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RESULTS OF CLINICAL STUDIES ON THE USE OF TONSILOTREN IN CHILDREN WITH CHRONIC TONSILLITIS

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Chronic tonsillitis (CT) is a quite frequent childhood illness; its incidence ranges from 20% in the general population to 43% among frequently ill children [1-3]. Chronic tonsillitis in children is frequently accompanied by impairment of the child's overall development, systemic complications, declining school performance and changes in the threshold of social adaptation.

The problem of a rational treatment of children is not a simple one. Doctors are often confronted with the need to choose between local treatment or systemic antibacterial therapy and sometimes tonsillectomy. Important factors in achieving the best therapeutic effect include not only direct action on the pathogenetic factors of the main disease, but also prompt prophylaxis of systemic changes. Evidence obtained from numerous studies which have demonstrated the active involvement of the palatine tonsils in systemic and local immune responses support a clear priority to be given to therapeutic rather than surgical methods of treatment and a search for new and more effective conservative therapy for patients with chronic tonsillitis [4-6].

Most methods of conservative treatment do not promote long-term sanitisation of the tonsils which increases the risk of complications. Selection of treatment of chronic tonsillitis requires consideration of its clinical form. Conservative treatment is used for the compensated as well as the decompensated form when it manifests itself in recurrent angina. The most widely used and effective type of conservative treatment is lavage of the crypts of the palatine tonsils with antiseptic solutions in combination with physiotherapeutic procedures. However, given that tonsillitis is a systemic infectious-allergic disease, it is important to use agents with systemic anti-inflammatory actions, promoting increases in the body's natural resistance, along with immunocorrective agents [4, 7, 8]. Tonsilotren, a complex homoeopathic remedy, is one such substance.

The purpose of our study was to evaluate the efficacy and tolerance of Tonsilotren in 6-18 year old patients with chronic compensated tonsillitis (CCT), decompensated tonsillitis (CDT), occurring as recurrent angina and chronic compensated tonsillitis with tonsillocardiac syndrome (CDT + TCS), which was conducted within the framework of a multicentre open randomised parallel clinical trial.

The clinical trials were conducted in six independent clinical sites in Ukraine: The A.A. Bogomolets National Medical University (Kiev), the State Medical University in Donetsk, the Vinnitsa National University, the Kharkov Medical School for Postgraduate Training , the Crimea State Medical University (Simferopol) and the "Ukrainian Medical Dental School in Poltava" Higher State Educational Institution (Poltava).

Materials and methods

The trial which included 143 patients, was conducted from November 2006 to November 2008. In accordance with the study design, patients were divided into the three groups identified above. Patients were followed over a period of 18 months by a paediatrician and an otorhinolaryngologist. At the initial stage, the ENT doctor identified the type of CT: compensated, showing only local signs identified by pharyngoscopy or decompensated, when in addition to the local signs the patient's showed signs of decompensation such as recurrences of tonsillitis (3 or more per year), paratonsillitis or tonsillitis-associated myocardial dystrophy.

According to the treatment procedure the patients were divided into two groups, the experimental and the control. Patients in the experimental group received three courses of Tonsilotren for 60 consecutive days, starting on day 1 – 180 ± 5 and 360 ± 5 respectively. The formulation was administered according to the following schedule: 1 tablet 3 times daily under the tongue to dissolve slowly in the mouth half an hour before or after meals. Children of both the experimental and control groups received local conservative treatment for CT – lavage of the crypts of the palatine tonsils with 0.02% furacillin solution (100-120 ml per procedure) as three courses of 10 consecutive days combined with ultrasound treatment of the tonsils.

Treatment efficacy was evaluated in terms of changes in point scores for general symptoms as well as individual symptoms characteristic of CT. General symptoms (changes in body temperature, decreased appetite, fatigue, pain in the cardiac area, and intermittence of the cardiac rhythm) were evaluated on a 4-point scale and the total points score was calculated. The severity of symptoms characteristic of CT (caseous detritus or liquid pus in the crypts, wedge-shaped swelling and stagnant hyperaemia of the margins of the palatine arches and commissure, friability or sclerosis of the tonsillar surface, scarring of the paratonsillar tissue, regional lymphadenitis) were assessed using a 5-point scale with calculation of the total score.

