

# Use of natural and homeopathic remedies in children ailments

Stephen Buskin<sup>1</sup>, María Pilar Riveros Huckstadt<sup>2</sup>, Silvia Salatino<sup>3</sup>

## Abstract

*In recent decades the use of CAM (Complementary and Alternative Medicine) has increased significantly, not only among adults but also in the pediatric population. Perceived efficacy of homeopathic or natural treatments, fear of drug adverse effects, dissatisfaction with conventional medicine, and the need for more personal attention are the main reasons given by parents who treat their children with homeopathy.*

*In the present paper the use of natural and homeopathic remedies for the treatment of children ailments are considered. In particular we focus on minor disorders of early childhood with a major impact on the well-being of the whole family, namely infant colic, teething, upper respiratory tract infections (URTIs) and tonsillopharyngitis. The results of recent studies on homeopathic products for the treatment of these disorders are presented and discussed.*

**Keywords:** Homeopathy; Children; Infant colic; Teething; Upper respiratory tract infections (URTIs); Tonsillopharyngitis

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## INTRODUCTION

The National Institutes of Health (NIH) has defined complementary and alternative medicine (CAM) as “a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine” [1,2]. The National Center for Complementary and Alternative Medicine (NCCAM) classifies CAM therapies into five categories: alternative medical systems (homeopathic and naturopathic, Chinese, and Ayurvedic medicine), mind-body interventions, biologically based therapies (herbs, foods, etc.), manipulative and body-based methods, energy therapies [1,2].

In recent decades the use of CAM (Complementary and Alternative Medicine) has increased significantly, not only among adults but also in the pediatric population.

Zuzak et al. recently conducted a pan-European review about CAM in pediatrics, re-

alized by combining data published in international journals, data from local or national surveys in original language conveyed by local experts, and expert perspectives about CAM availability, quality, use and popularity in their countries. According to this study, conducted in 20 European countries, 56% of the European population in general has used CAM at least once during the year preceding the survey. For the pediatric population the rate was similar (52%), confirming the growing interest in CAM reported by pediatricians and institutions. Homeopathy and herbal medicine was identified as the most popular CAM therapies in Europe [3].

In the United States the percentage of healthy children seen in outpatient pediatric clinics that uses CAM is between 20-40% and rises to values above 50% in the case of children with chronic diseases, almost always in conjunction with mainstream care [4].

An interesting analysis on the extent of homeopathic prescriptions in children was

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conducted by Ekins-Daukes and colleagues in Scotland. Majority of these prescriptions were made for children under 1 year of age (8.0/1000 registered children) and the most common conditions for which homeopathic medicines were prescribed were colic (85%), cuts and bruises (52%), teething (49%), dermatological conditions (32%), earache (21%), influenza and upper respiratory tract infections (16%), cough (16%), vomiting (16%), irritability (15%) and diarrhea (12%) [5].

Recently an international survey was performed in order to provide insights into physician's attitude towards the use of homeopathy and natural remedies in pediatric practice. 582 general pediatricians and general practitioners treating pediatric conditions in 6 countries (Germany, Spain, Russia, Bulgaria, Colombia, Israel) were involved. Herbal medicine and homeopathic products amounted to 17% and 15% of total prescriptions in pediatrics, respectively. Upper respiratory tract infections (URTIs), infant colic, sleep disturbances and recurrent infections were the main causes for which natural remedies and homeopathic products were used. In the majority of cases they are used as complementary treatment together with conventional drugs. The study confirms high interest of physicians in natural remedies and homeopathy, however their knowledge level is heterogeneous. The concern about side effects and the use for themselves are the main factor that drives parents to the use of homeopathy and natural remedies [6].

Perceived efficacy of homeopathic or natural treatments, fear of drug adverse effects, dissatisfaction with conventional medicine, and the need for more personal attention are the main reasons given by parents who treat their children with homeopathy [4].

Recognizing the increasing use of CAM in children, many institutions, like the American Academy of Pediatrics (AAP), have decided to provide information and support for health professionals. In the 2001 AAP Periodic Survey of Fellows, 73% of pediatricians agreed that it is the role of pediatricians to provide patients/families with information about all potential treatment options for the patient's condition, and 54% agreed that pediatricians should consider the use of all potential therapies, not just those of mainstream medicine, when treating patients [7].

Efforts to include education and training for CAM therapies in medical school programs have also become popular in some European countries [8,9].

Despite the long tradition of homeopathy, and its spread around the world, the debate on this issue is always very heated. In recent years a number of studies have been published on the effectiveness of homeopathy in children. For example, several studies conducted in different countries on the management of acute respiratory infections and acute otitis media showed a significant rapid improvement upon homeopathic medications compared to conventional treatment and less use of antibiotics [10-12].

Some researchers have highlighted an interesting peculiarity: publication bias in CAM research is «opposite that of conventional medicine; that is, negative studies are more likely to be published in well-known journals, and positive studies are more likely to be published in non-English language and often complimentary medicine journals» [13]. The most controversial aspect of homeopathy is the ultra-dilutions and the lack of reliable data on the mechanism of action. Theories on the possible explanation of mechanism of action of homeopathy within the context of nanomedicine have been recently published, although still hotly debated [14]. A recent publication by Rutten et al. explores the current evidence for homeopathy reporting three meta-analyses by Kleijnen, Linde and Cucherat published from 1991-2000 that reached positive conclusions and a review by Shang in 2005 that reached negative conclusions [15-19].

In the present paper the use of natural and homeopathic remedies for the treatment of children ailments are considered. In particular we focus on minor disorders of early childhood with a major impact on the well-being of the whole family namely infant colic, teething, upper respiratory tract infections (URTIs) and tonsillopharyngitis. The results of recent studies on homeopathic products for the treatment of these disorders are presented and discussed [20-24].

## INFANT COLIC

### Definition

A common definition of infantile colic comes from Morris A. Wessel and colleagues, the so-called "rule of 3": a condition of a healthy, well-fed baby in which it shows periods of intense, unexplained crying lasting more than at least 3 hours a day,

on at least 3 days (per week), of at least 3 weeks [25].

The prevalence of infantile colic given in the scientific literature widely varies and ranges from 5–40%, depending on the study methodology, the population and the definition of infantile colic used [26].

Although benign and self-limiting, it is associated with higher levels of maternal stress and anxiety: the impact of prolonged and inconsolable crying in children with infantile colic causing sleepless nights, stress, frustration and exhaustion, especially in first-time parents [27–29].

