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Revisión

Effectiveness of inulin intake on indicators of chronic constipation; a meta-analysis of controlled randomized clinical trials

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Abstract

Background: **Constipation is an intestinal dysfunction. Prebiotics, such as inulin, can improve bowel function by positively influencing intestinal biota.**

Aim: **To analyze the scientific evidence for the role of inulin in improving bowel function in patients with chronic constipation.**

Methods: **A meta-analysis of randomized controlled clinical trials was conducted, grounded on a literature search for the period 1995-2013 (descriptors: inulin & constipation) on PubMed, ScieLo and Central Trials Register Cochrane databases. A total of 24 articles were found, 5 of them were selected for this meta-analysis, involving 252 subjects (experimental group: n = 144, control group: n = 108). The quality of the studies was assessed using the Jadad scale.**

Results: **We found a significant overall effect of inulin on stool frequency (DEM = 0.69, 95%CI: 0.04, 1.34), stool consistency (Bristol scale) (DEM = 1.07, 95% CI: 0.70, 1.45), transit time (DEM = -0.57, 95% CI: -0.99, -0.15) and hardness of stool (RR = 0.42, 95% CI: 0.26, 0.70). Pain and bloating do not improve with inulin intake.**

Conclusions: **inulin intake has a positive effect on bowel function.**

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Key words: *Inulin. Constipation. Bowel function. Randomized controlled clinical trial. Meta-analysis.*

EFICACIA DE LA INGESTA DE INULINA SOBRE LOS INDICADORES DEL ESTREÑIMIENTO CRÓNICO; UN META-ANÁLISIS DE ENSAYOS CLÍNICOS ALEATORIZADOS CONTROLADOS

Resumen

Introducción: **El estreñimiento es una disfunción intestinal. Los prebióticos, como la inulina, pueden mejorar la función intestinal influyendo positivamente en la biota intestinal.**

Objetivo: **Analizar la evidencia científica del papel de la inulina en la mejora de la función intestinal en sujetos con estreñimiento crónico. Material y método: se realizó un meta-análisis de ensayos clínicos aleatorizados controlados que fueron seleccionados en una búsqueda bibliográfica en el período 1995-2013 (descriptores: inulina & estreñimiento) en PubMed, ScieLo y el Registro Central de Ensayos Clínicos de Cochrane. Se encontraron 24 artículos, de los que 5 fueron seleccionados para este meta-análisis, que involucran a 252 sujetos (grupo experimental: n = 144; grupo control: n = 108). La calidad de los estudios fue evaluada con la escala Jadad.**

Resultados: **Se ha encontrado un efecto global significativo de la inulina sobre la frecuencia de las deposiciones (DEM = 0,69, IC 95%: 0,04; 1,34), la consistencia de las heces (Escala de Bristol) (DEM = 1,07, IC 95%: 0,70; 1,45), el tiempo de tránsito (DEM = -0,57, IC 95%: -0,99; -0,15) y la dureza de las heces (RR = 0,42, IC 95%: 0,26; 0,70). El dolor y la distensión abdominal no mejoran con la ingesta de inulina.**

Conclusiones: **La ingesta de inulina tiene un efecto positivo sobre la función intestinal.**

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Palabras clave: *Inulina. Estreñimiento. Función intestinal. Ensayo clínico aleatorizado. Meta-análisis.*

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Abbreviations

C: Cases.
Gr: Gram.
M: Mean.
Ml: Milliliter.
NR: Not reported.
P: Placebo.
RCT: Randomized clinical trial.
RR: Relative risk.
SD: Standar Desviation.

Introduction

Constipation is a common dysfunction characterized by a large combination of symptoms, among which hardness of stool, an incomplete sensation of evacuation, abdominal pains, swelling and distension, are included.[1]

In the clinical scope, constipation is established based on the diagnostic criteria Roma III,[2] being necessary the achievement of, at least, two of the following in more than 25% of the stool frequency: a) effort; b) hard or compact stool; c) incomplete sensation of evacuation; d) sensation of blockage or obstruction; e) manual manoeuvres for evacuation; or f) less than three stool frequency per week. The epidemiological studies show figures of prevalence of this disorder, with values oscillating between 4, 4%[3] and 81%[4] considering the population characteristics, although, the majority of studies indicate a prevalence around 15% on adult population in occident.[5,6] This bowel dysfunction negatively influences the quality of life of the individuals affected[7,8] and could be related to an increment in the risk of suffering colorectal cancer.[9,10]

In the past decade, interest for prebiotics, which are defined as non-digestible substances (food fibre), has increased considerably, resulting beneficial for the health of the individual, as they stimulate the growth or the activity of a certain number of the bacteria in the colon.[11] Prebiotics are fermentable oligosaccharides which are specifically designed to change the compositions and the activity of the intestinal microbiota, such as bifidobacterium and lactobacillus,[12] whose presence has been related to a beneficial effect on the consistency and the pH of the faeces, as well as the stool frequency.[13,14] The ingestion of food fibre, thus, presents itself as a non-pharmacological option for the treatment of constipation.

