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Effectiveness of cinnamon bark extract in the treatment of allergic rhinitis

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ABSTRACT

OBJECTIVE

The purpose is to evaluate the effectiveness and safety of intranasal cinnamon extract (CE) in the management of patients with allergic rhinitis (AR).

METHODS

This is a systematic review, using the standard methodological procedures recommended by Cochrane to search six databases: Cochrane, PUBMED, EMBASE and LILACS, from database inception up to May 2020, to identify randomized controlled trials evaluating the use of CE in treatment for AR.

RESULTS

We included two trials involving a total of 100 participants. The studies were at low risk of bias. All studies had similar participant selection criteria and outcome measurement, enabling a meta-analysis. Both studies used a validated instrument (Rhinoconjunctivitis quality of life questionnaire – RQLQ) for this primary outcome (SMD -1.06; 95% confidence interval (CI) -1.58 to -0.59, P <0.0001). .All studies resulted in at least some clinical benefit with the use of CE compared to placebo. None of the included studies reported any significant adverse effects.

CONCLUSIONS

Despite the evidence from two studies showed certain positive effects of response for CE under evaluation in treatment of AR. We found no evidence regarding the effectiveness of intranasal cinnamon bark extract for allergic rhinitis. Well-conducted randomized clinical trials using CE are needed to further advance our understanding of the effectiveness for AR.

DESCRIPTORS

Allergic Rhinitis. Cinnamon. Rhinitis. Allergy. Meta-analysis.

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INTRODUCTION

Allergic rhinitis (AR) is one the most common chronic conditions worldwide, affects approximately 500 million people worldwide, with a higher incidence in westernized industrialized countries. It usually requires years of symptomatic treatment because allergies are chronic, beginning in child-hood and lasting through late adulthood. It is estimated that AR affects approximately 113 million people in Europe and 30 to 60 million in the United States[1]. The estimated direct cost of AR in 2005 was $11.5 billion according to the Medical Expenditure Panel Survey, a longitudinal survey that collects detailed information on health care use and expenditures in the United States[2].

The disease process itself is initiated when an individual is exposed to an allergen that stimulates immunoglobulin E (IgE)-mediated inflammatory responses in the nasal mucosa. This leads to allergen sensitization and the development of an atopic reaction that symptomatically manifests as rhinorrhea, pruritus, sneezing, and nasal congestion[3].

Pharmacological treatment with antihistamines and topical corticosteroids has been shown to reduce symptoms, but does not change the course of the disease. Allergen specific immunotherapy (TIA) is the only curative treatment so far, but it is very long-lasting and not recommended for multiple sensitizations or food allergy (together) due to the risk of serious systemic side effects. Many patients resort to complementary and alternative therapies such as acupuncture, traditional Chinese medicine, homeopathy and herbal therapy for disease management with more or less evidence against its effectiveness[4].

Cinnamon extract (CE) derived from cinnamon bark has been reported to exert antioxidative, antineoplastic, antidiabetic, anti-inflammatory, and anti-allergic effects in vivo and in vitro[5–9]. CE inhibits histamine release and synthesis of lipid mediators during allergic disease. For example, in vivo studies in patients with seasonal allergic rhinitis demonstrated anti-allergic properties of CE after allergen provocation concerning nasal symptoms and prostaglandin D2 release. Most recently, studies suggest that CE might be a promising antiallergic therapeutic agent especially for atopic dermatitis patients but also in the context of anaphylaxis and airway inflammation[10].

To the current date, a limited number of randomized controlled trials have evaluated the effectiveness of CE for the treatment of AR, usually with conclusions in favor of its use. No systematic review was carried out in order to assess its benefits in AR management, with the potential to improve the patient's quality of life and reduce medications in use. The current study seeks to systematically review the role of CE as an adjunctive treatment for AR.

METHODS

A comprehensive systematic literature review was performed using the standard methodological procedures recommended by Cochrane to search four databases: Cochrane - Central Register of Controlled Trials - CENTRAL, PUBMED, EMBASE, LILACS, from database inception up to May 2020, to identify randomized controlled trials evaluating the use of cinnamon bark in treatment for Allergic Rhinitis. The search was limited to studies performed on humans. The search criteria included the Medical Subject Headings (MESH) terms "rhinitis" and "cinnamon".