Despite being a very common disorder, the causes are not yet completely clarified. Etiopathology of this condition includes both gastrointestinal and non-gastrointestinal factors, such as hypersensitivity to baby formula, alteration in gut microflora, excessive gas in the intestine, intestinal hypo- / hypermotility, immature digestive system, over-stimulation and (hyper-)sensitivity to the environment, reflection of problems in parent-infant interaction, maternal smoking.

## Treatment

The above possible causes of infantile colic have led to a variety of available treatments, ranging from pharmaceutical therapies, dietary interventions, behavioral strategies, and physical remedies. At first, the most commonly recommended approach is to discuss the usually natural and self-limiting character of infantile colic with parents and to offer some methods to parents for calming the baby.

Pharmaceutical therapies includes simethicone, dicyclomine hydrochloride and cimetropium bromide, but results from literature on simethicone and dicyclomine for infantile colic do not suggest these to be effective or appropriate treatment options [30–33]. A trial by Savino et al. found cimetropium bromide more effective than placebo in reducing the duration of crying in children with infantile colic but there were reported side effects in terms of increased sleepiness [34,35]. Safety is a critical issues in infants, and a major concern for parents: in literature there have been reports of infants who experienced serious adverse events, such as serious respiratory symptoms seizures, syncope, pulse rate fluctuations and muscular hypotonia after taking dicyclomine hydrochloride syrup; no causal relationship has been established but dicyclomine hydrochloride is now contraindicated in infants < 6 months and in nursing mothers [35,36]. Recent re-

Active ingredient	Therapeutic action / characteristics
Chamomilla D6	<ul style="list-style-type: none"> <li>• Infant colic with flatulence (infant gaseous colic)</li> <li>• Hypersensitivity to pain</li> <li>• Restlessness together with dissatisfaction</li> </ul>
Cina D6	<ul style="list-style-type: none"> <li>• Spasms of the gastrointestinal tract</li> <li>• Aversion to breast-milk (ingestion causes colic and diarrhoea; the baby frequently spits up sour milk)</li> <li>• Marked irritability, physical and mental</li> </ul>
Colocynthis D6	<ul style="list-style-type: none"> <li>• Colic / colicky pain better by pressure and heat (warm applications)</li> <li>• Gripping pain around the navel</li> </ul>
Lac defloratum D6	<ul style="list-style-type: none"> <li>• Digestive disorders due to intolerance of milk</li> <li>• General aggravation of symptoms from drinking milk</li> </ul>
Magnesium chloratum D6	<ul style="list-style-type: none"> <li>• Constipation with dry, pellet-like stool</li> <li>• Problems to digest milk (especially during difficult dentition)</li> </ul>

search is now targeting the promising role of *Lactobacillus reuteri* in the treatment of infantile colic [37,38].

Nutritional interventions are closely related to the type of feeding received by the child. In case of breast-fed infants, a monitored low allergen maternal diet avoiding cow's milk and dairy food with appropriate intake of vitamins and minerals may be suggested, while the first-line for bottle-fed infants is represented by formulas based on partially hydrolyzed whey proteins with prebiotic oligosaccharides [39].

A considerable number of behavioral strategies and physical remedies resulting from tradition and practical experience are suggested, such as offering an atmosphere of security to the baby, decreasing stimulation, offering "white noise", massaging or rocking the baby. Despite the lack of evidence published in the literature, this type of remedies may be useful for some children [39].

In the absence of standard of care for treatment of infant colic, CAM has assumed an increasingly important role in the management of infantile colic. In particular, it is recognized the use of herbal supplements (i.e. containing chamomile, fennel, vervain, licorice, balm-mint) [40,41] and homeopathic products [42].

## Colikind® (use and dosage)

Colikind® (Deutsche Homöopathie Union, DHU, Karlsruhe, Germany) is natural combined medication that is indicated for the treatment of infantile colic and flatulence. It is composed of a combination of 5 single remedies: Chamomilla D6, Cina

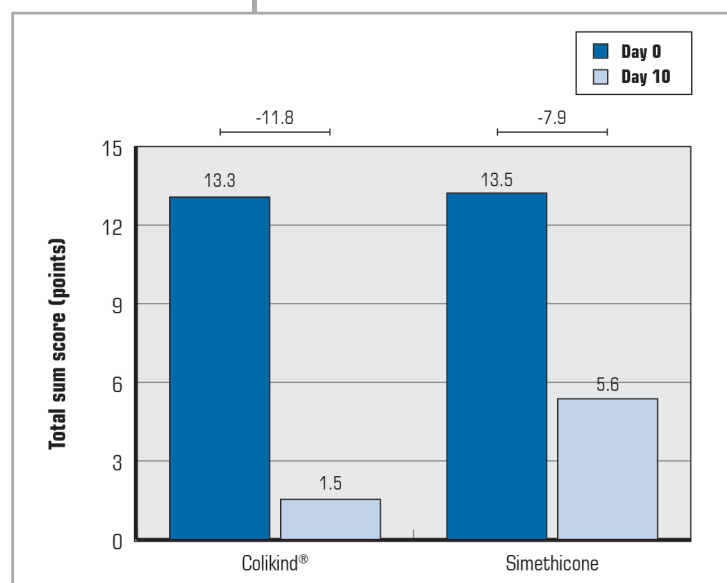
**Table I.** *Colikind®* active ingredients and therapeutic action

**Table II.** Treatment options [20]

Colikind® group (n = 100)	Simethicone group (n = 100)
Children 0-6 years	
Acute symptoms: 3 drops / hour (max. 6 times a day) Afterwards: 3 drops 3 times a day	1 measuring spoon of the emulsion taken 3-5 times a day during meals (from a baby bottle or mixed with food and drink)

**Table III.** Subjective complaints and objective symptoms assessed in the study [20]

<b>Subjective complaints</b>	<ul style="list-style-type: none"> <li>• Unexplained restlessness</li> <li>• Sleep and appetite disturbances</li> <li>• Increased crying while feeding</li> <li>• Regurgitation</li> <li>• Vomiting</li> <li>• Stool softening</li> <li>• Constipation and flatulence</li> </ul>
<b>Objective symptoms</b>	<ul style="list-style-type: none"> <li>• Abdominal bloating</li> <li>• Intestinal rumbling</li> <li>• Tenderness and intestinal spasm on palpation</li> <li>• Changes in stool</li> <li>• Dryness of the skin and mucosa</li> <li>• Skin pallor</li> <li>• Coating and geographism of the tongue</li> </ul>

**Figure 1.** Decrease in total sum score (subjective + objective symptoms). Adapted from [20]

D6, Colocynthis D6, Lac defloratum D6 and magnesium chloratum D6 [43]. In Table I Colikind® active ingredients and therapeutic action are reported.