Inulin is a prebiotic substance which functions in the same way as food fibre. It is a polysaccharide present in roots, tubers and plant rhizomes of common usage (chicory, garlic, artichoke, etc.), which is made by molecular chains of fructan of type $\beta(2 \leftarrow 1)$, causing significant changes in the compositions of the intestinal microflora and improving intestinal habits.[15]

Although the evidences seem to indicate towards a beneficial effect of inulin on intestinal habits of people who suffer from constipation, there are few clinical trails that provide enough guaranties in this sense. The aim of this study is to undertake a meta-analysis from the randomized clinical trails (RCT) in which the effect of inulin ingestion is analysed through the bowel function of people suffering from constipation.

Material and methods

Criteria of inclusion

The clinical trails which have been sellected are randomized studies which include one or more independent control groups and, one experimental group to which a food substance containing inulin was administrated. A placebo substance (maltodextrin, lactose, etc.) was applied to the control groups, as specified on table I. The resulting values are indicators of the bowel function related to constipation (stool frequency, consistency, transit time, abdominal pain and bloating).

Criteria of exclusion

Duplicated studies, revisions, observational studies, clinical cases and crossed randomized clinical trails, have been excluded.

Research strategies and data extraction

A bibliographical search has been made on the following data bases: *PubMed, Central Registry of randomized clinical trials from Cochrane and ScieLo.* The terms of the search have been "inulin & constipation" ("inulina & estreñimiento"). The research has been carried out independently by two reviewers, reaching a consensus on the search results. In cases of disagreement, the participation of a third reviewer has been requested. The dates of publication have been enclosed between 1995 and 2013. 29 results have been obtained, from which 5 have been selected for this meta-analysis (fig. 1).[16-20] The others have been rejected for being randomized controlled clinical trails,[10] for lack of data in the results[5] or for being crossed controlled clinical trails.[4] A search and article selection diagram has been drawn (fig. 1). For data extraction, a data base has been created for the different selected RCT, in which the results of each case has been registered. Subsequently, the results have been put together and grouped by common variables in the different studies. The variables, which were only present in one study, have been excluded, selecting only that data found at least in two of the RCT.

Statistic analysis

Data analysis has been made using Epidat® 3.1. Software. The categorical variables were analysed using

Table I
Characterstics of the selected trials

Trial	*Cases C/P*	*Age (years) Range M; ± Sd*	*Gender M/F*	*Intervention*	*Placebo*	*Conclusions*
López-Román et al., 2008[16]	16/16	47 ± 15	4; 28	Semi-skimmed milk (1/2 litre/day), 2 g/100 ml inulin, 2 g/100 ml MRD, 20 days	Semi-skimmed milk with vitamins A y D, 20 days	Improvement of the situation of primary cronic constipation idiopatic following Roma II criterion
Pilipenko et al., 2009[17]	(20 x 3)/16	18-72; 43.78	8; 68	Group 1: 150 g enriched yogurt (1.21 g/100 g); Group 2: 300 g enriched yogurt (0.31 g/100 g); Group 3: 200 g kefir (4 g/100 g). 14 days	Standere diet with an increment of diatetic food fiber (vegetables and dried fruit), 14 days	The insertion of inulin improved the health indicators related with constipation
Linetzky et al., 2012[18]	28/32	18-65	Women	15 g/day inulin, 3 weeks	15 g/ day maltodextrin, 3 weeks	The effects on the clinical indicators of constipation are comparable to those of the maltodextrin group
Weber et al., 2013[19]	20/24	4-12	na	Mixture of food fiber (Stimulance, "Milupa"), 12.5% inulin; 3.8 g of dilute fiber in 200 ml of milkshake for children > 18 kg; 7.6 g on children > 18 kg, twice/day, 4 weeks	Same dosage of maltodextrin, 4 weeks	The mixture of food fiber increases stool freacuency and hardness
Isakov et al.,	20/20	na	na	Enriched yogurt (1.23 g/100 g), 125 ml twice/day, 2 weeks	Standered yogurt, 125 ml twice/day, 2 weeks	Enriched yogurt reduces the time of bowel transit and increases stool consistency

Charecteristis of the studies: Consecutively showing a sample of each study (cases/controls); age (shown on the age range, on average and/or standard deviation); distributions of the participant's gender; type of intervention: placebo characteristics; conclusions of the different studies.