The following dynamic examinations included ECG and EchoCG (before treatment and 180, 360 and 540 days of follow-up). During the follow-up, cleanliness and the frequency and severity of recurrences of angina and acute respiratory illnesses were also assessed.

Assessment of treatment efficacy was based on the criteria of the Integrative Medicine Outcome Scale, (IMOS), and patient satisfaction was assessed using the Integrative Medicine Patient Satisfaction Scale, (IMPSS), where patients may report as being very satisfied, satisfied, neutral, dissatisfied or very dissatisfied.

A vital part of the study was assessment of the tolerance of Tonsilotren and monitoring of adverse events.

Results and discussion

The study included essentially identical numbers of boys (53.3%) and girls (46.7%). The children were uniformly distributed in groups, as follows: 31.3% had CCT, 32.8% had CDT, and 35.9% had CT + TCS.

The change in the general condition of children with CT when under observation in both the experimental and control groups were positive (**Table 1**).

Analysis of the study results showed that overall points scores were significantly different from baseline during treatment in the experimental and control groups of children with CCT: however the result was twice as good in the experimental as in the control group. Already by day 240 children treated with Tonsilotren showed a 2-fold decrease in the total points score ($p<0.01$), while the index of change in the control group was less marked, although still significant ($p<0.05$).

Similar changes were seen in patients with CDT: the integral index decreased significantly during treatment by a factor of 3.5 in patients receiving complex treatment, compared with a 1.6-fold decrease in the control group.

At screening, the severity of general symptoms in patients with CDT + TCS was greater than in the other groups. During the study, only a slight improvement in the general symptoms in children in the reference group were noted, complaints of fatigue, decreased

appetite, periodic sub febrile body temperature and cardiac symptoms continued, while significant reduction in the total index by a factor of 2.8 was registered in the experimental group ($p<0.01$).

The persistent presence of the infectious agent in the tonsils is known to be a source of chronic intoxication and allergenisation of the organism. Toxic effects on the organism in CT leads to the formation of inflammatory products, i.e., exo- and endotoxins, due to activation of microbial growth in the tonsillar tissues and dissemination of toxins via the haematogenic and lymphogenic pathways. This mechanism plays a key role in the severity of intoxication symptoms (malaise, increased fatigue, reduced concentration and memory, depression, etc.) and may subsequently cause complications. It should be noted that these same intoxication factors can aggravate the pathogenesis of any other disorder, including those with no aetiological association with CT. V.T. Palchun's findings have demonstrated the direct and continuous penetration of live microbes and their metabolic products into the vascular system of the tonsils in chronic tonsillitis. Autoradiography has confirmed the presence and growth of live microbes in the walls, lumens and parenchyma of tonsillar vessels which testifies to the activity and aggressiveness of the infection focus while in healthy humans no proliferation of microflora from the crypts to the parenchyma, vessel walls or lumens was observed [9,10].

Our results show that the frequencies of symptoms of increased fatigue in the study groups at screening were essentially identical, these being present in 63% of children receiving Tonsilotren and 62.5% of the reference group. On the last day of the study, this symptom was present in 7.2% of patients of the experimental group but persisted in essentially one third of children in the control group. This led us to the conclusion that the treatment of focal tonsillar infection should take cognisance of not only sanitisation of the lymphoid apparatus of the pharynx, but also a method of healing and strengthening the body as a whole. The positive effect of changes in overall status, especially in children with CDT, was obtained indirectly, through normalisation of any pathological changes at the *locus morbi*. Thus, the overall score for caseous detritus at the end of the study was significantly lower in the experimental group: we found it to be 10 times less frequent in experimental children with CCT (**Table 2**) and CDT (**Table 3**) ($p<0.01$).

In otorhinolaryngological terms, this effect of local treatment was interpreted as an improvement in the drainage function and sanitisation of the tonsils. Normalisation of the structure of the palatine tonsils was indicated by decreased signs of thickening, friability, and sclerolisation of their surfaces: at completion of the study, these symptoms were 2 times less frequent in the experimental group of children with CCT (**Table 2**) and CDT (**Table 3**) ($p<0.01$).

Similar changes were seen in relation to regional lymphadenitis. Better average score indices (more than 3-fold, $p<0.01$) were recorded in CCT, CDT, and CDT + TCS patients receiving Tonsilotren treatment. Smaller but still significant positive changes were seen in patients of the control group.

