A comparative in vitro study on the effects of the product Citrus e fructibus / Cydonia e fructibus as a whole and the single agent drugs Citrus e fructibus and Cydonia e fructibus separately, on immunological parameters of seasonal allergic rhinitis

Published: 13-07-2010
Last updated: 02-05-2024

Primary objective:To investigate the effects of the three investigational products (1.Citrus e fructibus / Cydonia e fructibus as a whole, single preparations 2. Citrus e fructibus and 3. Cydonia e fructibus) on the changes in SAR related...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Allergic conditions
Study type	Observational invasive

Summary

ID

NL-OMON34748

Source
ToetsingOnline

Brief title
In vitro effects of Citrus/Cydonia versus only Citrus or only Cydonia

Condition

- Allergic conditions

Synonym
hay fever, Seasonal allergic rhinitis

Research involving
Human

Sponsors and support

Primary sponsor: WALA Heilmittel GmbH
Source(s) of monetary or material Support: Farmaceutisch bedrijf

Intervention

Keyword: Cytokine, PMBCs, Seasonal Allergic Rhinitis

Outcome measures

Primary outcome

Analysis in the culture supernatants of PBMCs:

•Proliferation capacity

•Cell viability

•Cell toxicity

•Total production capacity of seasonal allergic rhinitis related cytokines:

IL-10, IL-12, IL-1ß, TNFα, IFN-γ, IL-5, IL-13, IL17A

Secondary outcome

Not applicable

Study description

Background summary

Since the beginning of the 20th century the anthroposophic pharmaceutical product Citrus/ Cydonia, which was first described in the book *Grundlegendes für eine Erweiterung der Heilkunst* (Steiner and Wegman 1924), is produced and prescribed to many patients with seasonal allergic rhinitis (SAR) or hay fever.
A survey on clinical experiences, carried out among a group of 39 general practitioners in the Netherlands, indicated that Citrus/Cydonia is profoundly effective (De Bruin and Baars, 2001). Firstly, a permanent effect from the treatment with Citrus/Cydonia comp. was experienced, which indicates that the

patients in question are claiming to lastingly suffer less from hay fever or even that they are free from complaints. Secondly, the effect occurred within a period of two weeks, up to three months, after the actual treatment. Thirdly, the effect was optimal after a treatment of several years. In a therapeutic causality report, positive effects with Citrus/Cydonia were observed in a group of 13 patients suffering from grass pollen mediated hay fever (Baars and De Bruin, 2005). In most patients, Citrus/Cydonia comp. injections were given before the onset of and during the grass pollen season and symptom severity did not increase during the pollen season. Furthermore, 69% of the patients reported an improvement of symptoms. In addition, a prospective, observational study on the effect of a Citrus/Cydonia nasal spray on hay fever symptoms reported positive results without side effects in 140 patients (Rother and Oexle, 2008). In a recent randomized comparative clinical trial with two parallel groups of grass pollen SAR patients, the clinical and immunological effects of two routes of administration (nasal spray (NS) versus subcutaneous injection (SI)) of Citrus/ Cydonia 1% were compared. The results demonstrate that Citrus/ Cydonia 1% for the treatment group as a whole (both the NS group and the SI group) and in both routes of administration separately are able to execute both clinically and statistically significant SAR symptom severity reduction. The SI route of administration induces a larger effect than the NS route of administration (Baars et al., in prep.).
Recently, the immunological pathways underlying the positive effects of Citrus/Cydonia in patients with seasonal allergic rhinitis were studied (Baars and Savelkoul, 2008). Therefore, peripheral blood mononuclear cells (PBMCs) were isolated from the blood of a healthy and an allergic donor and the effect of Citrus/Cydonia comp. on differentiation capacity and Th1 (e.g. IFN-*) and Th2 (e.g. IL-5) cells was examined. Citrus/Cydonia showed a selective effect on the differentiation of T-cells by producing relatively more IL-10 than IL-12. Furthermore, it also had an effect on the induction of regulatory (IL-10 producing) T-cell subsets. It was therefore concluded that the medicinal product Citrus/Cydonia can potentially restore the disturbed immune state of allergic rhinitis patients by modulation of the Th1-Th2 balance. In the described randomized comparative clinical trial with two parallel groups of grass pollen SAR patients, the immunological data are consistent with the notion that Citrus/ Cydonia comp. 1% treatment will result in the induction of a more regulatory capacity in the immune system. The pattern of immunological data demonstrates that the treatment by the SI route of administration induced a better controlled and anti-allergic immune responsiveness compared to the NS route. The immunological results are in line with the clinical results of this study (Baars et al., in prep.). This immunotherapeutic potency and the positive results from the observed clinical cases, form the rationale to further evaluate the effects of Citrus/Cydonia medicinal products in seasonal allergic rhinitis.