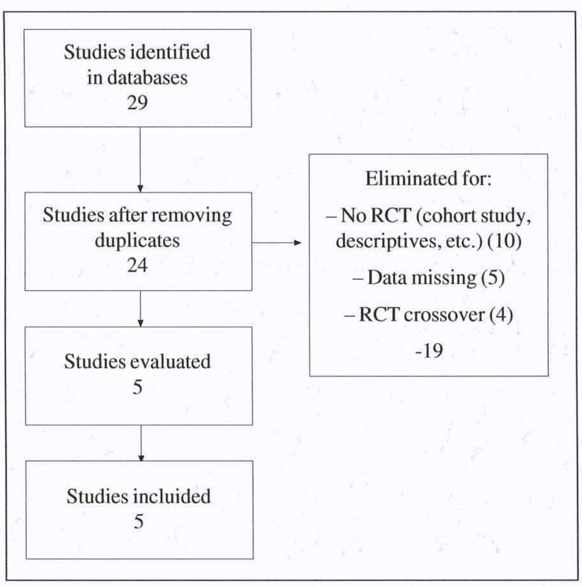

Fig. 1.—Diagram of selection of studies, representing how the studies were excluded and motives.

the relative risk (RR) procedure, while the constant variables have been analysed using the procedure of differentiation of standardized measures. A confidence interval of 95%, as well as the heterogeneity Dersimonian and Laird's Method has been calculated. When the result of the study was significant, the model of randomized effects was applied, employing the model of stable effects in the other cases. The publication bias was evaluated using Egger and Begg's test.

Results

Characteristics of the included studies

This study includes 5 articles which involve 252 subjects (144 in the experimental group and 108 in the control group). The general characteristics of this study, as well as those related to the interventions employed and the results of the trails can be found on table I.

Table II *Analysis of the quality of the trials by Jadad scale*						
Trial	*Randomized*	*Randomization method*	*Doble-blind*	*Blinding*	*Withdrawal*	*Total*
López-Román et al., 2008[16]	Yes	No	Yes	No	No	2
Pilipenko et al., 2009[17]	Yes	No	No	–	No	1
Linetzky et al., 2012[18]	Yes	No	Yes	No	Yes	3
Weber et al., 2013[19]	Yes	Yes	Yes	No	Yes	4
Isakov et al., 2013[20]	Yes	No	No	No	No	1

Describes the qualify of the studies bases on the punctuation (0-5) of the Jadad scale, based on the various characteristics of the studies.

Analysis of the quality of the trials

The *Jadad Scale* has been applied for the evaluation of clinical trails, in which the following aspects have been evaluated: existence of randomization, description of the randomization method, adequacy of the method, doble-blind, description of the blinding technique, adequacy of the test and description of the faults of the study. The maximum punctuation is 5, indicating the highest quality of the study. On table II, it can be observed that none of the selected articles reach the highest punctuation. None of them describe the procedure of blinding and only the article of Weber et al.[19] describes the randomization method.

Meta-analysis of the stool frequency

The five selected studies contain data to evaluate weekly stool frequency. The heterogeneity test has displayed a result statistically significant (χ^2_4 = 21,92; p = 0,000), which suggests the use of the model of randomized effects. The global test of this model indicates a significant effect upon the administration of inulin in the weekly stool frequency (fig. 2). Nevertheless, an existing bias of publication has been found, as shown on *Egger's test* (t_3 = 6,632; p = 0,007). Also, the sensibility analysis (table III) shows lack of robustness on the meta-analysis results, due to the dependency laying on the results of all the studies included.

Meta-analysis of the consistency (Bristol Scale)

In this test, three studies have been included. The heterogeneity test does not allow to reject the invalid hypothesis of the homogeneity of the studies (χ^2_2 = 2,17; p = 0,338), thus, the model of fixed effects has been applied. The global test of this model indicates a significant effect upon the administration of inulin in stool consistency according to