These Tables clearly demonstrate the therapeutic effects of this formulation. It should be noted that ***the natural components used in Tonsilotren*** provide a multifaceted and pathogenetically based therapeutic action:

- *Atropinum sulfuricum (atropine sulphate)* – decreases tonsillar parenchymal oedema, decreases pain on swallowing and has an antipyretic effect.
- *Hepar sulfuris (acclimated liver sulphur)* – anti-oedema action and accelerates crypt sanitisation. Effective in the treatment of recurrent purulent inflammation, accelerates clearance of the tonsils in abscesses and purulent plugs, eliminates inflammatory reactions of the lymphoglottal ring.
- *Kalium bichromicum (potassium bichromate)* – anti-oedema effect on the mucosa, anti-inflammatory action, eliminates the sensations of burning and a dry sore throat.
- *Silicea (silicon)* – has immunomodulatory action mediated by increases in phagocytosis and normalisation of lymphocyte subpopulations. It accelerates recovery, prevents recurrences of illness, and normalises the structure of the tonsils.

- *Mercurius bijodatus (mercury iodide)* – has lymphotropic action, decreasing oedema and inflammation in lymph nodes, has an anti-inflammatory effect on the mucosa, and promotes reductions in tonsillar hypertrophy.

Decreases in the frequency of local signs of CT such as caseous detritus, hyperaemia of the arches, and regional lymphadenitis, provided evidence of sanitisation of the tonsils, supported by decreases in the level of endogenous intoxication and improvements in general wellbeing in children treated with Tonsilotren.

The group of children with CDT combined with TCS deserves special attention. Results obtained from previous studies show that among children with carditis, streptococcal infection of the oropharynx was seen in up to 50-60% of cases and staphylococcal infection was seen in up to 15-25%. Published data identify a significant risk of developing carditis, acquired heart diseases, acute rheumatic fever and juvenile rheumatoid arthritis in children with chronic streptococcal pharyngeal infection. Studies reported by Y. Talmon, A. Samet et al. (2007) showed that of the 100 patients with acute tonsillitis studied, one was diagnosed with carditis and five had signs of cardiopathy [11]. In the case of chronic infection, the incidence of cardiac manifestations was up to 74%.

The basis for the formation of tonsillocardiac syndrome is altered reactivity of the macroorganism. Metabolic myocardial disturbances predominate over inflammatory changes – with formation of the so-called cardiomyocyte metabolic insufficiency. Myocardial contractile activity in patients with TCS undergoes changes of the energy-dynamic insufficiency type (hypodynamic syndrome) the severity of which depends primarily on the severity of the clinical signs of cardiomyopathy [12, 13]. Early reversible pathological changes, amounting to functional cardiopathy, require correction to prevent the development of serious disturbances of cardiovascular system activity in patients with CT.

Our results identified significant improvement in cardiac symptoms in the experimental group of children with CDT and functional cardiomyopathy. Along with decreases in the frequency of cardialgia and interruptions in cardiac activity, positive changes in the ECG were recorded (**Figure**).

Clinical and instrumental data provided evidence of decreases in ECG signs of metabolic disturbances in both groups during treatment. Lengthening of the P-Q interval, deformation of QRS complexes, and T wave were diagnosed significantly less often in children receiving complex treatment. These ECG changes were twice as rare in the experimental group than in controls. It should be noted that children of the control group more often showed changes in conductivity from baseline values during treatment, while these changes were essentially not seen in children of the experimental group.

Tolerance of Tonsilotren was good in all patients and no side or undesirable effects were seen. Patients were satisfied with their treatment results (on the Integrative Medicine Patient Satisfaction Scale).

Tonsilotren is one of the most tested agents, as it has been used with success in Germany and other EC countries for more than 50 years. Previous studies have demonstrated a 75-90% therapeutic efficacy of this agent in acute tonsillitis and 60-78% in chronic recurrent angina (S. Becker and D. Kunstman, 1995).

