

Revisión

Past and current trends in soy supplementation: a bibliographic study

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Abstract

The aim was to determine in what areas the therapeutic application of soy predominates in clinical trials and to assess the emerging fields of its use by means of an analysis of bibliographic resources. A search was performed in the MEDLINE database up to 31 december 2004, limited to the Title/Abstract field, and Clinical Trials as the type of publication. The abstracts from the publications selected (n=86) were reviewed and different variables were assessed. A total of 3280 subjects were included: 15% men and 59% women (71% postmenopausal). The studies were performed basically in healthy individuals (71%). Twenty five percent of the studies investigated plasma levels of different metabolites and 21% determined hormone or lipid profiles. After the year 2000 a new population focus was detected, with the publication of two studies in elite gymnasts and judoists, with positive results. The present observations indicate that soy supplementation in the competitive sports elite may be an emerging application.

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Key words: Soy. Supplementation. Clinical trial. Database. MEDLINE

TENDENCIAS PASADAS Y ACTUALES EN LA COMPLEMENTACIÓN CON SOJA: UN ESTUDIO BIBLIOGRÁFICO

Resumen

El objetivo del estudio fue determinar cuales son las áreas de aplicación terapéutica de la soja que predominan en los ensayos clínicos y valorar los campos emergentes de su uso mediante un análisis bibliográfico. Para ello se realizó una búsqueda en la base de datos de MEDLINE hasta el 31 de diciembre de 2004 limitando la búsqueda en los campos Título/Resumen y Ensayo clínico como tipo de publicación. Se obtuvieron todos los resúmenes de las publicaciones seleccionadas (n=86) eliminando los duplicados y se valoraron estadísticamente algunas variables reseñadas en ellos. Se incluyeron un total de 3280 sujetos: 15% de hombres y 59% de mujeres de las cuales un 71% eran menopaúsicas. Un 71% de los individuos se consideraron como sanos. Un 25% de los estudios habían investigado los niveles de algunos metabolitos plasmáticos y en un 21% de ellos los perfiles de lípidos u hormonas. A partir de las publicaciones del año 2000 se detectó un nuevo campo de aplicación con la publicación de dos estudios en deportistas de élite, gimnastas y judocas con resultados positivos. Las observaciones indican que la suplementación de la dieta de los deportistas de competición con proteína de soja puede ser una aplicación emergente.

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Palabras clave: Soja. Suplementación. Ensayo clínico. Bases de datos. MEDLINE.

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Introduction

Soy (glycine max) is a legume native to east Asia and has been part of the human diet for more than 5000 years. The benefits of this protein, which is extensively used in China and Japan, became widely known in the Western world at the end of the 20th century and now soy consumption is extensive, particularly among vegetarians. Currently, soy is situated at the apex of the food pyramid for this population¹.

The term *soy* refers to the legume as well as the plant protein. The soybean is rich in this polypeptide and has a PDCAAS (protein digestibility corrected amino acid score) of 0.91, which is very close to 1.0, the highest score possible for a protein²; nevertheless, it is currently recognized that to validate the nutritional value of a protein, other complementary methods are required³.

The first bibliographic references appearing in MEDLINE concerning its use date to the decade of the 1950's⁴ and the first data regarding its clinical use began to emerge in the 1980's⁵. Fifteen years had elapsed until, in 1995, the results of meta-analyses and the administration of soy in specific diets, indicated the effect of soy on reducing blood cholesterol levels⁶. In 1999 the Food and Drug Administration (FDA) recognized that consumption of 25g daily of soy protein results in a decrease in cardiovascular risk, particularly when associated with a diet low in saturated fats⁷. In addition, over the last 20 years several reviews have reported the health benefits of soy in menopausal women^{8,9}. It is clear that the interest in this protein is increasing.

The present study was designed to determine the predominant areas in which soy is currently used for therapeutic applications and to assess the emerging fields of its use by means of an bibliographic analysis of clinical trials involving administration of this protein in the diet.

Material and methods

An integrated bibliographic search was performed in the MEDLINE database up to 31 december 2004, using the terms *soy consumption* and *soy supplementation*, limited to the *Title/Abstract* field and *Clinical Trials* as the type of publication. A total of 64 and 61 references were retrieved, respectively, which formed the basis of this study. Thirty-nine abstracts from the total of 125 were excluded, 2 that had been repeated in the two searches and 37 that did not deal with the central subject of soy administration.

The abstracts from the publications selected (n=86) were reviewed and the following variables were studied: year of publication, number of patients studied, sex, clinical situation, diagnosis, days receiving treatment, amount of soy and isoflavons administered, methods, results and conclusions. In addition, we counted the number of study publications appearing in

the journals classified in the Journal Citation Reports within the Subject Category of Nutrition and Diagnostics.

The conclusions of the abstracts with regard to soy use were classified as *positive* or *negative*. The latter option was applied when no beneficial effect was found or when the findings were inconclusive.

The descriptive calculations and statistical analyses were performed with the Pearson Chi-square test and Spearman correlation coefficient using SPSS 8.0 for Windows. Significance was set at a P-value of .05.

Results

Among the studies assessing soy administration, 65% were performed in the present decade of 2000, 25% in the 1990s and 9% in the 1980s and no references before this period were retrieved.

In 29% of the studies both sexes were included, in 15% only men and in 59% only women; among the latter 71% were performed in menopausal women. The total of clinical trials retrieved included 3280 subjects and 6136 days in treatment.

Considerable variations were observed in the dose of soy protein administered, with values ranging 10 to 125 g/day, and no correlation was found between the amount administered and its potential beneficial effect.