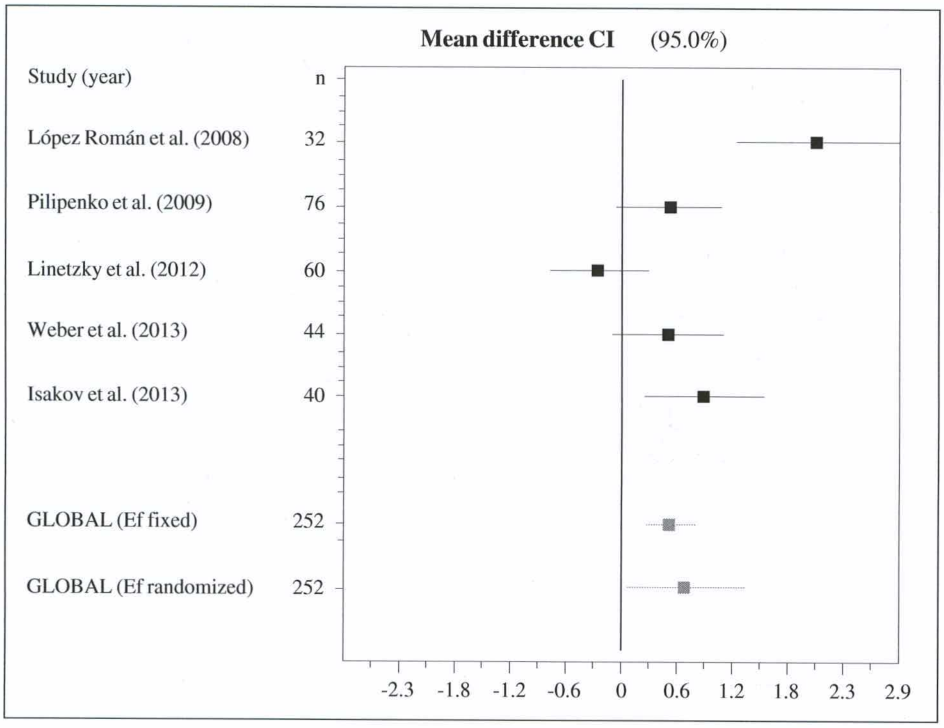

Fig. 2.—Graphic representation of the effects in the different trials and global estimation of the effects of the stool frequency meta-analysis.

Table III
Meta-analysis results: individual, global test and sensibility

	Experimental group			*Control group*					
				Stool frequency (weekly)					
Study	*M*	*Sd*	*n*	*M*	*Sd*	*n*	*Weight %*	*DEM (IC 95%)*	*Sensibility*
López-Román et al., 2008[16]	5.6	1.17	16	3.5	0.84	16	17.27	2.07 (1.21-2.93)	-43.87
Pilpenko et al., 2009[17]	5.39	2.18	60	4.27	2.1	16	20.95	0.52 (-0.04-1.08)	9.1
Linetzky et al., 2012[18]	5.95	2.5	28	6.7	3.83	32	21.5	-0.23 (-0.74-0.28)	33.92
Weber et al., 2013[19]	7.65	3.16	20	6.35	2.17	24	20.42	0.49 (-0.11-1.09)	9.84
Isakov et al., 2013[20]	6.58	3.5	20	4.27	1.4	20	19.86	0.87 (0.22-1.51)	-4.71
Total			144			108		0.69 (0.04-1.34)	
				Stool consistency (Bristol scale)					
Study	*M*	*Sd*	*n*	*M*	*Sd*	*n*	*Weight %*	*DEM (IC 95%)*	*Sensibility*
López-Román et al., 2008	4.53	0.85	16	3.28	1	16	41.25	1.24 (0.65;1.82))	-10.72
Pilpenko et al., 2009	3.67	0.9	60	2.62	0.6	16	34.74	0.69 (-0.05;1.33)	18.98
Isakov et al., 2013	3.1	1.3	20	2.4	0.6	20	24.01	1.35 (0.58-2.11)	-8.01
Total			96			52		1.07 (0.70-1.45)	
				Transit time (minutes)					
Study	*M*	*Sd*	*n*	*M*	*Sd*	*n*	*Weight %*	*DEM (IC 95%)*	*Sensibility*
Pilpenko et al., 2009	115.57	25.83	60	132.8	41.9	16	56.98	-0.58 (-1.14;-0.02)	
Isakov et al., 2013	109	30.4	20	12.7	34.1	20	43.92	-0.56 (-1.19;0.07)	
Total			80			36		-0.57 (-0.99;-0.15)	
				Abdominal pain					
Study	*M*	*Sd*	*n*	*M*	*Sd*	*n*	*Weight %*	*DEM (IC 95%)*	*Sensibility*
Pilpenko et al., 2009	1.32	0.53	60	1.25	0.4	16	51.82	0.14 (-0.41;0.69)	
Isakov et al., 2013	1.1	0.3	20	1.4	0.5	20	48.18	-0.73 (-1.37;-0.09)	
Total			80			36		-0.28 (-1.12;0.57)	
				Abdominal distension					
Study	*M*	*Sd*	*n*	*M*	*Sd*	*n*	*Weight %*	*DEM (IC 95%)*	*Sensibility*
Pilpenko et al., 2009	1.53	0.73	60	1.8	0.6	16	55.75	-0.38 (-0.93;0.17)	
Isakov et al., 2013	1.8	0.9	20	1.6	0.5	20	44.25	0.27 (-0,35;0.90)	
Total			80			36		-0.09 (-0.51;0.32)	
				Stool consistency (hardness)					
Study	*n*	*%*	*n*	*%*	*Weight %*		*RR (IC 95%)*		
Pilpenko et al., 2009	20	40	24	83.3	21.78		0.27 (0.09;0.80)		
Isakov et al., 2013	16	21.4	16	71.4	78.22		0.48 (0.27;0.85)		
Total	36		40				-0.42 (0.26;0.70)		

