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Effects of the consumption of rice from non-KBD areas and selenium supplementation on the prevention and treatment of paediatric Kaschin–Beck disease: an epidemiological intervention trial in the Qinghai Province

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SUMMARY

Objective: Based on the aetiological hypothesis of Kaschin–Beck disease (KBD), different interventions were adopted, and the preventive and therapeutic effects of interventions was observed and evaluated in this trial.

Design: A total of 358 children from seven villages of Qinghai Province in China were examined, and 280 children aged 6–11 years old were eligible for the trial. The children were divided into three groups that received either no intervention ($n = 64$), 150 kg/person of rice from non-KBD areas ($n = 103$) or 7 kg/family of selenium–iodine salt ($n = 113$) for 12 months. Data were collected and used to calculate the proportion of patients with X-ray lesions, the proportion of new patients and the metaphyseal repair rate. All indicators were analysed with Pearson chi-square or Fisher's exact tests. The registration number of this trial is ChiCTR-PNRC-12002309 (http://www.chictr.org).

Results: After interventions, the proportion of patients with X-ray lesions increased dramatically in the control group and decreased significantly in two intervention groups; significant differences were seen between the control group and two intervention groups ($P < 0.05$). Moreover, significant differences were observed in the proportions of new patients and the metaphyseal repair rates between the control group and two intervention groups ($P < 0.05$). Additionally, the proportion of new patients was lowest and the metaphyseal repair rate was highest in group B.

Conclusions: The effects of eating rice from non-KBD areas and selenium supplementation on the prevention and treatment of paediatric KBD were notable, the consumption of rice might be the most effective and safest intervention and should be encouraged.

Introduction

Kaschin–Beck disease (KBD) is a chronic, endemic and little-known form of osteoarthropathy[1] that mainly occurs in children aged 5–15 years old. The primary pathologic changes of KBD are chondrocyte degeneration, necrosis and losses of the deep-zone of articular and growing plate cartilage[2]. These changes develop continuously and cause severe dysarthrosis in the joints[3,4]. KBD has crippled and stunted the growth of hundreds of people in China[5].

Although KBD has been studied for more than 150 years, its aetiology remain uncertain[6]. Some researchers believe that T-2 toxin is the main causal substance of KBD[7,8]. The causative agent of

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KBD enters the patient's body through contaminated food. In addition to T-2 toxin, selenium deficiency is also thought to be an important risk factor for KBD[9–11]. The addition of selenium to the diet might promote metaphyseal restoration in paediatric KBD patients, and this particular effect has previously been well-documented and confirmed in previous studies[12,13]. Moreover, a recently published study indicated that environmental conditions, such as microtrauma and cold, can worsen KBD, although these factors do not cause KBD[14].

Many years ago, the Chinese government has launched a massive effort and series of etiotropic measures to prevent and control KBD, these measures include selenium supplementation[12] and relocation[15]. According to our monitoring report[16–19], the incidence of KBD has been markedly reduced, but new patients continue to occur in western regions of China, particularly in the Qinghai and Sichuan provinces and Tibet Autonomous Regions. Presently, KBD is more severe and prevalent in the Qinghai Province, new paediatric patients of KBD are still being found in this province[20].

The currently available treatments for KBD are limited to nonspecific interventions, such as exercise, pharmacologic management of the symptoms, and surgical treatment for severe adult KBD[21–24]. Non-steroidal anti-inflammatory drugs and analgesics are heavily used to alleviate patients' pain because these agents are inexpensive. However, these agents are accompanied by a high risk of adverse events[22]. Therefore, the identification of effective preventive and therapeutic measures for KBD is an important step toward improving the management of this disease.

Based on the main aetiology of KBD detailed above, a 12-month, controlled study of continuous health care intervention was conducted. The aim of this trial was to observe and evaluate the effects of two interventions, i.e., having local residents eat rice from non-KBD areas and selenium supplementation, on the potential causes of KBD.