Colikind® is available in drops. The medication can be used on its own or in combination with prescribed medication. Colikind® drops should be kept within the mouth before swallowing. In babies and small children, the drops can also be diluted in a little bit of water and administered with a plastic spoon. An interval of approximately 30 minutes should be kept between the intake of Colikind® and eating or drinking [43].

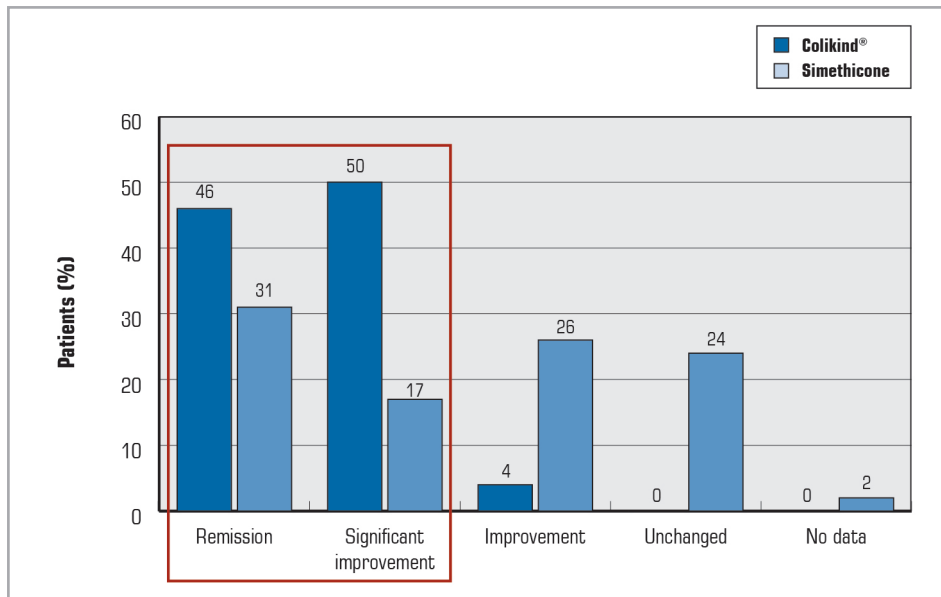
In case of acute condition, Colikind® can be administered at a dose of 3 drops up to a max. of 6 times a day; after improvement, treatment can be continued with 3 drops 3 times a day [43].

### From literature

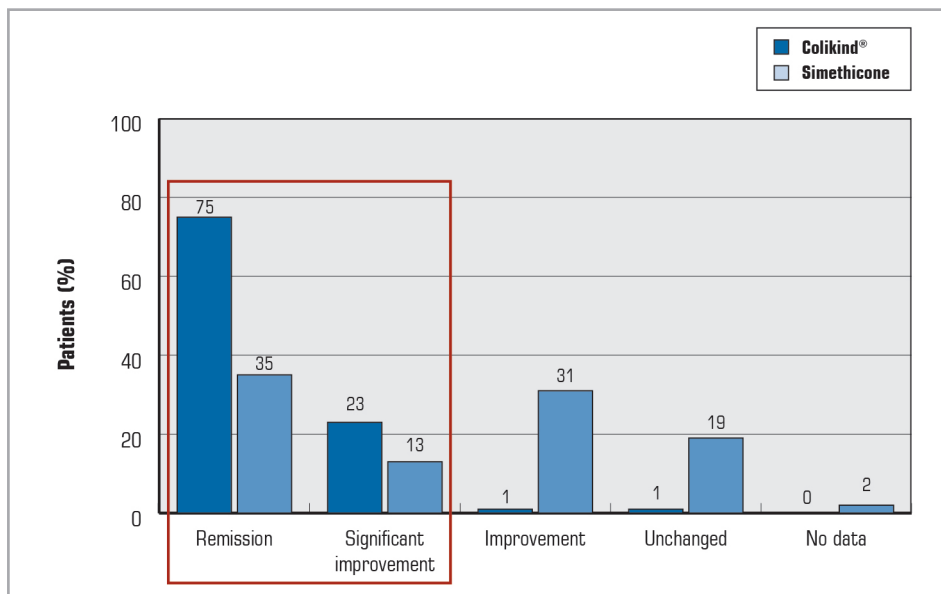
In 2010 an open, prospective, multicenter, comparative study on Colikind® was published by Ilyenko and colleagues [20]. Aim of the study was the evaluation of the effectiveness, safety and tolerability of Colikind® compared to simethicone in children with infantile colic and/or meteorism. The study population was 200 pediatric patients aged 2 months to 6 years of both sexes. Table II summarized the treatment options.

Comparative evaluation of the efficacies of the study agents was performed in terms of changes in the severity of subjective complaints and objective symptoms at 3, 7, and 10 day after the start of treatment. In Table III subjective complaints and objective symptoms are reported. Clinical symptoms were assessed by the physician at each visit, while overall outcome of treatment, treatment satisfaction, safety and tolerability of study medication were assessed both by physicians and parents.

On day 10, both treatment groups showed a significant improvement of their subjective and objective symptoms, whereas Colikind® showed to be significantly more effective ( $p < 0.0001$ ). Consequently, the decrease



**Figure 2.** Overall outcome of treatment on day 10, assessed by physicians. Adapted from [20]



**Figure 3.** Overall outcome of treatment on day 10, assessed by parents. Adapted from [20]

in total sum score (subjective complaints + objective symptoms) was more pronounced in the group of children treated with Colikind® (Figure 1).

After 10 days of treatment, 96 % of patients treated with Colikind® showed a “remission” or a “significant improvement” of symptoms according to the physicians’ assessment (Figure 2).

Parents’ assessment of overall outcome after 10 days of treatment with Colikind® was even better.

In total, 98 % benefitted from the treatment with Colikind® - thereof 75 % of patients showed a “remission” of symptoms (Figure 3).

Significantly more parents were “very satisfied / satisfied” with treatment in the Colikind® group compared to the Simethicone group ( $p < 0.001$ ). In addition, none of the parents in the Colikind® group was “dissatisfied” with treatment, whereas this applied to 22 % of parents in the Simethicone group. Tolerability of Colikind® was rated “very good” or “good” in all patients, whereas in the Simethicone group, there were 6 % of parents and 7 % of physicians who rated tolerability only as “satisfied”. In the study group treated with Colikind® 1 adverse event (AE) but no drug-related AE (i.e. adverse drug reaction (ADR)) was reported. In the control group 5 children (5/100, 5 %) treated with Simethicone were observed to suffer from an



AE, whereas 1 event was assessed as being related to the intake of Simethicone (ADR).