Join data of all the analysis – Stool consistency (hardness), abdominal distension, stool consistency (Bristol scale), transit time (in minutes), abdominal pain, stool frequency (weekly) – for the experimental group and control group, expressed in each of the cases in average, standard deviation, number of samples; the % of the weight of each study in the neta-analysis; and the standardized difference of the averages. In those cases where more than two studies were able to be included, sensibility has been included.

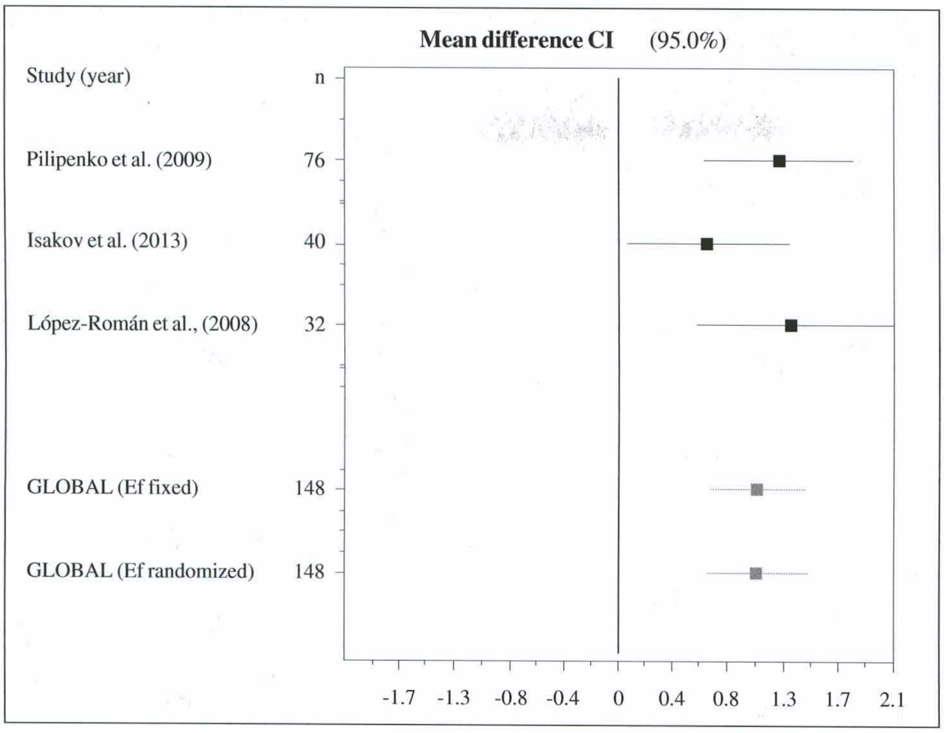

Fig. 3.—Graphic representation of the effects in the different trials and global estimation of the meta-analysis effect of stool consistency (Bristol scale).

Bristol Scale (fig. 3). The Egger test value ($t_1 = 0,252$; $p = 0,843$) allows to dismiss the presence of a publication bias. Nonetheless, the sensibility analysis (table III) points out an anomaly related to the robustness of the meta-analysis results, due to the variability of the global result dependent of each study included.

Consistency's meta-analysis (hardness)

In this meta-analysis, 2 studies have been included. The model of fixed effects has been applied due to the non-signification of the test to study the heterogeneity of the studies included ($\chi^2_1 = 0,84$; $p = 0,361$). The global test confirms the existence of a significant effect in the administration of inulin upon stool consistency-hardness (fig. 4). The value of Begg test ($z = 0,00$; $p = 1,000$) indicates absence of a publication bias. A sensibility analysis has not been developed because only two studies were included.

Meta-analysis of transit time

For the meta-analysis of transit time (in minutes), two studies have been used. According to the heterogeneity test, the application of the model of fixed effects ($\chi^2_1 = 0,00$; $p = 0,961$) is adequate, advising the use of the model of fixed effects. The global test of this model shows a significant effect of the administration of inulin in the reduction of transit time (fig. 5). The Begg test value ($z = 0,00$; $p = 1,000$) allows to dismiss the presence of a publication bias. A sensibility analysis has not been developed because only two studies were included.

