Complementary Therapies in Clinical Practice 28 (2017) 181–191

Contents lists available at ScienceDirect

Complementary Therapies in Clinical Practice

journal homepage: www.elsevier.com/locate/ctcp

Effectiveness of an add-on treatment with the homeopathic medication SilAtro-5-90 in recurrent tonsillitis: An international, pragmatic, randomized, controlled clinical trial

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ARTICLE INFO

Article history:
Received 28 April 2017
Accepted 11 May 2017

Keywords:
Homeopathy
Recurrent tonsillitis
Tonsilotren
SilAtro-5-90
Acute throat infection
Randomized controlled trial

ABSTRACT

Objective: To investigate the effectiveness and safety of the homeopathic product SilAtro-5-90 in recurrent tonsillitis.
Methods: In this international, pragmatic, controlled clinical trial, 256 patients (6–60 years) with moderate recurrent tonsillitis were randomized to receive either SilAtro-5-90 in addition to standard symptomatic treatment, or to receive standard treatment only. The primary outcome was the mean time period between consecutive acute throat infections (ATI) within 1 year (analyzed via repeated events analysis).
Results: During the evaluation year, the risk of getting an ATI was significantly lower (hazard ratio: 0.45, proportional means model, $p = 0.0002$, *ITT*) with SilAtro-5-90 compared to control. Tonsillitis-specific symptoms were significantly reduced ($p < 0.0001$, *ITT*) and the need of antibiotics to treat acute throat infections ($p = 0.0008$; *ITT*) decreased. 3 non-serious adverse drug reactions were reported for SilAtro-5-90.
Conclusions: An integrative treatment approach where SilAtro-5-90 is given alongside mainstream symptomatic treatment may bring therapeutic benefit to patients suffering from recurrent tonsillitis.
Trial registration: ISRCTN registry: Registration number ISRCTN19016626, registered 23 January 2013.

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[2] Membership of the TocTo research group is provided in the acknowledgments.

http://dx.doi.org/10.1016/j.ctcp.2017.05.005

1. Introduction

Tonsillitis is a common condition, particularly in childhood, which is caused mainly by a viral or by a bacterial acute throat infection (ATI) and which is typically associated with sore throat [1]. Diagnosis of tonsillitis is mostly clinical and it is difficult to determine whether the cause is viral or bacterial [1–3]. Recurrent tonsillitis has been defined as the repeated occurrence of acute tonsillitis episodes followed by periods with only very few, or without any, symptoms [4]. Due to the frequent episodes of sore throat, fever, general illness, sleepless nights, impaired daily functioning and absence from school or work associated with it, recurrent tonsillitis is recognized to have a significant impact on families' daily life and healthcare costs [5–7].

Surgical removal of the tonsils (tonsillectomy) is a widely applied procedure in recurrent tonsillitis [5]. Whereas the "Paradise criteria" with 7 episodes of ATIs in 1 year, 5 episodes each year in 2 consecutive years, or 3 episodes each year in 3 consecutive years were considered as recommendation for tonsillectomy for a long time [3,8,9], the most recent guidelines merely advise to focus on the number of ATIs during the last 12 months: tonsillectomy is a therapeutic option when a patient has had 6 or more ATIs during this period and not at all, if a patient has had less than 3 ATIs. In case patient had between 3 and 5 ATIs, tonsillectomy may be an option if patient develops further ATIs during the next 6 months thereby reaching the number of 6 ATIs [4].

In recent years, however, the clinical efficacy of tonsillectomy has been under debate. Studies have shown that tonsillectomy can reduce the number of ATIs, but the effect is modest and mainly observed in children who are more severely affected. Simultaneously, the risks of the procedure have to be considered, as tonsillectomy is associated with a small but significant risk of primary and secondary hemorrhage, and in addition it is particularly painful for adults [2,5]. Moreover, it needs to be considered that even tonsillectomized patients can still suffer from sore throat, due to inflammation of other pharyngeal lymphoid tissues [5,10]. It is concluded that more randomized controlled trials (RCTs), with adequate long-term follow-up, are necessary to clarify the benefits of tonsillectomy versus non-surgical treatment in patients with recurrent tonsillitis [10].

Although antibiotics are still commonly prescribed for acute and for recurrent throat infection, reducing unnecessary use of antibiotics has become a priority to cope with the problem of antibiotic resistance. It has been shown that even if antibiotics reduce the incidence of tonsillitis-associated complications like rheumatic fever and acute glomerulonephritis, routine aggressive antibiotic use in resource-rich countries, where these diseases are rare, is not justified [2,11]. In this context, it has recently been reported that there is insufficient evidence for the effectiveness of antibiotics for preventing recurrent sore throat [12].

