INT. J. BIOL. BIOTECH., 3 (3): 547-550, 2006.

ORIGANUM VULGARE INHALER IN THE TREATMENT OF CHRONIC RHINOSINUSITIS, A DOUBLE BLIND PLACEBO CONTROLLED RANDOMIZED CLINICAL TRIAL

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ABSTRACT

Symptoms of chronic rhinosinusitis (CRS) are cumbersome and refractory to most systemic medications and even after surgical intervention, the recurrence of symptoms are frequent. In order to study the beneficial effects of *Origanum vulgare* inhaler in releasing the symptoms, this study was conducted at Boo Ali Sina Hospital Sari, Iran. Sixty four patients were recruited and allocated equally in case and control groups matched for age,sex and duration of symptoms.15.6 and 25 percent of cases and controls had history of sinuses surgery. All symptoms including headache,nasal congestion, sinus pain, post nasal discharge, eye pain, purulence in nasal cavity and cough were significantly reduced after the intervention except for hyposmia and nasal discharge($p<0.00$).No side effect was reported. Inhalation of 75% hydroalcoholic extract of Origanum vulgare effective in releasing most symptoms of CRS.

Key word: *Origanum vulgare*, chronic rhinosinusitis, inhaler, Iran

INTRODUCTION

Chronic rhinosinusitis (CRS) is among the most common illnesses in the world (Anonymous, 1994). Symptoms including headache, nasal congestion, sinus pain, post nasal discharge, eye pain, purulence in nasal cavity, caugh, nasal discharge and hyposmia are cumbersome and difficult to treat (Krouse, 2002). Treatment of CRS cost, more than 2 billion $ annually in the USA (Anonymous, 1994). If untreated, it may cause some local and serious complications such as subperiosteal, orbital abscesses, cavernous sinus thrombosis, orbital, preorbital cellulitis, osteomyelitis and meningitis (Choi and Grundfast, 2001; Pickard, 1988). Classic treatments of CRS antibiotics, decongestants, mucolytics, antihistamins and sinuses surgery if indicated, however, recurrence is common (Krouse, 2002; Clerico, 2001; Ivker *et al.*, 2002; Nuutinen *et al.*, 1986). *Origanum vulgare* (Wild marjoram) which belongs to the Laminaceae family (Bown, 1995; Leung and Foster, 1996) has been used in Italian cookery (Bremness, 1994) and also in herbal medicine as antifungal (Leung and Foster, 1996; Stile *et al.*, 1995; Biondi *et al*., 1995) and antibacterial (Stile *et al.*, 1995; Biondi *et al*., 1995) agent, but never as inhaler. In order to study the effects of inhalation of the 75% hydroalcoholic extract of *O. vulgare*.

MATERIALS AND METHODS

It was double blind, placebo controlled clinical trial performed from April to December 2005. The study was approved by the medical ethics committee of Mazandaran University of Medical Science. The subjects attended the ENT clinic of Boo Ali Sina Hospital with suggestive symptoms and signs and proven to have CRS by CT scan or FESS were enrolled for the study. After explaining the trial, an informed consent form was signed by each patient. Then a questionnaire was completed. The patients were randomly allocated to cases and control groups matched for sex, age and chronicity of the symptoms. The exclusion criteria of the study were age under 15, fever or signs of acute infection, known immunodeficiency states and history of eye allergy. *Origanum vulgare* was gathered in summer from Kojor Mountain (North of Iran) and identified by an experienced botanist. The aerial organ of the plant dried, macerated and undergone a 75% hydroalcoholic extract and finally standardized by Emerson method (Hartke *et al.*, 1982).The active ingredient and placebo were both prepared in similar dark glass bottles. The subjects were instructed to use the medication by the medicine to about 250 ml of boiling water and inhale it for 15 minutes, three times a day for two weeks. The placebo has contained no active substance. Two telephone calls for each patient were made to enhance the compliance. After two weeks a doctor blind to groups asked for symptoms,

possible side effects and examined the patients for signs and filled a separate form. Chi square was used to analyze the effects of the intervention and $p<0.05$ was considered statistically significant.

RESULT

Sixty four patients (32 cases, 32controls) have participated in the study. Basic characteristics of patients prior to the intervention are shown in table1, and were statistically not different. The effects of *O. vulgare* inhaler on the symptoms of CRS are shown in table 2.All signs and symptoms of CRS were relieved except nasal discharge and hyposmia.No side effects were reported.