Meta-analysis of abdominal pain

In this case, two studies have been included. The heterogeneity test indicates that the model which should be applied is that of randomized effects ($\chi^2_1 = 4,03$; $p = 0,045$), advising the use of the model of fixed effects. According to the global test of this model, a significant effect of the administration of inulin in the reduction of abdominal pain does not exist (fig. 6). The Begg test value ($z = 0,00$; $p = 1,000$) indicates the absence of a publication bias. A sensibility analysis has not been developed because only two studies were included.

Meta-analysis of abdominal distension

Once again, Pilipenko et al.[17] and Isakov et al.[18] studies have been included. The model of fixed effects has been applied due to the non-signification of the test to study the heterogeneity of the studies included ($^2_1 = 2,39$; $p = 0,122$). The global test does not allow the affirmation of the existence of a significant effect in the administration of inulin in the reduction of abdominal distension (fig. 7). The Begg test value ($z = 0,00$; $p = 1,000$) indicates the absence of a publication bias. A sensibility analysis has not been developed because only two studies were included.

Discussion and conclusions

The results obtained in the mate-analysis show that the administration of inulin produces a significant bene-

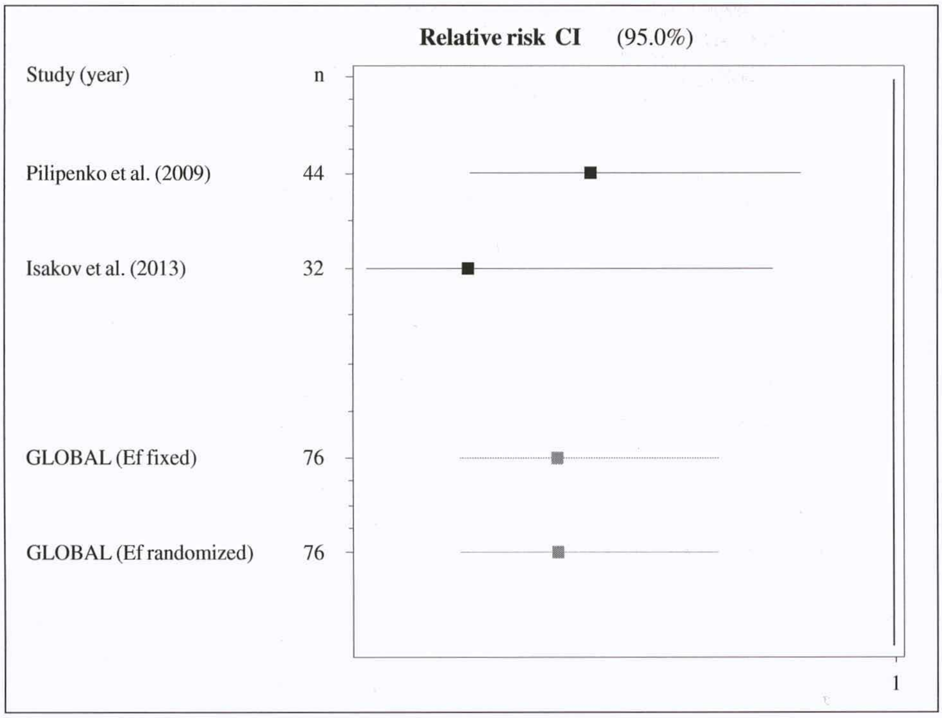

Fig. 4.—Graphic representation of the effects in the different trials and global estimation of the meta-analysis effect of the stool consistency (hardness).