According to the results of this study, both medications (Colikind® and Simethicone) were effective and safe and can thus be recommended. However the Authors highlighted that in the Colikind® group more benefits were reported, such as quicker remission, faster decrease in the degree of the severity of subjective complaints and objective symptoms, the greater parents' satisfaction, the tolerability and the excellent safety profile of Colikind®, emphasized by the lack of adverse drug reaction.

## TEETHING

### Definition

Teething is known as a natural process by which the first teeth appear in children. A variety of symptoms has been shown to accompany teething, including fever, pain, irritability, sleep problems, mouthing/biting, drooling, decreased oral intake, gum inflammation, runny nose, and diarrhea [44].

The onset of the primary incisors is usually around 6-12 months: in the same period the circulating maternal humoral immunity decreases, and the child's own humoral immunity develops [45]. The simultaneous presence of these events often makes this period difficult and distressing for both the child and their respective parents and accompanied by a number of relatively minor symptoms [45]. Teething symptoms in children can create much distress in parents [21].

### Treatment

There are many remedies used by parents to relieve the symptoms of teething, often derived from tradition or experience of friends and family.

Pharmacological therapies include topical local anesthetics (i.e. lidocaine based preparations and topical benzocaine gel), topical choline salicylate-based products, and systemic analgesics. However, a standard of care is not established in the treatment of teething disturbances, use of some medications might be associated with unwanted side effects and for some topical teething gels cases of potential life-threatening risks have been reported [21,46]. In 2011 the US Food and Drug Administration (FDA) has released a document to recommend not to use benzocaine products on children < 2 years without medical advice [47].

Non pharmacological remedies include teething rings, pacifier, hard food like bread, frozen fruits and vegetables. The relief derived from the low temperature of the objects, that cause local vasoconstriction, and by the pressure exerted on the gums through the biting on hard objects [21,45]. These remedies are widely used and have few contraindications. It is crucial, however, to be very careful to avoid the choking risk. It is also recommended to use only sugar-free objects and not to add medicine to food or feeding bottles, as their dosage cannot be checked.

### Dentokind® (use and dosage)

Dentokind® (Deutsche Homöopathie-Union, DHU, Karlsruhe, Germany) is a complex homeopathic product containing five individual homeopathic substances: Belladonna D6, Chamomilla D6, Ferrum phosphoricum D6, Hepar sulfuris D12 and Pulsatilla D6 [48]. It is indicated for the treatment of teething symptoms such as irritability, restlessness, earache, painful gums, mild fever and softened stools in babies and children. It is available as tablets allowed to dissolve slowly in the mouth. For usage in small children, tablets can be dissolved in a little bit of water. For children < 1 year the suggested dosage is 1 tablet every hour, up to a maximum of 6 tablets a day, in acute condition; the treatment can be extended after improvement at a dosage of 1 tablet, 3 times a day. For children 1-6 years the suggested dosage is 2 tablets every hour, up to a maximum of 12 tablets a day, in acute condition; the treatment can be extended after improvement at a dosage of 2 tablet, 3 times a day. An interval of at least half an hour to meals should be kept [48].

### From literature

In 2015 a prospective, multicenter, randomized, open-label, comparative, controlled clinical trial on the clinical use of Dentokind® was published by Jong and colleagues [21]. The study, required for Dentokind® marketing authorization in Russian Federation, compared Dentokind® to another homeopathic product already authorized in the Federation. The study population consisted of 200 pediatric patients up to 6 years of age.

Dentokind® was administered orally for seven days. Children aged up to one year received Dentokind® tablets with a dos-

age regime of one tablet every hour up to six tablets per day (acute symptoms). After symptoms reduced one tablet three times a day was administered. Children aged 1-6 years received two tablets every hour up to a maximum of twelve tablets per day (acute symptoms). After symptoms reduction the dosage was two tablets three times per day. The other homeopathic medication was administered rectally for a period of seven days. For children aged up to six months the maximum daily dose was two suppositories a day. Children older than six months of age received a maximum of four suppositories (at a body temperature of  $\geq 37.5^{\circ}\text{C}$ ) a day. When body temperature normalized one suppository was used for further 3-4 days 1-2 times per day (with preventive purpose).

Primary endpoints were changes in total severity scores of subjective complaints (TSSC) and changes in total severity scores of clinical signs (TSCS) after treatment with study medication for 3-5-7 days. In Table IV subjective complaints and clinical signs are reported.

In the Dentokind group the assessment of TSSC recorded a reduction from 7.0 (baseline median value) to 3.0 (Day 3-5) and 1.0 at Day 7, while in the control group TSSC values decreased from 5.0 (baseline median value) to 3.0 (Day 3-5) and 1.0 at Day 7.

The study showed a reduction also in the TSCS values, which decreased from 6.0 (baseline median value) to 3.0 (Day 3-5) and 1.0 (Day 7) in the Dentokind group, and from 5.0 (baseline median value) to 4.0 (Day 3-5) and 1.0 (Day 7) in the control group.

#### Subjective complaints

- Unmotivated anxiety
- Gingival tenderness and appetite disorder
- Otalgia
- Stool softening
- Sleep-onset insomnia and frequent awakenings

#### Clinical signs

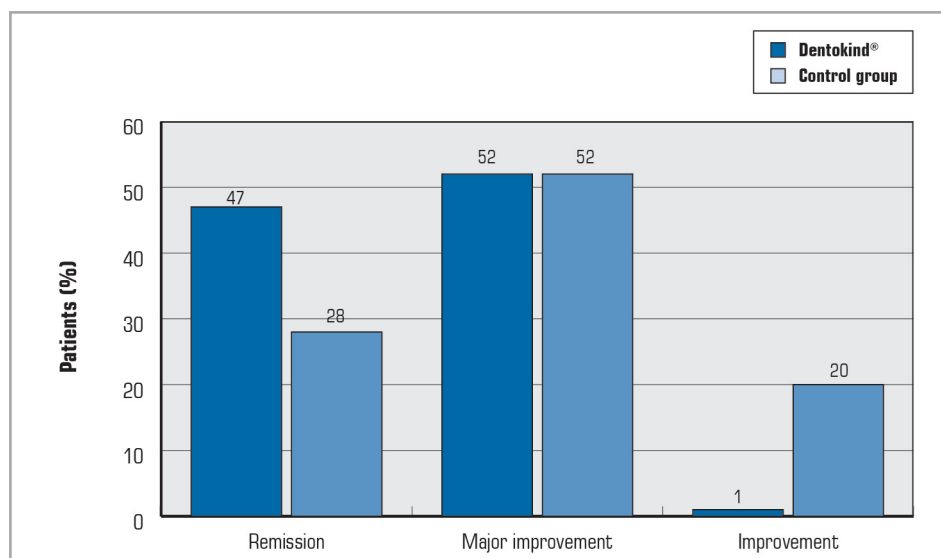
- Skin pallor
- Gingiva hyperemia
- Gingiva swelling
- Hematoma and hyperemia around the mouth
- Drooling and hyperthermia

Improvement of individual complaints and individual signs after 7 days of treatment was observed in both treatment groups-except for the complaint sleep-onset insomnia. Compared to the other homeopathic medication improvement of the individual complaints gingival tenderness and appetite disorder and of the signs gingival hyperemia and gingival swelling was observed in significantly more children of the Dentokind® group (Armitage Trend Test:  $p < 0.05$ ; FAS).

