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Review article

Effectiveness of dietary supplements in spinal cord injury subjects

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ABSTRACT

Background: Individuals with spinal cord injury (SCI) consume more dietary supplements than the general population. However, there is limited information regarding the clinical effectiveness of dietary supplements in SCI population.
Objective: To systematically review the effectiveness of dietary supplements for the prevention or treatment of health-related conditions associated with SCI.
Methods: Randomized or non-randomized controlled clinical trials were selected, comparing the effect of any dose and form of a dietary supplement (defined by the Dietary Supplement Health and Education Act), with either no treatment, placebo, or other medication. Data Sources included the Cochrane Database, DARE, LILACS, CINAHL, EMBASE, MEDLINE, OTSeeker, PEDro, PsycINFO, SpeechBITE, ScienceDirect, Scopus, clinicaltrials.gov, Google Scholar, and OpenGrey. Two reviewers independently classified articles from January 1970 through October 2015, and 18 articles were selected.
Results: Due to the heterogeneity of outcome measures across studies, a meta-analysis was not conducted. However, high-quality evidence showed that cranberry supplementation is not effective for prevention of urinary tract infections (UTIs) in SCI. Moderate-quality evidence supported a beneficial effect of vitamin D, alpha-lipoic acid, and omega-3 supplementation, although replication of results is needed. There were conflicting results for the effect of creatine supplementation on improvement of motor outcomes. Low-quality evidence does not permit assessment of the effectiveness of melatonin, whey protein, vitamin C, and Chinese herb in SCI.
Conclusions: There is sufficient data suggesting that cranberry supplementation is ineffective for prevention of UTIs in individuals with SCI. There is insufficient data to support or refute the use of any other dietary supplement in individuals with SCI.

Individuals with spinal cord injury (SCI) have a number of medical comorbidities, in addition to motor and sensory neurologic deficits. Depending on the level and extent of the injury, persons with SCI may have unique health problems including osteoporosis, gastrointestinal tract dysfunction, autonomic dysregulation, cognitive deficits, respiratory conditions, orthostatic hypotension, and neurogenic bladder/bowel, among others.[1] Furthermore, the muscle atrophy produced by inactivity, and the lack of motor innervation,[2] are associated with metabolic disturbances including dyslipidemia; insulin resistance; glucose intolerance; diabetes mellitus; and reduced levels of testosterone, T3 thyroid hormone, vitamin D, and calcium.[3,4] Comorbidities common to individuals with SCI are important to consider when administrating medication or dietary supplements.

Individuals with SCI consume dietary supplements at a greater rate than the general population.[5] Opperman et al. applied an open-ended structured questionnaire to collect demographic information from 77 community-dwelling adults with chronic SCI in Ontario, Canada. Seventy one percent of respondents reported using supplements at least once, and 50.6% were regular supplement users. The top 3 supplements consumed were multivitamins (25%), calcium (20%), and vitamin D (16%).[5] The elevated consumption may be due in part to the widespread availability of dietary supplements. The United States (US) Food and Drug Administration (FDA) regulates dietary supplements as a special category of food (not as drugs), and thus, they are easily available over-the-counter and through the internet, without a medical prescription.

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Moreover, there is a widespread perception among patients that non-traditional medicine is 'natural' and therefore intrinsically safe.[6]

According to the Dietary Supplement Health and Education Act (DSHEA) of 1994 (Public Law 103-417),[7] a dietary supplement is "a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients: (A) a vitamin; (B) a mineral; (C) a herb or other botanical; (D) an amino acid; (E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or (F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E)".[7] Although dietary supplements are reported to be widely consumed by patients with SCI, there is no scientific evidence of the effectiveness of any of the aforementioned dietary supplement categories in the SCI population. Furthermore, dietary supplement consumption may have potential risks such as severe adverse reactions, drug interactions, masking a severe disease, risk of addiction, and abuse.[8] Finally, the US FDA does not require manufacturers to demonstrate the efficacy or safety of dietary supplements, which ethically obliges clinicians to test the effectiveness of those supplements in a particular target population before recommending them as a harmless option.

The aim of this review was to systematically assess the effectiveness of dietary supplements to prevent or treat comorbidities common to individuals with SCI.