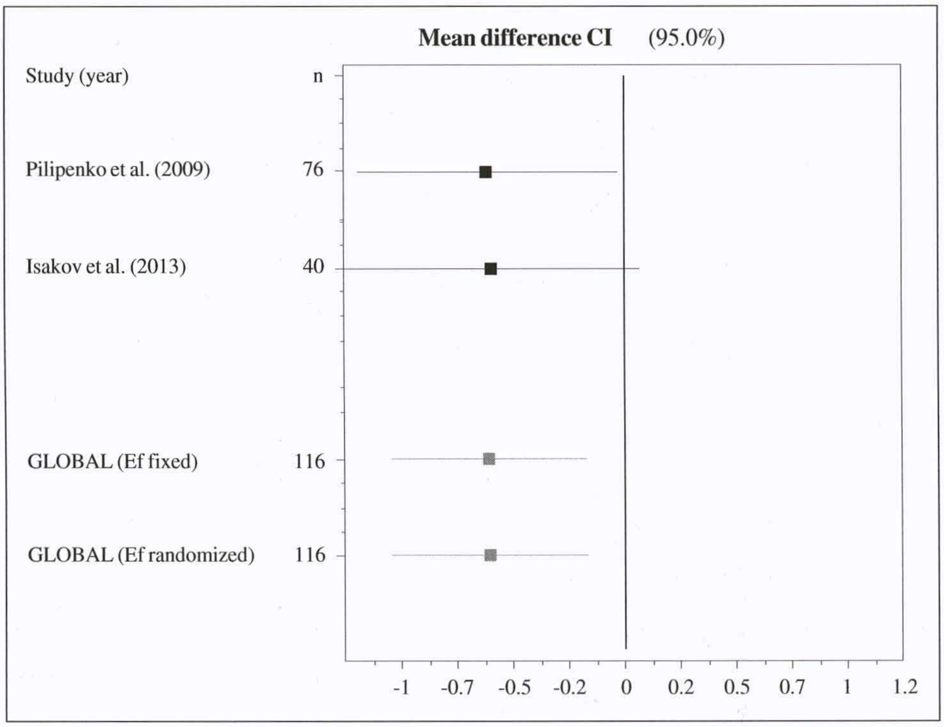

Fig. 5.—Graphic representation of the effects in the different trials and global estimation of the meta-analysis effect of transit time.

ficial effect upon various indicators of the intestinal function of evacuation in individuals with chronic constipation. An increase in the number of weekly stool frequency, a higher stool consistency according to the Bristol Scale, a lower intestinal transit time, as well as a reduction on the stool consistency has been observed. This demonstraits the beneficial effects of the ingestion of inulin for patients who suffer from chronic constipation in indicators that constitute essential aspects in this disorder. Nonetheless, the clinical trials examined have not produced a conclusive result in the reduction of abdominal pain and abdominal distension.

In relation to stool frequency, the results of this meta-analysis are in agreement with the ones observed in other studies.[21-25] Nevertheless, when evaluating the tolerance of inulin in one of the randomized crossed clinical trails

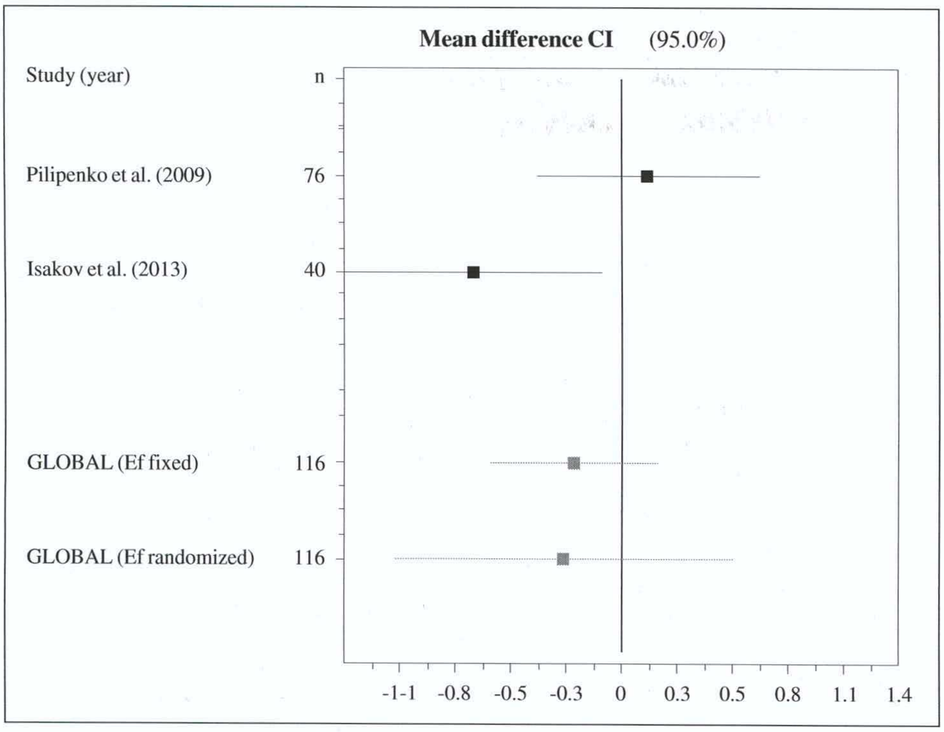

Fig. 6.—Graphic representation of the effects in the different trials and global estimation of the meta-analysis effects of abdominal pain.