Only randomized controlled trials including patients with Allergic Rhinitis, with specified point evaluation standards, defined outcome measures and provision of efficacy or safety information were reviewed. The exclusion criteria were a high risk of bias, if providing insufficient data, if focused on patient with asthma, if combined therapy contained interventions, that examined mixed non-allergic or rhinosinusitis RA or included patients with any significant clinical condition or abnormality.

Two authors (GS and BGS) independently screened the citations identified and selected those judged possibly relevant by both for full-text reading. In case of disagreement or uncertainty of study relevance based on title and abstract screening, we also retrieved the full-text article. The two independent review authors read each full paper, extracted the data and assessed each for possible inclusion according to the selection criteria. Any inconformity was solved by consensus. End point indicators were determined by assessing the most common used scales from data characteristic.

Data was then extracted from individual studies and assembled in a standardized database using Cochrane Review Manager 5.3 software version (The Cochrane Collabo-ration, Oxford, UK). Mean values, standard deviations and sample sizes were used for each comparable objective criterion. This data was then formatted into forest and funnel plots to illustrate the relative strength of treatment effects and assessment of publication bias, respectively. Risk of bias was assessed according to the Cochrane Collaboration's tool. We decided to drop studies with a high risk of bias. When applicable, results are described in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines for reporting systematic reviews and meta-analyses, with 95% confidence intervals (CI) reported throughout. A p value of <0.05 was considered significant for all statistical tests.

RESULTS

The literature search retrieved a total of 84 articles. A title and abstract review followed by exclusion of any duplicate publications resulted in 65 remaining articles for full-text review. After closer examination of the titles and abstracts of these references, we obtained full paper copies for 5 citations that were potentially eligible for inclusion in the review. We excluded two studies that experience the effects in mice[11–12] and one that used EC on a composition, mixed with Malpighia glabra and Bidens pilosa (ClearGuard™)[13]. None studies were excluded because of a lack of quantifiable data or insufficient study description. We found no ongoing studies and no studies are awaiting assessment (Figure 1).

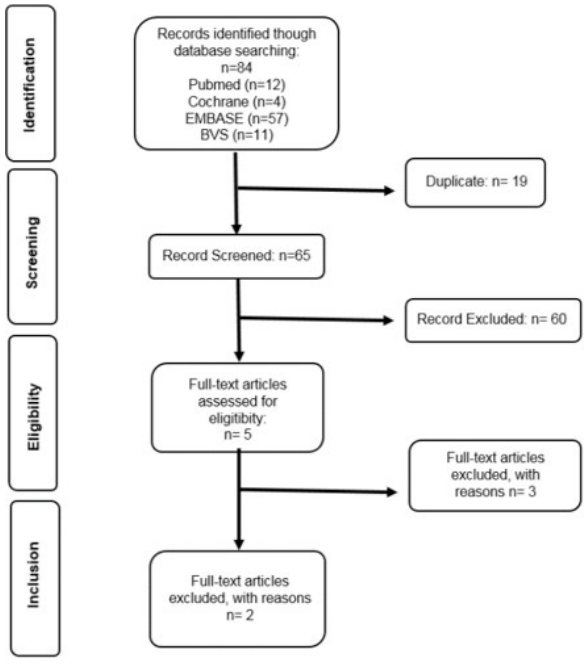

Figure 1. Process of study identification and selection.

Ultimately, the selection process included two articles in the study, involving a total of 100 participants[14–15]. Both studies were reported to be placebo-controlled and randomized. The included studies had similar participant selection criteria and outcome measurement, enabling a meta-analysis. The studies were at low risk of bias.

Each trial included two groups of participants: one was treated with intranasal cinnamon extract (Cinnamonum zylanicum bark (TAPP-CZ) on Walanj, et al[14] and Cinnamonum zylanicum Syn: Cinnamomum verum (IND02) on Steels, et al[15] and the other with placebo (control group). In both studies, participants were instructed to take one shot per nostril in the morning and evening twice daily, using the same dosage (1g/L), for 4 weeks on the first study and 7 days on the second.