After 7 days of treatment children treated with Dentokind® had a 5-times higher odds of showing improvement in total severity score of subjective complaints than children treated with the other homeopathic medication and a 2.5-times higher odds of showing improvement in the total severity score of objective clinical signs.

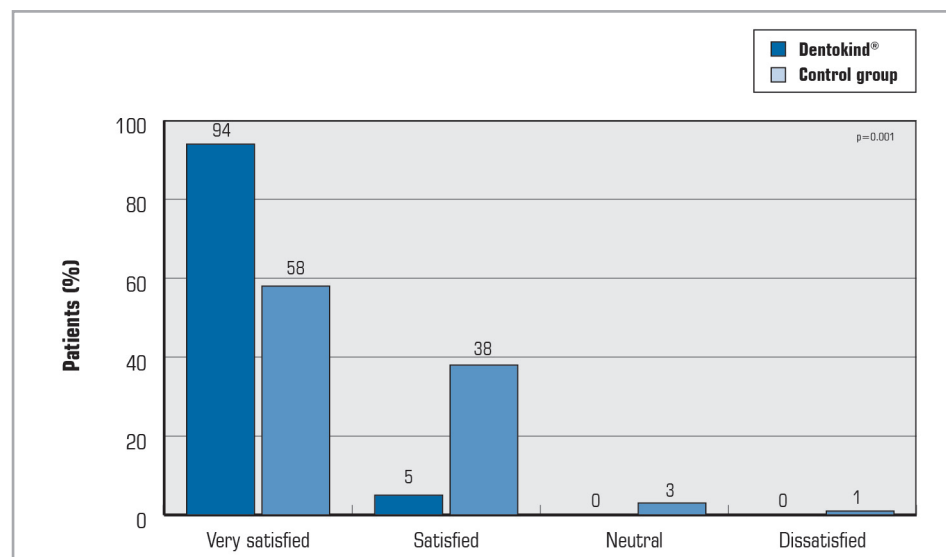
After 7 days of treatment with Dentokind® almost all parents and investigators ( $n=99$  out of 100 each) of the Dentokind® group rated “no complaints” or “major improvements” (Figure 4). Almost all parents ( $n=99$  out of 100) of the Dentokind® group were very satisfied or satisfied with the treat-

**Table IV.** Subjective complaints (TSSC) and clinical signs (TSCS) assessed in the study [21]



**Figure 4.** Overall outcome on day 7, assessed by physicians. Adapted from [21]

**Figure 5.** Treatment satisfaction on day 7, assessed by parents. Adapted from [21]



ment. In comparison with the other product, the treatment satisfaction in Dentokind® group was significantly better (Armitage Trend Test:  $p < 0.0001$ ; FAS) (Figure 5).

During the treatment period 1.5% children experienced AEs. The AEs occurred in 3 children of the control group. In Dentokind® group no AEs occurred. Almost all parents and investigators rated the tolerability of Dentokind® as “very good” or “good”. Compared to the control group the outcome in the Dentokind® group was significantly better (Armitage Trend Test:  $p < 0.0001$ ; FAS).

The study demonstrated that Dentokind® reduced total severity scores of subjective complaints, including individual symptoms such as unmotivated anxiety, gingival tenderness, appetite disorders and otalgia in teething children after 7 days of treatment. Total severity scores of clinical signs also lowered after 7 days of treatment in both groups. Dentokind® seems therefore a “pragmatic treatment alternative” to conventional OTC teething gels for symptoms relief of painful teething in children [21].

## UPPER RESPIRATORY TRACT INFECTIONS (URTIs)

### Definition

Upper respiratory tract infections (URTIs) or common colds represent the most frequently occurring illness in the world. Although they are usually self-limiting conditions, they are a leading cause of missed

days from work and school, with a relevant economic burden [49].

Sore throat, runny nose, general malaise, fever, nasal congestion and cough are most common symptoms [22].

The specific immune status of children in the first years of life makes them especially vulnerable to viral infections [50]. In literature about 4–8 episodes of viral infection per year per child are recorded [50]. The majority of URTIs are caused by viral pathogens, most commonly rhinoviruses, but also influenza viruses [22].

URTIs are even the most frequent cause of antibiotic prescriptions in pediatric outpatient care. This represents a serious health problem globally since inappropriate use of antibiotics has a strong impact the increase of bacterial respiratory pathogens [51,52].

### Treatment

Since there is no approved specific therapy for URTIs, treatment is mainly symptomatic. The most common pharmacological treatments are antipyretics, anti-inflammatory drugs, expectorants, decongestants, and cough suppressants [21]. A number of other remedies are available, such as vitamins, herbal supplements and homeopathic medicine. Data relating to the Germany showed that about 7% of all pediatric prescriptions for the respiratory tract system are not officially licensed for use in children [53].

As mentioned above, a key issue concerns the prescription of antibiotics, that are widely prescribed, but often inappropriate; overuse can lead to the development



of community-acquired resistant pathogens which are an increasing and serious health burden [50]. The results of a nationwide US survey published in 2004 showed 38% of more than 6.5 million visits (primary practice, outpatient, and emergency department) by children and adults with a sole diagnosis of influenza were associated with antibiotic prescriptions. Studies limited to children demonstrated even higher rates of antibiotic treatment in children diagnosed with viral infections [54].

There are many factors that contribute to an inappropriate antibiotic prescription, including diagnostic uncertainty, lack of knowledge, socio-cultural and economic pressures, meeting parental expectations [51].

Natural remedies, and homeopathy in particular, can be used in the management of URTIs. An integrative approach to these infections may help reduce excessive antibiotic prescription [55].

### Influcid® (use and dosage)

Influcid® (Deutsche Homöopathie-Union, DHU, Karlsruhe, Germany) is a homeopathic preparation containing a fixed combination of 6 homeopathic single substances: Aconitum D3, Bryonia D2, Eupatorium perfoliatum D1, Gelsemium D3, Ipecacuanha D3 and Phosphorus D5 [56]. Launched in Germany in 1928, now it is marketed in 22 countries worldwide [22].