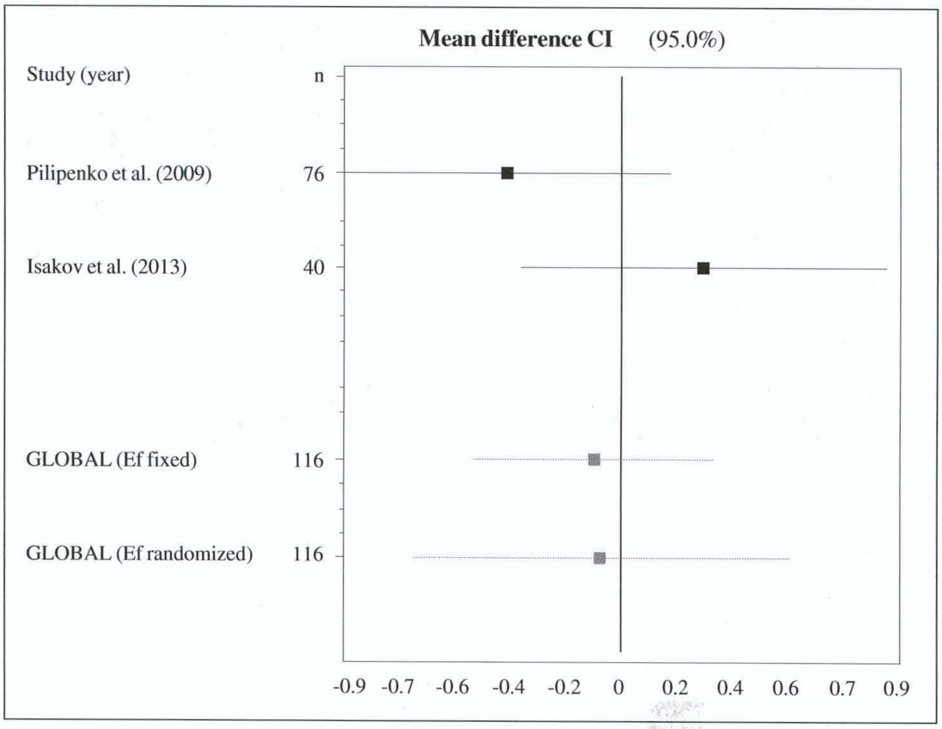

Fig. 7.—Graphic representation of the effects in the different trials and global estimation of the meta-analysis effects of abdominal distension.

made upon 84 patients, it was observed that stool frequency, although being a highly significant indicator of constipation, did not contribute decisively to the perception of the beneficial effects of the ingestion of this substance, as its most beneficial effects were indicated upon flatulence and stool consistency.[26]

As far as the stool consistency according to Bristol Scale, our study confirms the findings of other clinical trails which have not been included in this meta-analysis, for being crossed data that confirms the efficiency of inulin ingestion upon the increment of stool quality.[21,25] One of the characteristics which better indicates stool quality is consistency, and in individuals with constipation, it presents itself hard, complicating evacuation. The ingestion of inulin has been associated, in our study, with a reduction of hardness in stool frequency, which is in accordance with what was found in other studies,[22,24,25] although there are other studies that have not found significant differences in the hardness of stool between the groups that were administrated inulin and the placebo.[21,23]

Another positive effect for the individuals with constipation, related to the ingestion of inulin, is the reduction of intestinal transit time, in accordance with the findings of other authors,[21] for which the mechanisms associated with a higher speed in intestinal transit could be related to an increase in the peristaltic contractions, a reduction in anti-peristaltic contractions or a reduction of the contractions of the left colon. Other factors associated, could be the volume increment of the stool because a reduced re-absorption or the increment of the quantity of endoluminal bacteria, which represents approximately 60% of faecal volume. Nonetheless, other studies seem not to have found a positive effect upon the speed of intestinal transit as a consequence of inulin ingestion.[23]

In relation to pain symptoms and abdominal distension, our study has not been able to establish a positive effect in inulin ingestion, as opposed to what was found in other studies.[21,22,25] Nevertheless, in another experimental study, it has not been established that inulin ingestion is associated with a reduction of pain and abdominal distension,[24] showing the existing variability in the results on these indicators of constipation.

Therefore, it can be affirmed that, considering the examined clinical trails, inulin ingestion produces a beneficial effect upon bowel function of individuals with constipation in the frequency, consistency, quality, and transit time. Moreover, the administration of this product has not been linked with relevant adverse effects for the health of the patients, being a substance which is well tolerated by the organism in recommended dosages.[26] However, we should continue the investigation of the effects of inulin in bowel function, as the results of this meta-analysis is based upon a reduced sample of randomized clinical trails, this reflects the lack of scientific production related to this subject. These circumstances reduce the robustness of the conclusions, which need to be supported by clinical trails that recruit a greater amount of patient samples.

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