All participants were adults over 18 years with diagnostic of seasonal allergic rhinitis. Walanj, et al[14] included 40 participants, separated uniformly in respect of demographic and baseline parameters such as gender and weight, but not the age. Mean age of patient on placebo group (39.85) is significantly more (P < 0.05) than that of active group (32.10). Steels, et al[15] included 60 participants, that the two groups were evenly matched for age (42.8 ± 14.82 years, active group; 43.7 ± 14.19 years, placebo group).

Both studies used defined outcome measures, particularly the measurement of the Rhinitis Quality of Life Questionnaire (RQLQ), which allowed for direct comparison and meta-analysis, and, individually, the Nasal Symptom Score (NSS) and Total Nasal Symptom Score (TNSS), the Pittsburgh Sleep Quality Index (PSQI), labor productivity (Work Productivity and Decrease in Activities - Specific Allergy) (WPAI-AS) and Specific Health Problem (WPAI: SHP).

The meta-analysis demonstrated a significant improvement in RQLQ global score in the intervention groups compared to the placebo (standard mean difference [SMD] - 1.06; 95% confidence interval (CI)-1.58 to -0.54, P<0.0001), as well as in RQLQ nasal symptoms (SMD - 1.11; 95% CI, -1.65 to -0.57, P<0.0001), RQLQ eye symptoms (SMD – 0,86; 95% CI, -1.27 to -0.45, P<0.0001), RQLQ non-hay fever symptoms (SMD -1.01; 95% CI, -1.71 to -0.35, P<0.005) and RQLQ practical problems (SMD -0.78; 95% CI, -1.34 to -0.22, P<0.007) (Figure 2).

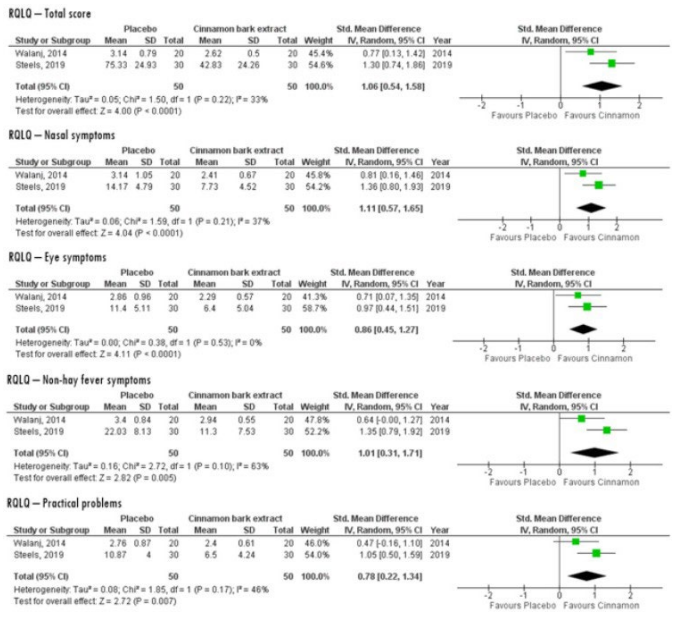

Figure 2. Comparison. Cinnamon bark extract versus placebo Outcome 1. Rhinitis Quality of \Life Questionnaire (RQLQ). Cl = confidence; St = standard deviation.

Walanj, et al[14] revealed similar findings using the data from TNSS (SMD -0.91; 95% CI, -1.57 to -0.26, P<0.006). The difference between CE and placebo was significant clinically and statistically. However, when the NSS parameters were analyzed separately, only the sneezing (CID = 1.09) and nasal drainage (CID = 1.13) scores were significant clinically and statistically (P < 0.05). The mean NSS or TNSS scores were not significantly different from corresponding values of placebo group at follow-up visit (4-weeks after the treatment was finished) (Figure 3).

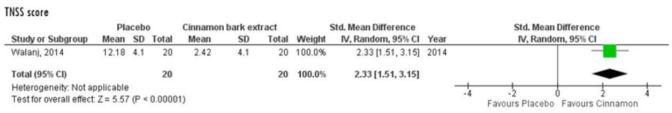

Figure 3. Comparison. Cinnamon bark extract versus placebo Outcome 2. Total Nasal (TNSS). Cl = confidence interval; St = standard deviation.