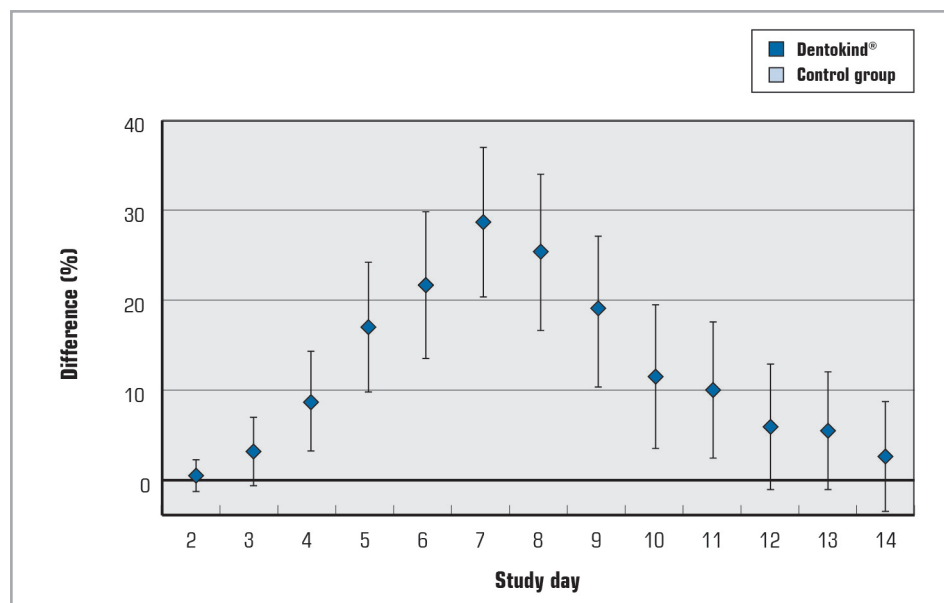
In acute conditions, the suggested dose is 1 tablet every 2 hours, up to a maximum of

8 tablets per day, until improvement occurs; for subsequent treatment the dose is 1 tablet 3 times per day. The same dosage (1 tablet 3 times per day) is suggested for prevention of infections. Tablets should be dissolved slowly in the mouth: for small children, they can be dissolved in a little bit of water. An interval of at least half an hour to meals should be kept [56].

Efficacy and safety of Influcid® (IFC) in the treatment of flu-like infections and URTIs were demonstrated in several studies: in the multicenter open study conducted by Heger on a total of 600 patients (333 adults and 267 children) with URTIs, about 90% of patients reported an improvement after 3 days [57].

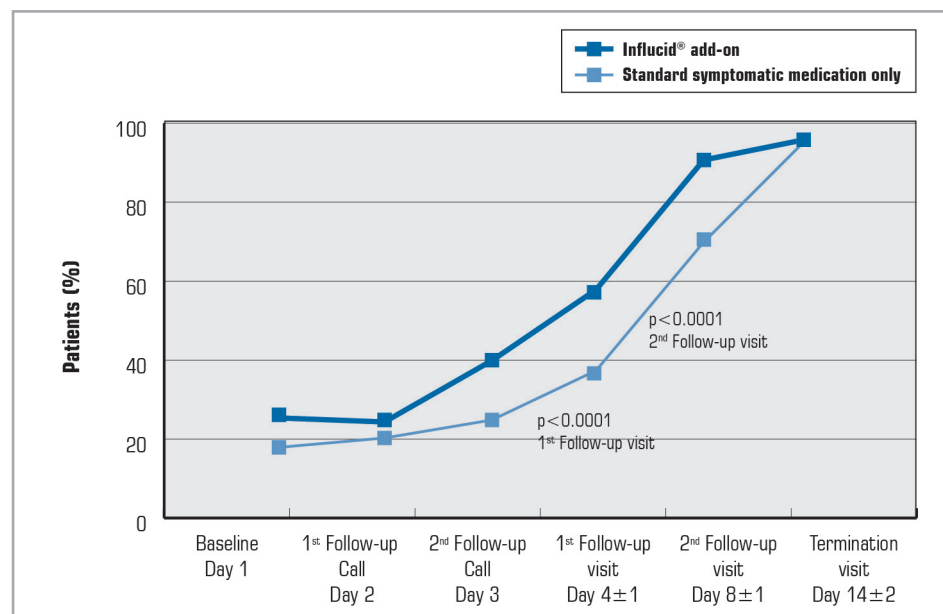
### From literature

In 2015 a randomized, standard-treatment controlled, parallel group, open, multicenter and multinational clinical trial was published by Thinesse-Mallwitz and colleagues [22]. Aim of the study was to evaluate the effectiveness and safety of IFC as an add-on to symptomatic standard treatments of URTIs. A total of 523 patients presenting with clinical signs and symptoms of an URTI with a duration up to 24 h, accompanied by fever were randomized. The standard treatment (ST) group received paracetamol, ambroxol and/or oxymetazoline; the IFC group received the same symptomatic treatment plus IFC for 7 days. Patients evaluation was performed by investigators at baseline (day 1), and on day 4, 8,

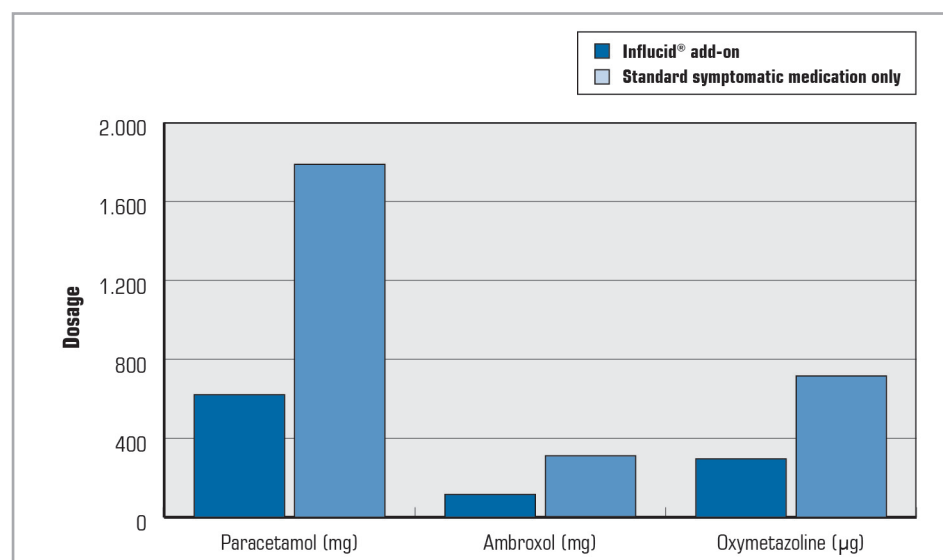


**Figure 6.** Between-group differences in the percentage of treatment responders (IFC minus ST) by study day (including 95% CIs) Adapted from [22]

**Figure 7.** Ability to perform normal daily activities. Adapted from [22]



**Figure 8.** Cumulated intake of standard symptomatic medication. Adapted from [22]



15. During the first 72 hours, patients  $\geq 12$  years took 12 tablets a day (1 tablet every hour) while patients  $< 12$  years took 8 tablets per day (1 tablet every 2 hours); during the following 96 hours the IFC dosage was 2 tablets 3 times a day for patients  $\geq 12$  years and 1 tablet 3 times a day for children.