Patients and methods

Test sites and subject selection

The Qinghai Province consists of 30 counties and seven autonomous counties and is located in northwestern China. Paediatric KBD to be prevalent in some villages of Xinghai, Guide, Tongde, and Banma counties, and the detection rate is higher than the lower limit (5%) prescribed in the Chinese Determinative and Hierarchical Criteria of KBD Areas[25]. In accordance with the principles of matching natural and social factors, such as geologic environments, economic situation and educational standards, villages were included if they met the following eligibility criteria: (1) the villages were in active and non-controlled endemic areas affected by KBD according to the prevalence of paediatric KBD in Qinghai Province from 2003 to 2006[16–20], (2) all local families used self-produced wheat or barley as their staple food, and (3) no interventions for the prevention or treatment of KBD had been provided to any local children in the 12 months prior to the trial. Ultimately, seven villages in Guide and Xinghai counties were chosen as the test sites. These villages were Xiemalang Village, Xinjianping Village of Guide County, Shanglujuan Village, Xialujuan Village, Shang Village, Zhong Village, and Road North of the Xia Village of Xinghai County.

Based on the radiologic and clinical diagnostic criteria for KBD[26], clinical and radiologic examinations were performed for the children 6–14 years of age who were living in the above-mentioned villages to investigate the prevalence of KBD in these villages. After the examinations, the eligible individuals were selected. The inclusion criteria were children aged 6–11 years who had lived in the test site for more than 3 years. Children with other joint diseases, such as joint inflammation, metabolic bone diseases, neoplasia, osteoporosis, or osteomalacia and those who declined to participate in the survey were excluded. Ultimately, 280 children entered the study cohort.

Group setting and interventions

This intervention trial was an epidemiological quasi-experiment. According to the geographic distributions, the proportion of patients with X-ray lesions and the populations of each village, the seven villages were divided into three groups and assigned to receive different interventions. Based on humanitarian concerns, the intervention measures were provided to five of the more serious KBD villages. The subjects who lived in Xinjianping and Zhong villages did not receive any intervention. The types of staple foods consumed by these participants were typical, and the salt that they consumed was commercially available iodised salt (the potassium iodate content were 25–30 mg/kg). The children who lived in the Road North of the Xia and Xiemalang villages were assigned to consume rice from non-KBD areas (150 kg for each child) and commercially available iodised salt. The children who lived in Shanglujuan, Xialujuan, and Shang villages were instructed to eat selenium–iodine salt (the potassium iodate content were 25–30 mg/kg and sodium selenite content were 3–5 mg/kg, 7 kg for each family) and typical staple foods. For each subject, the amount of staple food consumed was not restricted, but the salt intake was restricted to 5–7 g/d. The trial lasted for 12 months.

This study was conducted in accordance with the Helsinki Declaration II, and was approved by the Institutional Review Boards of Harbin Medical University (HMUIRB2011002) and the Administration Village Committee. The registration number in the Chinese Clinical Trial Registry is ChiCTR-PNRC – 12002309 (http://www.chictr.org). Written informed consent was obtained from the parents or guardians of all children.

Outcome measurement

The lesions and their subsequent repair and remodelling processes in the growing cartilage result in variety of radiological changes in the hands and wrists of patients with KBD[27,28]. Thus, X-ray is the gold standard for the diagnosis and grading of KBD. The changes in the metaphysis and distal ends of the phalanges in the hands of paediatric KBD patients were main radiological outcomes (see Fig. 1, Images B and C). In general, metaphyseal changes are easy to repair and to return to normal (see Fig. 1, Image A), and changes in the distal ends of the phalanges in hand are not. In this trial, orthophoric radiographs of the right hands and wrists (the right hands and wrists of the subject in a position they vertically faced the tube ball of X-ray machine) of the children were obtained at 0 (baseline) and 12 months (endpoint) and at any time at which abnormality occurred.

Based on above X-ray measures, the proportion of patients with X-ray lesions (i.e., the number of children with X-ray lesions/the total number of subjects), the metaphyseal repair rates (i.e., the number of cured KBD patients/the total number of paediatric KBD patients in each group throughout the trial), and the proportions of new patients (i.e., the number of new patients/the total number of paediatric KBD patients in each group throughout the trial) were calculated. The proportion of patients with X-ray lesions was used to reflect the occurrence and prevalence of KBD, the metaphyseal repair rates was used to evaluate the therapeutic effects of the interventions and the proportions of new patients were used to assess the preventive effects of the interventions.

Quality control

Double-blinded diagnoses were utilised to ensure the accuracy of the baseline data. To identify eligible patients, five exports or