Osteoarthritis and Cartilage 20 (2012) 605–613

Osteoarthritis and Cartilage

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

Review

Sodium selenite for treatment of Kashin-Beck disease in children: a systematic review of randomised controlled trials

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ARTICLE INFO

Article history:
Received 22 November 2011
Accepted 16 February 2012

Keywords:
Kashin-Beck disease
Therapy
Sodium selenite
Systematic review

SUMMARY

Objective: To assess the effectiveness and safety of sodium selenite in treatment of patients with Kashin-Beck disease (KBD).
Methods: We searched for all publications between January 1966 and October 2011 using seven electronic databases. All randomized controlled trials (RCTs) assessing the effects of sodium selenite on KBD vs no treatment or placebo were included. For dichotomous data, odds ratios (OR) and 95% confidence intervals (CI) were estimated according to the intention-to-treat principles. For continuous data, mean difference (MD) was used for outcomes pooled on the same scale.
Results: A total of 10 RCTs involving 2244 patients were included. The methodological quality of the included studies was low. When comparing the outcome of sodium selenite treatment group vs the control group, the OR of repairing rate of metaphyseal lesions was 5.63 (95% CI: 3.67–8.63) and repairing rate at the distal end of phalanges was 2.98 (95% CI: 1.32–6.70) based on X-ray assessment, which was statistically significant difference in favour of sodium selenite. In one RCT which reported data on clinical improvement, no statistically significant difference was observed in the treatment vs control group (OR 1.50, 95% CI: 0.43–5.30). Se content in hair was (MD 0.11, 95% CI: 0.09–0.13) which was statistically significant higher in selenium group.
Conclusions: Current evidence suggests that sodium selenite is more effective than placebo or no treatment in patients with KBD. However, the evidence was limited by potential biases; thus, further high quality large-scale RCTs are still needed to evaluate the short term and long term effects of selenium.

Introduction

Kashin-Beck disease (KBD) is a chronic, endemic, degenerative osteoarthropathy with severe skeletal deformation and dwarfism[1–3]. It is endemic to certain areas of South-Eastern Siberia to North China, North Korea, Central China and Tibet[4,5]. A report published by the Chinese Ministry of Health in 2008 estimated a population of 105.28 million people living in 366 counties within the KBD regions, and approximately 714.8 thousands of those people were found to be affected with KBD. Overall, there are about 2.5 million people diagnosed with KBD in China, Russia and North Korea[6] Most clinical manifestations of the joints become apparent during childhood up to the age of 25 years. Affected individuals present with joint destruction leading to recurrent and commonly bilateral joint pain, movement restriction, and joint enlargement. Although most commonly seen in adults and often the group more severely affected, the worst forms of this disease tend to start in childhood, which may lead to dwarfism[1,7]. The resulting disability causes an important human and socioeconomic burden to both affected children and adults.

From the different hypotheses regarding etiological factors, four factors have been convincingly associated with the disease: selenium deficiency, grain contamination with mycotoxin-producing fungi, water pollution with organic material, and fulvic acid. However, none of the proposed explanations are entirely satisfactory; thus, it appears that KBD has a multifactorial origin[8,9].

So far, only palliative measures exist for treatment of KBD. Successful surgical treatments to correct joint defects have been reported by Chinese and Russian orthopaedists[10–12]. Recently, physical therapy aimed at increasing mobility and functioning has

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1063-4584/$ – see front matter
doi:10.1016/j.joca.2012.02.012

started in Tibet[13]. Medications for symptomatic relief include non-steroidal antiinflammatory drugs for pain relief.

Selenium supplements have been given in some highly endemic areas for a long time. A meta-analysis including five randomised control trials (RCTs) and 10 non-RCTs assessed the efficacy of selenium supplementation for prevention of KBD in children. The odd ratios (OR) and number needed to treat (NNT) favoured selenium supplement for prevention of KBD in children[14]. Some clinical trials using selenium for treatment of KBD have also been carried out. However, there is no systematic review evaluating the effects of selenium treatment for patients that are already affected with KBD disease. The aim of this systematic review was to synthesize the results from RCTs to assess the effectiveness and safety of sodium selenite in treatment of patients with KBD.