The primary outcome was “treatment response” defined as a combination of mean axillary body temperature  $\leq 37.2^\circ \text{C}$  and absence or very mild degree of symptoms.

Patients in the IFC group showed an attenuated and shortened course of illness: at day 4 a percentage of 76.8% in the IFC group was free of fever vs 56.7% in the ST group and 17.0% had absence or very mild symptoms vs 7.5% of ST group.

Considering the entire study period of 14 days, data highlighted a more prompt occurrence of “treatment response” in the IFC group (Figure 6).

As a consequence to the significantly better response to treatment, patients in the IFC group showed a shorter time to symptom alleviation (1-2 days), a faster resumption of normal activities (IFC 48% vs ST 28%) and a significantly lower median disease severity (Figure 7). Simultaneously, significantly less standard symptomatic medication was needed in the IFC group (Figure 8). Safety results confirmed the good tolerability of IFC.

According to authors' conclusions, IFC as an add-on therapy improved response,

shortened the duration of URTIs, and lowered symptoms severity. The results suggest that IFC enhanced the self-recovery of the patients, and partly replaced the need for conventional symptomatic treatment.

## TONSILLITIS AND PHARYNGITIS

### Definition

Tonsillopharyngitis is an infection of the palatine tonsils and pharynx that can be either acute or chronic. Acute pharyngitis is caused by Group A beta-hemolytic streptococcus (GABHS) in the 15-30% of cases in children, and in 5 to 20 percent in adults [58]; the remaining cases are considered viral [59]. Tonsillopharyngitis is a common reason for pediatric health care visits: in the USA, approximately 10% of children seen by medical care providers each year have pharyngitis, and 25-50% of these children have GABHS pharyngitis [60]. Among school-aged children, the incidences of acute sore throat, swab-positive GABHS, and serologically confirmed GABHS infection are 33, 13, and 8 per 100 children/years, respectively [58].

The signs and symptoms of acute tonsillitis can be similar to other infectious causes (e.g. painful swallowing, sore throat, cervical lymphadenopathy), while chronic tonsillitis is characterized by more specific symptoms (e.g. enlarged tonsils, caseous detritus or liquid pus in the crypts, ridged thickening and chronic hyperemia of the edges of the palatine arches).

Diagnosis is based on clinical findings. To positively identify whether the etiology is bacterial or viral, a rapid strept test (RST) or a throat swab culture can be performed.

If tonsillopharyngitis is not properly treated, serious complications, as rheumatic fever and related cardiovascular disorders or post-streptococcal glomerulonephritis, can occur.

### Treatment

The goals of treatment are to: attenuate the severity of symptoms, shorten the course of disease, reduce the number of disease-related absences in school or at work, help prevent serious complications, and improve the quality of life [61]. The treatment of tonsillitis, both in acute and in chronic form, is based on pharmacological measures, as symptomatic medications, antipyretics and analgesics, and on other measures, as gargling, throat

compresses, and ultrasound. Only GABHS infections diagnosed by RST or culture should be treated with antibiotics [62]. According to a recent US study [63], antibiotics were prescribed during 60% of pharyngitis visits for children, while bacteria are responsible for pharyngitis only in 37% of cases: the inappropriate antibiotic treatment, suggested by this study, is becoming a major issue, in relation to development of resistances and hypersensitivity. To date, the management of bacterial pharyngitis remains controversial, and there is a lack of uniformity between different guidelines [64].

Tonsillectomy is indicated for repeated GABHS tonsillitis and severe acute tonsillitis persistent despite antibiotics. According to a recent Cochrane review, the results of surgery are controversial: the effects are modest, and they should be balanced with the risks related to the surgical procedure [65].

As for the other URTIs, natural remedies and homeopathy are used for tonsillitis and pharyngitis: according to data from a recent international survey, conducted on 138 pediatricians, general practitioners and ear-nose-throat specialists in 7 countries, homeopathic remedies were prescribed as a supportive therapy by 62% of participants in case of acute tonsillopharyngitis, and by 59% of participants in case of chronic tonsillopharyngitis [55].

### Tonsilotren® (use and dosage)

Tonsilotren® (Deutsche Homöopathie Union, DHU, Karlsruhe, Germany) is a homeopathic complex composed of a combination of 5 single remedies: Atropinum sulfuricum D5, Hepar sulfuris D3, Kalium bichromicum D4, Mercurius bijodatus D8, and Silicea D2 [66]. In acute tonsillitis, the suggested dosage for children < 1 year is 1 tablet (250 mg) 3 times a day; for children 1-11 years, the initial dose is 1 tablet every 2 hours (maximum 8 times a day) and the subsequent dose is 1 tablet 3 times a day. In chronic tonsillitis, the dosage for children < 12 years is 1 tablet 3 times a day: the treatment should continue for 6-8 weeks in 3-4 treatment cycles per year. Tonsilotren® can be used on its own or in combination with prescribed medication. An interval of approximately 30 minutes should be kept between the intake of Tonsilotren® and eating or drinking [66].