Study objective

Primary objective:

To investigate the effects of the three investigational products (1.Citrus e fructibus / Cydonia e fructibus as a whole, single preparations 2. Citrus e fructibus and 3. Cydonia e fructibus) on the changes in SAR related immunological parameters in PMBCs as isolated from seasonal allergic rhinitis patients.

Secondary objective:
To investigate whether there are statistically significant differences between each of the three investigational groups on the changes in immunological parameters in PMBCs as isolated from seasonal allergic rhinitis patients and healthy subjects.

Study design

A comparative in vitro laboratory study with peripheral blood mononuclear cells (PBMCs) isolated from blood of participants

Study burden and risks

Possible risks that can be expected during blood withdrawal are very low and well known. Since a little amount of blood will be drawn once, the burden for the patients and healthy volunteers is very low as well.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

SAR patients:
•Written informed consent
•Sex: both men and women
•Age >= 18 and < 60 years
•Seasonal allergic rhinitis:
*Duration of at least 2 years
*High RAST grass pollen (>= 2) and high RAST birch pollen (>= 2)
*Suffering from the following nasal symptoms during the pollen season: sneezing, itching nose, nasal obstruction and watery nasal discharge
*Severity score of at least three of the four symptoms >= 2 (ranging from 0 = not present to 3= severe)
*The necessity to use antihistamines and/or corticosteroids for treatment of symptoms for previous (at least two) years.;Healthy volunteers:
•Written informed consent
•Sex: both men and women
•Age >= 18 and < 60 years
•RAST for grass and birch pollen = 0
•Absence of the following nasal symptoms during the pollen season: sneezing, itching nose, nasal obstruction and watery nasal discharge
•No history of SAR symptoms for at least 2 years

Exclusion criteria

SAR Patients:
•Chronic inflammatory autoimmune disease such as Type I - Diabetes Mellitus, Rheumatoid Arthritis, Multiple Sclerosis, Psoriasis or Crohn*s disease
•Allergic (hypersensitive) to one of the constituents of Citrus e fructibus / Cydonia e fructibus
•Asthma
•Use of other preparations containing Citrus and/or Cydonia extracts within the last two weeks prior to enrolment into the study
•Use of cromoglycates in the last month before study onset

•Concomitant pharmacological treatment indicated for seasonal allergic rhinitis such as antihistamines, corticosteroids or other preparations in the last two weeks before study onset
•Anti-allergy immunotherapy in previous years
•Participation in a further clinical trial at the same time or within the previous 4 weeks prior to enrolment into this study
•Pregnancy or lactation
•Severe internal or systemic disease (e.g. cardiac, hepatic, renal diseases)
•A known history of drug, alcohol and/or medication dependence or addiction;Healthy volunteers:
•Chronic inflammatory autoimmune disease such as Type I - Diabetes Mellitus, Rheumatoid Arthritis, Multiple Sclerosis, Psoriasis or Crohn*s disease
•Allergic (hypersensitive) to one of the constituents of Citrus e fructibus / Cydonia e fructibus
•Asthma
•Participation in a further clinical trial at the same time or within the previous 4 weeks prior to enrolment into this study
•Pregnancy or lactation
•Severe internal or systemic disease (e.g. cardiac, hepatic, renal diseases)
•Drug, alcohol and/or medication dependence or addiction

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-05-2010
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO Date:	13-07-2010
Application type:	First submission
Review commission:	METC Wageningen Universiteit (Wageningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL30944.081.10