The highest percentage of studies were performed in healthy individuals (71%), 16% were done in patients with hypercholesterolemia, 7% in cases of neoplasms (breast and prostate), and 6% in diabetes patients.

With regard to biochemical variables, 25% of the studies investigated plasma levels of various metabolites, particularly isoflavons, 21% determined hormone profiles and the same percentage lipid profiles. The circulatory system was studied in 14% of the trials retrieved and bone metabolism in 7%.

With regard to outcome, the results were considered positive in 66% and negative or neutral in 34%.

In the 1980s two studies appeared in obese patients with diabetes^{10,11} and one in vegetarians¹², whereas in the 1990s, three studies were done in Pediatrics¹³⁻¹⁵. No further studies were done in these specific populations after this time.

A significant correlation was found only between the number of clinical trials and the total of subjects studied ($r=0.362$); there was no association between the number of treatment days and positive results with the use of soy ($P=.5$)

After the year 2000 a new population focus was detected, with the publication of two studies in elite gymnasts and judoists, with positive results^{16,17}. A third reference was found in individuals practicing moderate intensity resistance exercise¹⁸.

Lastly, the frequency with which the articles appeared in specialized journals showed a higher presence in those with the greatest impact factor in the subject

category of Nutrition and Dietetics, such as the *American Journal Clinical Nutrition* (n=19) and the *Journal of Nutrition* (n=14).

Discussion

Emerging evidence points to the beneficial biological properties of soy, and for this reason the government of Japon in 1994 and the USA in 1999 approved its use as a product for special health use. A recent study has described favorable differences in the gene cluster concerned with lipid metabolism, genes related to energy metabolism and anti-oxidization enzymes in the liver of animals fed this protein as compared to casein-fed animals¹⁹. Along this line, reductions in plasma cholesterol, triglycerides, free fatty acids and glucose levels have been documented in obese mice fed a soy protein isolate diet²⁰.

The present study provides a general overview of the most reliable scientific production (clinical trials) related to the use of soy protein in health and disease. There is a great deal of current interest in this legume, which has led to increased marketing of related products and claims regarding its beneficial effects in a variety of conditions. Our interest with this study was to investigate the results of therapeutic application of soy protein based on information from the most reliable scientific source, clinical trials, in order to determine the state of the art regarding the current use of this protein.

The data analyzed were retrieved with a bibliographic search from a single medical database, MEDLINE. The additional use of other databases, such as PASCAL/BIOMED might have covered other related aspects (e.g. experimental studies, veterinary use); however, since MEDLINE provides the highest number of unique and relevant references in clinical medicine^{21,22}, we considered the use this database alone appropriate for the purposes of the present study. With regard to the specific field of nutrition, the use of MEDLINE together with EMBASE/Excerpta Medica, provides more extensive indexing coverage in the literature, although there is a high level of repetition among them. MEDLINE covers journals that contain 92% of the total number of references in the field of dietetics²³. We cannot attribute that this approach was the most all-inclusive; however, we can affirm that the number of references retrieved enabled us to determine the current and emerging fields in which soy is being applied. The literature search was based on keywords limited to the *Title* and/or *Abstracts* as the main data source. This is an effective strategy, which allows retrieval of the largest amount of relevant information with the least noise²⁴.

The appearance of references from clinical trials studying soy administration is relatively recent; there were none before 1980. The majority of these studies

were performed in healthy premenopausal and menopausal women and individuals with hypercholesterolemia. Work has also been done in patients with breast and prostate cancer, diabetic and obese diabetic patients, healthy vegetarians and in pediatrics. These efforts underline the scientific and conceptual support for the use of soy in the field of preventive medicine.

Among the factors that reaffirm the emerging importance of soy application, we cite the fact that 66% of the clinical trials retrieved considered the use of soy to be positive and 65% of the references have appeared since the year 2000. In addition, the total number of days in treatment among all the clinical trials retrieved was 6136 and this variable correlated significantly ($r=0.362$) with the number of subjects (n=3280) treated with soy, which suggests a certain homogeneity in the criteria of the various authors with regard to the duration of soy supplementation, situated at around three months.

With regard to the analytical variables studied in the clinical trials, they mainly referred to plasma isoflavone levels (as the active ingredient in soy), hormone or lipid profiles and, in a smaller percentage, to circulatory function or bone metabolism (closely linked to ageing), the most labile aspects in menopausal women and patients with hypercholesterolemia.

The use of soy by elite sports competitors only appeared in two references in one specialized sports journal. One of them focussed on a series of 12 judoists receiving soy supplementation for 4 weeks, and the other on a group of 15 female gymnasts undergoing exhaustive training and receiving soy during 4 months. The amount consumed differed in the two trials (0.5 and 1.0 g per kg of body mass respectively), but both reported positive results with the addition of soy^{16,17}. The finding of a reference in sports enthusiasts, who were also given soy protein as a dietary supplement, reinforces the idea of its preliminary implantation in this field¹⁸.

It should be remembered that soy is in fashion and governs strong economic interests. Dietetic soy supplementation still remains to be studied in other settings and fast access to information on the development of novel clinical options for its use would be of significant practical value. Alternative search strategies on MEDLINE, such as the free-text search tool²⁵, which are less specific, but encompass a wider range of references, could be useful to investigate all the sources of information possible.

In conclusion, the last 20 years have witnessed an increase in the study of dietary soy supplementation. The main populations involved have been healthy premenopausal and menopausal women and individuals with hypercholesterolemia. Our observations indicate that soy supplementation in the competitive sports elite may be an emerging application for this biologically valuable protein.

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