With the purpose of evaluating the labor productivity, Walanj, et al[14] used the WPAI-AS score, showing significant difference between groups after 4 weeks of treatment (SMD -0.79; 95% CI, -1.43 to -0.14, P<0.02) (Figure 4). However, this difference was not sustained at follow-up visit (4-weeks after the treatment was finished). Steels, et al[15] used the WPAI-SHP score, and noted a significant improvement in overall work productivity (SMD -0.75; 95% CI, -1.37 to -0.13, P<0.02) and a significant decrease in regular daily activity impairment (SMD -0.93; 95% CI, -1.56 to -0.29, P<0.004) in favor of the intervention group, even after only 7 days of treatment (Figure 5).

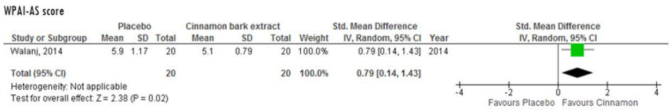

Figure 4. Comparison. Cinnamon bark extract versus placebo Outcome 3. Effect on Work Productivity and Impairment-Allergy Specific (WPAI-AS) score. Cl = confidence interval; St = standard deviation.

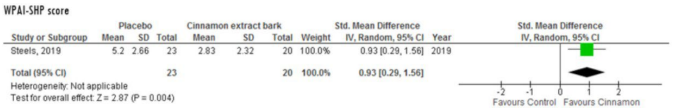

Figure 5. Comparison. Cinnamon bark extract versus placebo Outcome 4. Effect on Work Productivity and Impairment – Specific Health Problem *WPAI: SHP) score. Cl = confidence interval; St = standard deviation.

Exclusively, Steels, et al[15] used laboratory clinical parameters (biochemical and hematological analysis) as a second outcome, funding a wide range in IgE responses with a similar distribution of total Ig E levels in both groups. The groups were evenly matched for the number of allergen groups associated with raised IgE levels.

Few adverse events were reported among the included studies. Complaints including cough, fever, headache, body aches, throat irritation and swollen bottom lip were reported in select studies, but at rates that typically mirrored the placebo group. There were no serious/life-threatening adverse events and no patients required additional treatment or intervention.

DISCUSSION

This current systematic review and meta-analysis represents the most comprehensive analysis to date on the use of cinna-

mon extract for the treatment of allergic rhinitis. All studies resulted in at least some clinical benefit with the use of CE compared to placebo. A meta-analysis resulted in concordant results, showing a statistically significant improvement in global and specific symptom RQLQ scores.

However, some limitations prevent us from making generalized recommendations based on this data. The general group of participants remained quite homogeneous, but only two studies composed the analysis summating 100 participants. No participants under 18 years old were added to this group. Moreover, the outcome measures were mostly heterogeneous, limiting the evaluation.

Recently, much about the role of cinnamon in the human immune response has been studied to be completely defined. The available in-vitro and in-vivo evidence suggests that CZ has anti-microbial, anti-parasitic, anti-oxidant and free radical scavenging properties. In addition, CE seems to lower blood glucose, serum cholesterol and blood pressure, suggesting beneficial cardiovascular effects[1] 6. In mice models, the intranasal CE (TAPP-CZ) was used in experimental allergic rhinitis induced by ovalbumin and promoted a prophylactic potential, probably through the down regulation of IgE and histamine release[11]. Although, one of the included studies exposed a similar distribution of total Ig E levels in control and intervention groups.

The mechanism by which cinnamon may modulate atopic diseases remains poorly understood and additional translational studies will likely be needed to clarify this in the future. The current study suggests that CE have the potential to alter disease severity, symptoms, and quality of life in patients with AR. Positive outcomes were reported in a majority of studies with no significant adverse events.

CONCLUSION

Despite the studies have shown that cinnamon bark extract has beneficial effects on the treatment of allergic rhinitis, there are only a few studies in this topic, with a reduced number of participants (low quality evidence). We found no evidence regarding the effectiveness of intranasal cinnamon bark extract for allergic rhinitis. Well-conducted randomized controlled trials are needed, and should be encouraged, to further advance our understanding of the effectiveness of cinnamon bark extract in the treatment of allergic rhinitis.

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