A meta-analysis of previous studies addressing the efficacy and tolerance of Tonsilotren in children aged 3-14 years with acute and chronic tonsillitis in the Ukraine in 1995-1996, 1998, and 2000 showed that the treatment was clinically effective in 72.3-76.5% of patients; decreases in the severity of local signs of chronic tonsillitis were noted, along with decreases in the frequency of recurrences of quinsy and acute respiratory infections. The therapeutic effect in the control group given traditional treatment was only 53.0% (L. P. Chirkova, 2003).

Thus, chronic tonsillitis in children is not simply an inflammatory disease of the palatine tonsils, but a serious pathology involving suppression of the organism's nonspecific natural resistance factors with a high risk of developing serious complications.

The therapeutic effect of Tonsilotren is achieved via a complex action at multiple application points and is of interest to both paediatricians and otorhinolaryngologists in

relation to its use in the treatment of children with chronic tonsillitis and tonsillocardiac syndrome.

An analysis of multicentre trial results demonstrates that it is possible to treat children with different types of chronic tonsillitis effectively and to prevent both cardiac and other systemic complications.

Table 1. Changes in general status in groups of children during treatment (total points)

Diagnosis	Before treatment		Day 240 ± 5		Day 540 ± 5	
	Experimental	Control	Experimental	Control	Experimental	Control
CCT	15.5 ± 0.5 (n = 20)	16.4 ± 0.7 (n = 17)	7.7 ± 0.6** (n = 19)	12.2 ± 0.8* (n = 17)	4.4 ± 0.5** (n = 17)	9.6 ± 0.6** (n = 14)
CDT	17.2 ± 0.7 (n = 21)	17.6 ± 0.6 (n = 23)	7.8 ± 0.5** (n = 21)	13.2 ± 0.7* (n = 23)	4.7 ± 0.5** (n = 21)	11.0 ± 0.8** (n = 19)
CDT + TCS	20.3 ± 0.8 (n = 23)	21.0 ± 1.1 (n = 15)	12.0 ± 0.7** (n = 22)	16.0 ± 1.1 (n = 15)	7.3 ± 0.7** (n = 19)	13.0 ± 0.9 (n = 12)

Note: *p<0.05; **p<0.01 (horizontal comparison with pre-treatment values). CCT – chronic compensated tonsillitis; CDT – chronic decompensated tonsillitis; TCS - tonsillocardiac syndrome

Table 2. Changes in local signs in groups of children with CCT (total points)

Days	Caseous detritus / pus in crypts		Wedge-shaped swelling/ hyperaemia of the arches		Friability / sclerosis of the tonsillar surface		Commisures / scars with palatine arches		Regional lymphadenitis	
	E	C	E	C	E	C	E	C	E	C
Before treat-ment	2.4 ± 0.2	2.4 ± 0.2	2.4 ± 0.2	2.9 ± 0.2	2.6 ± 0.2	2.8 ± 0.2	2.1 ± 0.1	1.9 ± 0.2	1.9 ± 0.1	1.8 ± 0.1
240 ± 5	0.5 ± 0.1**	1.4 ± 0.3**	1.5 ± 0.1**	2.1 ± 0.3*	1.5 ± 0.1**	2.3 ± 0.3	1.3 ± 0.2*	1.8 ± 0.2	0.8 ± 0.1**	1.5 ± 0.2
540 ± 5	0.2 ± 0.2**	1.3 ± 0.3**	1.0 ± 0.1**	1.7 ± 0.3**	1.3 ± 0.2**	1.8 ± 0.2**	1.0 ± 0.2**	1.8 ± 0.3	0.5 ± 0.1**	1.0 ± 0.2