### From literature

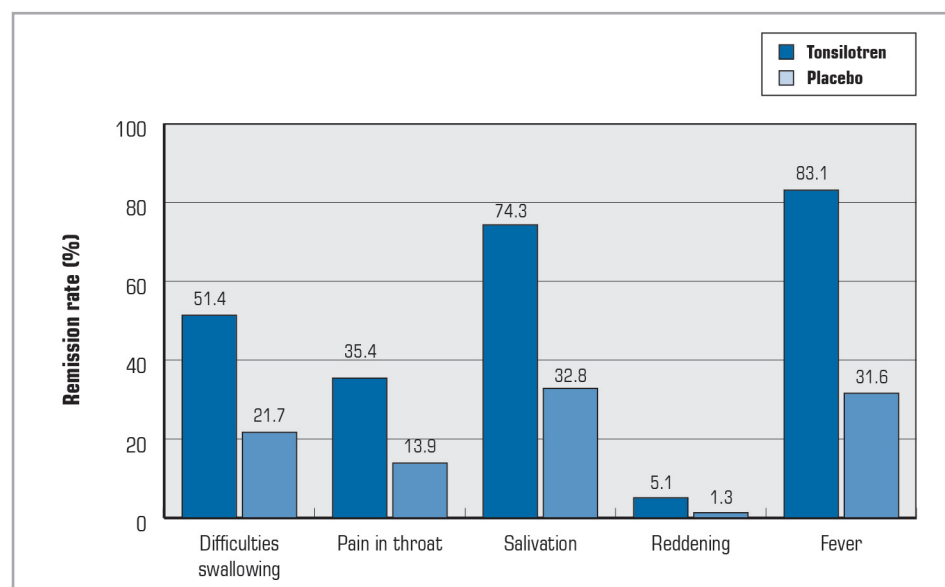
Tonsilotren® has been studied in a series of clinical studies, since the early nineties [23,24,67-73]. Here we present the main results of the two most recent studies in the pediatric setting, one in patients with acute tonsillitis [23] and one in patients with chronic tonsillitis [24].

Friese et al. [23] performed a multicenter, randomized, placebo-controlled, double-blind study on 158 patients aged 6-10 years affected by acute tonsillitis and without indication for an antibiotic treatment. The study group received Tonsilotren® at dosage of 1 tablet for hour (max. 12 times a day) until onset of improvement, afterwards the dosage was 1 tablet 3 times a day; the control group received placebo. The primary outcome criterion was the decrease of total sum score of tonsillitis typical symptoms from baseline to day 4; the 5 tonsillitis typical symptoms included difficulties swallowing, pain in throat, salivation, reddening and fever, rated on a 4-point-scale. Secondary outcome criteria were: the remission of tonsillitis typical single symptoms assessed on day 4, the time until onset of treatment effect, the outcome of treatment, and the safety and tolerability of Tonsilotren®. The overall observational period was 6 days.

The decrease of total sum score of tonsillitis typical symptoms from baseline to day 4 was significantly higher in the study group (- 7.2 vs - 2.7), as well as the remission of tonsillitis typical single symptoms assessed on day 4 (Figure 9).

Moreover, 92.4 % of patients showed a full recovery or at least a moderate improvement after 6 days of treatment, compared to the 43.1 % in the control group. The complete recovery rate was 75.9% in the study group vs 16.5% in the control group, and the deterioration rate was 3.8% in the study group vs 22.8% in the control group. Tonsilotren® showed an excellent safety and tolerability: no adverse event was related to the treatment and almost 100% of patients and physicians rated the tolerability as “very good” or “good”.

The most recent study on Tonsilotren® were performed by Palm and colleagues between January 2013 and April 2015, and the results were presented at the 13<sup>th</sup> Congress of the European Society of Pediatric Otorhinolaryngology (ESPO) [24]. A randomized, controlled, clinical trial was conducted in Germany, Spain and Ukraine on 256 patients aged 6-60 years (86 ≤ 12 years, 51 between 12-18 years, 119 ≥ 18 years) with moderate CT. Conventional symptomatic drugs should be prescribed to all the patients involved, while the test group received additionally Tonsilotren® for 3 treatment periods of 8 weeks. The estimated rate of diagnosed acute throat infections per year was the primary outcome measure; other outcome measures were the severity of CT symptoms and the antibiotics consumption due to acute throat infections. The primary outcome was significantly lower in the test group compared to the control group (0.59; 95%-CI: 0.41-0.85 vs. 1.35; 95%-CI: 1.09-1.66; p=0.0002; Poisson regression model) [24]. The CT symptoms occurred in a sig-



**Figure 9.** Remission of tonsillitis typical single symptoms assessed on day 4. Adapted by [23]

nificantly lower percentage of patients in the test group compared to the control group: difficulties in swallowing / sore throat were seen in 25% of test group vs. 52.5% of control group ( $p<0.0001$ ; Chi2 test), halitosis in 30.5% vs. 67.5% ( $p<0.0001$ ; Chi2 test) and caseous purulent plugs in the tonsillar crypts in 45.3% vs. 66.7% ( $p=0.0007$ ; Chi2 test) [24]. Significantly lower was also the antibiotics consumption due to acute throat infections: 37% in the test group vs. 58.2 in the control group (95%-CI: 9.13-33.36;  $p=0.0008$ ; Chi2 test) [24]. Positive results were also registered about the safety of Tonsilotren®: in the test group 225 adverse events were reported, three of these were related to Tonsilotren® [24].

## CONCLUSION

In recent years the use of herbal remedies and homeopathic products in children is highly increasing, as outlined by analysis carried out in the USA and in Europe [3-6]. Very often parents themselves decide to give their children these kind of remedies, especially in the early childhood years or for the treatment of mild ailments, such as those related to teething or infantile colic. The biggest concern for parents comes generally from the risk of adverse events due to conventional drugs; furthermore, for some disorders, there are no standard of care in mainstream medicine. In these cases the use of homeopathic products confer the advantage of having an excellent profile of safety and tolerability together with efficacy, as demonstrated by recent studies presented and discussed in this article [20-24].

Homeopathy can also be useful as adjunctive therapy for conventional drugs: recent

studies show that, even in children, very often homeopathic products are used together with conventional therapies. In these cases the use of homeopathic medicines demonstrated to alleviate symptoms, contributing to shorten the duration of the disease and decreasing the use of symptomatic drugs, as here reported by the study on Influcid [22]. In some pathologies, in particular, such as recurrent respiratory infections in children, the use of symptomatic drugs is very high, although not particularly effective. A recent Cochrane review confirmed the controversial results on non-prescription, over-the-counter (OTC) medicines for acute cough due to URTIs: in the absence of good evidence for or against the effectiveness of OTC medicines in acute cough, the Authors stressed the importance of prescribing these drugs with caution, to avoid the risk of adverse events [74].

There is a strong interest of pediatricians towards herbal products and homeopathic: many studies have reported a growing demand for validated information, also to better address the demands and needs of patients and their parents [7]. In recent years it has also increased the number of pediatricians and physicians who choose to treat themselves with natural and homeopathic remedies.

Although homeopathy is still debated, there are some studies that attest to the efficacy and safety in children. In this article we present and discuss six studies that have shown the effectiveness of homeopathic products for the treatment of infantile colic, teething, URTIs and tonsillopharyngitis [20-24]. As authors active in clinical practice we hope that such issues will be investigated with further trials and updated reviews on existing literature.

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