Materials and methods

Search strategy and eligibility criteria

We searched, without language restrictions, for all publications between January 1966 and October 2011 using electronic databases, which included Medline, Embase, Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, The Chinese Biomedical Database, Chinese National Knowledge Infrastructure, Chinese Science and Technique Journals Database, and Wan Fang database. The following MeSH and free words were used during the search: “Kashin-Beck disease”, “big bone disease”, “endemic osteoarthritis”, “Urov disease” and “selenium”, “Sodium selenite”, and “Se”. We also searched the references of review cited for additional articles that were missed by the computerized database search. Conference proceedings were checked for any relevant trials, and authors were contacted for details of unpublished and ongoing trials.

We included all RCTs that used sodium selenite alone vs no treatment or placebo, without age restrictions. Studies that were excluded consisted of: (1) no placebo or control group, (2) use of other types of selenium supplements (eg., selenium salt), and (3) use of sodium selenite in combination with other treatments (eg., vitamin E, vitamin C or both). Studies reporting mixed groups of participants (e.g., participants with and without KBD) were included only if the therapeutic effect data could be identified and extracted separately.

Data extraction

Data was extracted independently by two reviewers using a standard data extraction form; discrepancies were settled by discussion. The data extraction form included title, setting, country of origin, demographics, interventions (dosage, route of administration and duration of treatment), sample size and outcomes. The primary outcome was repairing rate of metaphyseal lesions and the distal end of phalanges in hands on X-ray films as well as clinical improvement. The secondary outcomes were Se contents in hair and adverse effects.

We assessed the methodological quality of each study using a four-item checklist: (1) reporting of a randomization method, (2) allocation concealment, (3) investigator blinding for assessment of outcomes, and (4) completeness of follow-up. The criteria were drawn from the Cochrane Collaboration tool for assessing risk of bias[15], and the descriptions provided by Wu and Liu[16].

Statistical analysis

For dichotomous data (e.g., improvement of metaphyseal lesions and the distal end of phalanges in hands on X-ray films), OR and 95% confidence intervals (CI) were estimated according to the

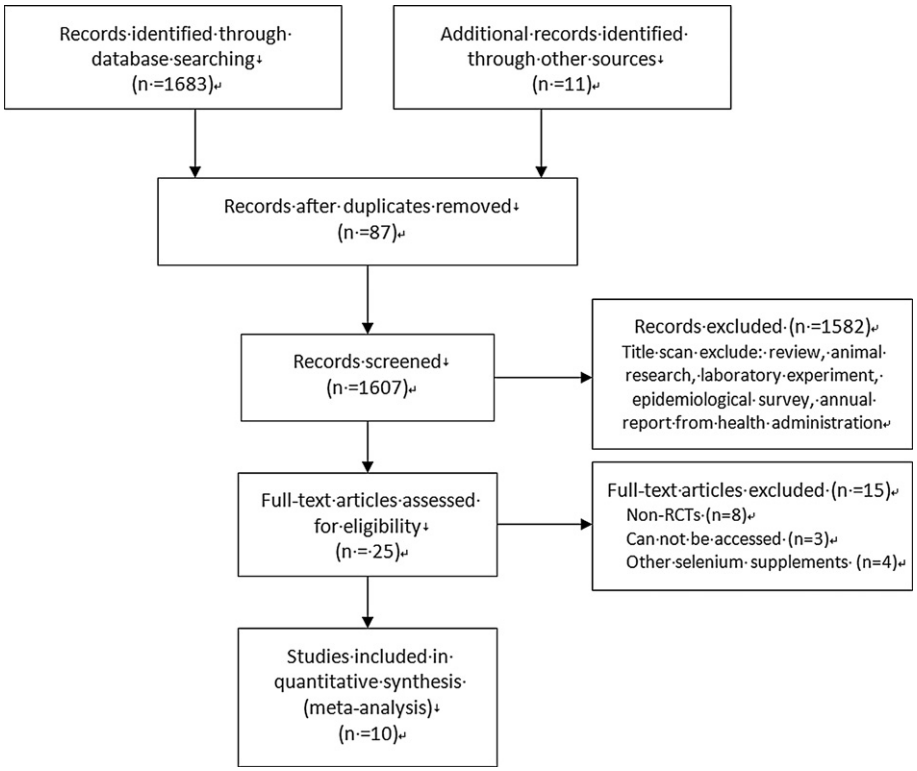

Fig. 1. Flow chart of study selection process.