Table 1. The characteristics of CRS patients receiving *Origanum vulgare* and controls, Boo Ali Sina Hospital, Sari Iran 2005.

Patients characteristics	**Controls N=32**	**Cases N=32**
Sex		
Female	16(50%)	16(50%)
Male	16(50%)	16(50%)
Age $(\bar{X} \pm S.D)$	36.56± 8.51	37.41± 10.05
Age of start of illness $(\bar{X} \pm S.D)$	30.88± 9.12	31.22± 9.02
Age of first treatment $(\bar{X} \pm S.D)$	31.34± 8.67	32.28± 9.33
Time of illness $(\bar{X} \pm S.D)$	5.94± 3.72	6.22± 3.96
Surgery	8(25%)	5(15.6%)

Table 2. the effects of Origanum vulgare inhaler versus placebo in CRS patients, Boo Ali Sina Hospital, Sari, Iran 2005.

Symptoms	**Controls**		**Cases**		**P**
	Before	**After**	**Before**	**After**	
Headache	18(56.3%)	18(56.3%)	22(68.8%)	0	0.000
Nasal congestion	21(65.6%)	13(40.6%)	20(62.5%)	0	0.000
Sinus pain	23(71.9%)	23(71.9%)	16(50%)	0	0.000
Post nasal Discharge	30(93.8)	30(93.8)	29(90.6%)	0	0.000
Eye pain	5(15.6%)	5(15.6%)	11(34.4%)	0	0.000
Purulence in Nasal cavity	12(37.5%)	12(37.5%)	11(34.4%)	0	0.000
Cough	9(28.1%)	5(15.6%)	10(31.3%)	0	0.01
Nasal discharge	10(31.3%)	2(6.2%)	6(18.8%)	0	NS
Hyposmia	6(18.8%)	6(18.8%)	8(25%)	8(25%)	NS

DISCUSSION

The study showed that 75% hydroalcoholic extract of *O. vulgare* inhaler was effective on CRS. The most important active chemicals of the plant are phenol compounds including thymol and carvacrol which have antioxidant (Lagouri and Boskou, 1996), antibacterial (Stile *et al.*, 1995; Biondi *et al*., 1995), antifungal ((Leung and Foster, 1996; Stile *et al.*, 1995; Biondi *et al*., 1995), antiseptic (Bremness, 1994) and ant parasitic (Force *et al*.,2000) properties. There are reports of their effects against *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeroginosa*, *Serratia macescence*, *Staphylococcus aurous* and *S. fecalis* (Biondi *et al*., 1995; Hammer *et al.*, 1999), *Proteos vulgaris*, *Bacillus subtilis*, *Aspergillus niger*, *Micrococcus cluteus* and *Candida albicans* (Stile *et al.*, 1995; Biondi *et al*., 1995 Hammer *et al.*, 1999). Also there are papers referring to the beneficial effects of *Origanum vulgare* extracts on different kinds of illnesses such as bronchitis, asthma, vomiting, diarrhea, cough, nervous

headache, muscle spasms and spider bites (Bown, 1995; Bremness, 1994; Leung, 1996). Thymol with a phenolic index of 50% is being used in local antiseptics such as oral wash solutions and vaginal douches is one of active ingredients of the plant (Remington, 1990). Leuteolin is another chemical of the plant which is active against carcinogen factor Trp-p-2 of *Salmonella thyphi* (Samegima *et al.*, 1993).Even an anticancer property was described for the plant (Milie and Milie, 1998). Avicenna noticed the effects of *O. vulgare* dark halos under eyes, pain and swelling of joints, headache and scorpion bite (Avecina, 1984). Nowadays some products of the plant are available including"Candismic", "Herbetom BB DG-103","Papahade","Broncol San" (It ballast and Bachelor, 1997; Treas and Evans, 1991; www.hipernatural. com/en/ pltoreganohtml). The extract is even effective against bacteria such as Ralstonia solanacearum pathogenic to tomato, potato, banana and tea plant (Pradhanage *et al.*, 2003; Momol *et al.*, 1999). *Origanum vulgare* extract inhalation was effective and safe in symptomatic relieved of CRS.The results of this study showed that the extract of *O. vulgare* has promising effects on the symptoms of CRS, and because of it, availability and low price, easy of use as well as lack of side effects. It is recommended to undertake a more comprehensive study on all aspects of the medical and pharmacological properties of the extract. Of course based on the results of this study *O. vulgare* can be recommended

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(*Accepted for publication June 2006*)