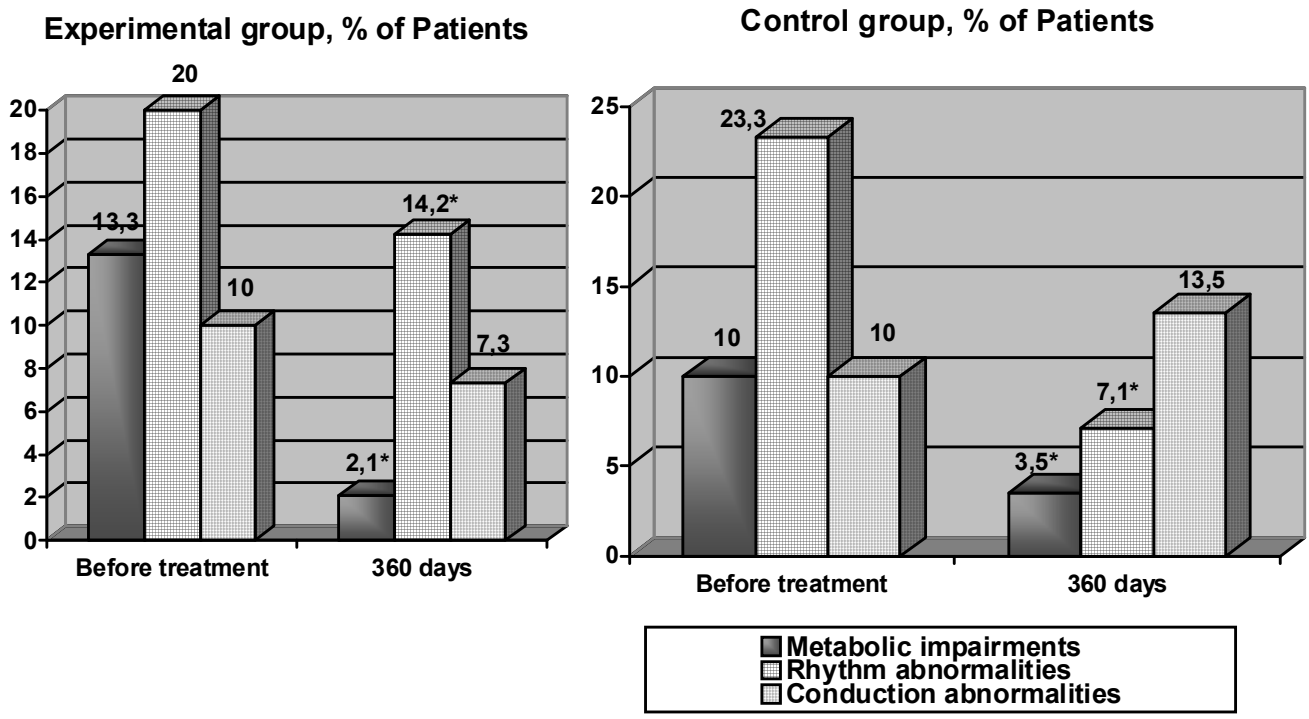
Note: *p<0.05; **p<0.01 (vertical comparison with pre-treatment values, horizontal comparison with control group)

Table 3. Changes in local signs in groups of children with CDT (total points)

Days	Caseous detritus / pus in crypts		Wedge-shaped swelling/ hyperaemia of the arches		Friability / sclerosis of the tonsillar surface		Commisures / scars with palatine arches		Regional lymphadenitis	
	E	C	E	C	E	C	E	C	E	C
Before	2.4 ±	2.4 ±	2.6 ± 0.2	2.6 ±	2.9 ±	2.7 ±	2.3 ±	2.1 ±	2.0 ±	2.1 ±

treat-ment	0.2	0.2		0.2	0.3	0.2	0.2	0.2	0.2	0.2
240 ± 5	0.5 ± 0.2**	1.7 ± 0.3*	1.4 ± 0.2**	1.9 ± 0.2*	1.7 ± 0.2**	2.3 ± 0.2	1.6 ± 0.2*	1.8 ± 0.2	0.7± 0.1**	1.6± 0.2
540 ± 5	0.2 ± 0.1**	1.4± 0.3**	1.1± 0.1**	2.0 ± 0.2*	1.4 ± 0.1**	2.0 ± 0.2*	1.1 ± 0.2**	1.8 ± 0.3	0.6 ± 0.1**	1.2 ± 0.2**

Note: *p<0.05; **p<0.01 (vertical comparison with pre-treatment values, horizontal comparison with control group)



Note: *p<0.05 compared with indices before treatment.

Figure. Changes in ECG indices in children of the study groups during treatment.

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T O N S I L O T R E N

Essential Tonsillitis Therapy

- Angina (catarrhal, lacunar, follicular)
- Chronic tonsillitis
- Tonsillar hypertrophy
- Accelerated healing following tonsillectomy

60 TABLETS

TONSILOTREN

A Homeopathic Medicinal Product
for the Prevention and Treatment
of Angina

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