Methods

This systematic review was conducted following The Cochrane Handbook for Systematic Reviews of Interventions Guidelines[9] and adhering to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[10] The study protocol was registered in PROSPERO (Prospective Register of Systematic Reviews) database (CRD42015028014), University of York.

Data Sources

Databases searched included The Cochrane Database, DARE, LILACS, CINAHL, EMBASE, MEDLINE, OTSeeker, PEDro, PsycINFO, SpeechBITE, ScienceDirect, Scopus, clinicaltrial.gov, Google Scholar, and OpenGrey. Quantitative articles, including randomized or non-randomized controlled clinical trials from January 1970 through October 2015, were included. The computerized search strategy was based on keywords including: "dietary supplements," "supplementation," "vitamin supplements," "mineral supplement," and "herbal supplement." These terms were combined with "spinal cord injuries," "spinal cord injury," "spinal injury," "paraplegia," and "tetraplegia."

Using the search keywords, the titles and abstracts were screened by two independent reviewers to identify potential relevant articles. Full text articles were independently examined to determine eligibility for inclusion. A third experienced reviewer resolved disagreements.

Article selection

Studies were included if they satisfied all of the following inclusion criteria[1]: all foreign language articles with English or Spanish abstracts, both randomized or non-randomized controlled clinical trials,[2] subjects of any age with acute or chronic SCI consuming any dose of dietary supplementation defined by the Dietary Supplement Health and Education Act (DSHEA)[7] in the following categories: (A) a vitamin; (B) a mineral; (C) a herb or other botanical; (D) an amino acid; (E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or (F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E),[3] studies comparing the effect of any dose of any form (pills, capsules, tablets, gel caps, liquids, powders, herbs, or other forms) of a dietary supplement with either no treatment, placebo, or another medication, and[4] any outcome measure (clinical or laboratory-related) used to demonstrate a dietary supplement's preventive or therapeutic effect for health-related conditions associated with SCI.

Data extraction

The following information was extracted and entered in an Excel file by two independent reviewers[1]: characteristics of the selected studies: sample size; age, gender, and diagnoses of participants; study design; goal of study; type of intervention; dosage of dietary supplement; assessment periods; and number of dropouts (Table 1), and[2] outcome measures of studies according to dietary supplement category (Table 2).

Quality assessment

The risk of bias in each included study (selection bias, performance bias, detection bias, attrition bias, reporting bias) was assessed by two independent reviewers following the Cochrane Handbook for Systematic Reviews of Interventions.[9] Additionally, quality assessment across studies was carried out using The Grading of Recommendations Assessment, Development, and Evaluation (GRADE)[11] (Table 3).

Results

Study selection

A total of 860 abstracts were initially identified. After removing the duplicates, 452 abstracts were selected. From these, 25 were identified as potentially pertinent and reviewed in full. Finally, 18 articles were selected that fulfilled the inclusion criteria (Fig. 1). The selected studies were conducted in USA (n = 10), Iran (n = 3), Spain (n = 1), Norway (n = 1), Australia (n = 1), China (n = 1), and Switzerland (n = 1).

Study characteristics

Table 1 summarizes the characteristics of the studies reviewed. The earliest and latest articles fulfilling the inclusion criteria were published in 1980 and 2015, respectively. Of 18 selected studies, 16 corresponded to randomized, double-blind, placebo-controlled clinical trials.[12–27] One study corresponded to a non-randomized cross-over clinical trial[28] and another corresponded to a randomized simple-blind clinical trial.[29] Although most of the articles included individuals from both genders, overall, there was a greater representation of male (n = 689) versus female (n = 115) individuals with SCI.

According to the dietary supplement category defined by DSHEA, 18 articles investigated the effectiveness of[1]: clause A (vitamins): vitamin C[28,29] vitamin D[23,2] clause C (herbs and botanicals): Chinese herb formula[17,3] clause E (a dietary substance for use by humans to supplement the diet): whey protein[15,26,4] clause F (a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause A, B, C, D or E): creatine,[13,14,19,20] cranberries,[18,21,25] melatonin,[16,22] omega-3,[12,24] and alpha-lipoic acid.[27] Articles investigating the effectiveness of a mineral (clause B) or an amino acid (clause D) in individuals with SCI were not found.