration), fungal contamination (the humidity of grains, fungi in cereals) and iodine status (urine iodine concentration) in the aetiology of KBD. Yulin District is one of the principal areas affected by KBD [14, 16, 18], and despite recent improvement this region remains severely affected when compared with the rest of China [16].

Materials and methods

A cross-sectional study was conducted during 1997 of 353 school children (aged 5–14 years) attending four rural village schools in Yulin District. Three villages known to be endemic for KBD and one village without KBD were selected. The study sample included over 80% of the 5- to 14-year age group in the four villages. Clinical and radiological examinations (right hand) were performed and KBD was confirmed by radiography [17]. Hair selenium concentration, cereal grain humidity and water content, contamination of cereals by fungi (Alternaria), and urine iodine concentration were determined. Selenium in hair was measured by fluorimetry after reaction with 2,3-diaminonaphthalene (modified Wilkie method) [15]. The cerium sulphate catalytic method was used for iodine determination in urine. Two-hundred and fifty gram cereal samples (barley) were collected from each family and stored in paper bags at 0–4°C while awaiting mycological examination. The humidity of the grain was determined on whole grains as in the Tibet study [2]. Their water content is the value obtained after grinding the grain [19]. Czapek-Dox agar at 28°C was used as the culture medium for fungi. *Alternaria alternata* was the predominant species identified and contamination was expressed as the percentage of grain samples in which this species was detected. For statistical analysis the urine iodine data had to be transformed logarithmically. One-way ANOVA (for continuous variables) or chi-square test (for categorical variables) were used for analysing data. Logistical regression analysis was used to estimate the adjusted odds ratio (OR) and 95% confidence intervals (CI) for KBD in relation to the hair selenium concentration, cereal fungal contamination and urinary iodine concentration in the villages where KBD was endemic. A *P*-value (two-sided) of <0.05 was considered as statistically significant. Analyses were performed using the SPSS statistical software version 8.0 (SPSS, Chicago, Ill., USA).

Results

Among the 353 children examined, 119 (33.7%) were confirmed as positive for KBD by radiography. The prevalence rate of KBD was 30.2%, 44.2% and 45.3% in the three endemic villages and was nil in the control village. The average age of the children was 9.6 years (range: 5–14 years) and 55% were male. Mean levels of hair selenium were significantly lower in the endemic villages than in the control village (87 vs. 159 ng/g). The same situation was observed for urine iodine (43 vs. 89 µg/l). The proportion of fungal contaminated cereal was higher among the children living in the endemic villages, but this difference was not statistically significant. There were no differences in age, sex and grain water content between the endemic villages and the control village. Within the three endemic villages (Table 1) the mean levels of hair selenium and urinary iodine were significantly lower among KBD-affected children than in those unaffected. The proportion of fungal contaminated cereal was significantly higher among KBD-affected children and these children were slightly, but significantly, older than those unaffected. There was no difference, however, for sex, grain water content and grain humidity between affected and unaffected children.

Three dichotomised (categorical) variables: hair selenium (≤85 ng/g, >85 ng/g), fungal cereal contamination (yes, no) and urinary iodine (<50 µg/l) were related to the risk of KBD in terms of odds ratios (OR). After adjustment for age and sex, the odds of KBD among hair selenium below 85 ng/g was 52 times higher than in those children with hair selenium above 85 ng/g. The occurrence of KBD among children with urine iodine below 50 µg/l was more than twice that in those whose urine iodine was in the normal range. Finally, the odds of KBD occurring in the fungal contaminated cereal group relative to the group not affected by fungal contaminated cereal was 2.5. After adjustment for dichotomised variables (hair selenium, urine iodine, fungal contamination, age and sex), the association of KBD with hair selenium and fungal cereal contamination remained significant, but the association of KBD with urine iodine was not.

Discussion

The role of selenium in KBD was discovered in the early 1970s [7, 9] and in our study the selenium status was assessed by analysis of hair – a biological material which is often used in epidemiological studies performed in China [3, 12]. Good positive correlations have been reported between the selenium content of hair and in blood and food grains in various areas of China [7, 13]. The present data are in agreement with previous reports and confirm the close relationship that exists between selenium deficiency and KBD [8, 13, 20]. There was a marked variation of the selenium status in the four examined villages of Yulin District, and this correlates well with the presence or absence of disease. Within the endemic villages selenium deficiency was more severe in children with KBD than in unaffected children. This contrasts with previous data from Tibet [10] where it was not possible to discriminate between affected and unaffected children within endemic villages according to their serum selenium.

There was no evidence of pronounced iodine deficiency disorders in the area studied. The mean urine io-

Table 1 Characteristics of KBD-affected and unaffected subjects living in villages where KBD is endemic

Characteristic	KBD-affected		KBD-unaffected		*P*-value[b]
	Value[a]	No.	Value[a]	No.	
Age (years)	10.0±1.9	119	9.2±1.9	176	0.002
Males (%)	55	119	58	176	0.57
Hair selenium (ng/g)	66±16	119	102±16	172	<0.001
Urine iodine (µg/l)	32 (26–40)[c]	111	52 (45–60)[c]	163	<0.001
Grain humidity (%)	8.3±1.8	87	8.9±1.7	80	0.06
Grain water content (%)	11.4±0.9	91	11.2±0.8	81	0.14
Cereal contamination (%)	63	91	41	87	0.005

[a] Results are expressed in % or as means ± SD except for urine iodine (geometric mean, 95% confidence interval)
[b] *P*-value derived from one-way analysis of variance or by the chi-square test
[c] To convert urine iodine into nmol/l, multiply by 7.87

dine concentration was at the limit of definition of deficiency (50 µg/l) in endemic villages, and well above that threshold value in the control village. The absence of any pronounced iodine deficiency contrasts with the severe iodine deficiency observed in Tibet [10]. Therefore KBD can occur in the absence of any iodine deficiency, even if this deficiency is likely to contribute to the clinical manifestations of the disease in Tibet [10]. The lower urine iodine concentration in KBD-affected children compared to that in unaffected children, which is not associated with iodine deficiency disorders, has no clear explanation. Even if, for methodological reasons, it is impossible to compare clinical data from Tibet [10] with those from Yulin in China, it seems that the lesions in KBD patients living in Yulin are less severe than in Tibetans.

Fungi present in cereals exposed to humidity for long periods have also been implicated in the pathogenesis of KBD [2]. Mycotoxins were not specifically measured, but it is known that grain humidity and the presence of fungal contamination in grain are directly associated with the presence of mycotoxins [6]. A greater load of mycotoxins (grain humidity, presence of Alternaria) was observed in our endemic villages as compared to the control village, and within the endemic villages. Its level was also more elevated in KBD-affected children than in those unaffected.

Our multivariate analysis of the risk factors showed that selenium deficiency was the principal factor linked to KBD in this district with an OR of 61, when compared to iodine deficiency or fungal contamination which only showed an OR of around 2. Therefore it appears that KBD in Yulin District is associated significantly with severe selenium deficiency, but not with iodine deficiency.

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