In the light of these discussions, the use of complementary and alternative medicine (CAM) in the treatment of recurrent tonsillitis may be an interesting option. A survey among pediatricians and other healthcare professionals has lately revealed that "natural remedies" are, among other things, also recommended in the management of recurrent tonsillo-pharyngitis [13]. In this survey, homeopathy was reported as a supportive therapy for recurrent tonsillo-pharyngitis by 59% of the respondents, phytotherapy by 28% and vitamins/nutritional supplementation by 37%. Studies have shown that some homeopathic medicinal products or (Chinese) herbal preparations may reduce symptoms of acute tonsillitis or pharyngitis [14–17]. In a randomized, controlled, double-blind trial in children with recurrent tonsillitis, homeopathic treatment was shown to significantly reduce the number of acute tonsillitis episodes [18]. However, more research in the treatment of recurrent tonsillitis with homeopathy is needed.

SilAtro-5-90 is a complex homeopathic medicinal product that is sold over-the-counter in many European and non-European countries for recurrent tonsillitis. It is applied according to the principles of homeopathy, a medical system that was developed 200 years ago by Samuel Hahnemann, a German physician and pharmacist. Homeopathy is one of the most frequently used CAM therapies in children as well as in adults [19–22]. First clinical experiences with SilAtro-5-90 in recurrent (chronic) tonsillitis were reported in the 1950s [23]. The first clinical studies with SilAtro-5-90 were conducted in the 1990s [24–27]. Among the latter was a multicenter observational study in which 1368 patients with tonsillitis were treated for 2 weeks with SilAtro-5-90, after which 605 patients with recurrent tonsillitis continued to take SilAtro-5-90 for a period of 6 weeks [24]. After the 6-weeks' treatment period 79% of the patients no longer reported throat complaints. In another multicenter, randomized, controlled, open-label study in 143 children with recurrent tonsillitis, the effectiveness of SilAtro-5-90 in addition to standard treatment (experimental group) was compared to standard treatment only (control group). In this study children were observed for 18 months, during which those from the experimental group were treated with SilAtro-5-90 for 3 cycles of 2 months. It was shown that the general symptoms of recurrent tonsillitis such as fatigue, decreased appetite and changes in body temperature, were reduced to a much greater extent in the experimental group than in the control group. In addition, the patients treated with SilAtro-5-90 had a more pronounced decrease of tonsillitis-specific symptoms compared to the children receiving standard treatment only [28].

The aim of the present study was to further explore the effectiveness and safety of SilAtro-5-90 in patients suffering from moderate recurrent tonsillitis (more than 3 ATIs per year, or 2 ATIs for 2 consecutive years). Since patients often use homeopathic medications, such as SilAtro-5-90, alongside mainstream medicine [13,29,30], a pragmatic comparative study design was chosen. After recruitment into the study, for a period of 1 year, patients received either SilAtro-5-90 for 3 treatment periods of 8 weeks, in addition to standard symptomatic treatment, or standard symptomatic treatment only.

2. Materials and methods

2.1. Trial design

A pragmatic, randomized, international, multicenter, open-label, controlled clinical trial with 2 parallel groups was conducted. The study complied fully with the International Conference on Harmonization (ICH) guidelines for Good Clinical Practice (GCP), ethical principles founded in the Declaration of Helsinki and all appropriate regulatory requirements. The study took place at 19 study centers (private practices or medical institutions) in 3 countries (5 centers in Germany, 6 centers in Spain, and 8 centers in Ukraine). The study protocol was approved by independent ethics committees in the respective countries: in Germany, on August 27, 2012 by the central ethics committee "Ethics Committee of the Bavarian State Medical Association"; in Spain, on November 16, 2012 by the central ethics committee "Ethics Committee of the Joined Foundation of the Catalonian Hospitals"; in Ukraine, between July 16, 2012 and April 01, 2013 by the local ethics committees of the "Vinnytsia Regional Clinical Hospital Named after M.I. Pirogov", "Vinnytsia Regional Children Clinical Hospital", "Poltava Regional Clinical Hospital Named after M.V. Sklifosofskyi", "Odessa National Medical University", "National Specialized Children Hospital OHMATDYT, Kyiv", "Kyiv City State Administration Children Clinical