Acta Biomed 2019; Vol. 90, Supplement 7: 30-35 DOI: 10.23750/abm.v90i7-S.8655

Original article

Broncalt®, class II medical device, in patients with chronic upper airways disease: a survey in clinical practice

*Gian Franco Cupido[1], Matteo Gelardi[2], Ignazio La Mantia[3], Salvo Emanuele Aragona[4], Claudio Vicini[5], Giorgio Ciprandi[6], and Italian Study Group on inflammatory otorhinolaryngological disorders**

[1]ENT Department, University of Palermo, Palermo, Italy; [2]Otolaryngology, Department of Basic Medical Science, Neuroscience and Sensory Organs, University of Bari Aldo Moro, Bari, Italy; [3]ENT Department, University of Catania, Catania, Italy; [4]Center of Regenerative Medicine, Humanitas Mater Domini, Castellanza (VA), Italy; [5]ENT Department, Forlì-Faenza Hospital, Italy; [6]Allergy Clinic, Casa di Cura Villa Montallegro, Genoa, Italy

Summary. Inflammation and infection are common pathogenic mechanisms involved in many otorhinolaryngological (ORL) chronic diseases. Broncalt® is a class II Medical Device containing: thermal water (Medesano, PR, Italy), hyaluronic acid, and grapefruit seed extract. It could exert a safe and effective anti-inflammatory, washing, and antimicrobial activity by virtue of these components. Therefore, the aim of the current survey, conducted in clinical practice of 84 Italian ORL centers, was to evaluate its safety and efficacy in the treatment of patients with chronic upper airways disease. The 1,817 (958 males, mean age 49 years) patients were evaluated at baseline (T0) and after one (T1) and two (T2) weeks of treatment, they were treated or not treated with Broncalt®. Signs and symptoms severity were measured by visual analogue scale. Broncalt® significantly, quickly, and safely diminished the clinical features in all sub-groups ($p<0.001$ for all). In conclusion, Broncalt® is a class II Medical Device able to exert a safe, quick, and effective activity in patients with chronic ORL disorders. (www.actabiomedica.it)

Key words: upper airways, chronic disease, thermal water, hyaluronic acid, grapefruit seed extract

Introduction

Chronic otorhinolaryngological (ORL) airways disorders are frequent in clinical practice. Chronic respiratory ORL illness include chronic rhinosinusitis, chronic rhinopharyngitis, chronic pharyngitis, chronic tonsillitis, and chronic laryngitis.

Chronic progression of an upper acute airways disease usually depends on worsening pathogenic factors, including host immune defect, virulence of

***Italian Study Group of inflammatory otorhinolaryngological disorders:** Aielli Federica, Albanese Gianluca, Alessi Vincenzo, Allosso Giuseppe, Antico Filippo, Antoniacomi Giovanni, Asprea Francesco, Azzaro Raffaele, Azzolina Alfio Alfonso, Benedetto Domenico, Bennici Ettore, Berardi Carlo, Bertetto Bruno Ivano, Blotta Pasquale, Bucci Alessandro, Bulzomì Antonio Giovanni, Caligo Giacomo, Cantaffa Antonio, Capelli Marco, Casaula Marco, Castagna Giovanni, Castellani Carla, Castellani Francesca, Chiarelli Raffaele, Ciabattoni Andrea, Colombo Giovanni, Cordier Aldo, Costanzo Marcello, Danza Carlo, De Luca Carlo Maurizio, Degli Innocenti Massimo, D'Emilia Mario, Dessì Roberta, D'Urso Marino, Emanuele Antonino, Falcetti Saverio, Falciglia Roberto, Ferraro Guglielmo, Fini Oscar, Franco Teresa, Frascadore Luigi, Fuggetta Alessandro, Gambardella Tullio, Iacolucci Carlo Maria, Ierace Michelangelo, Ingria Federico, La Paglia Alessandro, Lavazza Paolo, Leone Mirko, Livi Walter, Londei Salvatore, Lovotti Paolo, Maio Michele, Maniscalco Francesco, Martone Rosa, Melis Andrea, Mercurio Antonio, Milone Vincenzo, Montanaro Salvatore Carmine, Muià Fernando, Mussella Tommaso, Nacci Andrea, Naqe Nertila, Padovani Davide, Palma Antonio, Panetti Maria Luisa, Paoletti Matteo, Pellegrino Cataldo, Piccolo Marcello, Pizzolante Maurizio Cosimo, Sari Marianna, Scarpa Alfonso, Scotto di Santillo Leonardo, Serraino Eugenio Maurizio, Stabile Carlo, Tatti Maria Fatima, Tauro Francesco, Tombolini Alberto, Turso Giorgio Felice, Zaraca Giorgio

pathogens, autoinflammatory/autoimmune disorders, climate and environmental effects, concomitant pharmacological treatment, metabolic disease, etc (1-3). Therefore, the management of chronic upper airways disease is more complex than in acute ones and requires a careful work-up.

The treatment of chronic airways diseases is targeted to fight both infection and inflammation usually using antibiotics and anti-inflammatory medications. However, pharmacological medications may have contraindications and may implicate adverse events. Therefore, the option of complementary medicine is up-to-date in clinical practice.

Broncalt® is a new class II medical device containing salso-bromo-iodine thermal water (spring of Medesano, PR, Italy) 8%, hyaluronic acid (HA) 0.1%, and grapefruit seed extract 0.35%.

Recently, it has been reported that Broncalt® was effective in the treatment of postnasal drip-related cough in children with upper respiratory tract infections (4).

On the basis of this background, an Italian survey explored the pragmatic approach of a group of otolaryngologists in the management of chronic upper-airways disorders in clinical practice. Therefore, the aim of the current survey was to evaluate the efficacy and safety of Broncalt® in outpatients with chronic ORL diseases.

Materials and Methods

The current survey was conducted in 84 Italian ORL centers, distributed in the whole Italy, so assuring a wide and complete national coverage. Otolaryngologists were asked to recruit all consecutive patients visited because of chronic ORL disease.

Patients were consecutively recruited during the specialist visit. The inclusion criteria were: to have a diagnosis of chronic respiratory ORL disease, both genders, and adulthood. Exclusion criteria were to have comorbidities and concomitant medications able to interfere the evaluation of outcomes. As this survey was based on a real-world practice, the doctors had the complete liberty of choosing the preferred medications on the basis of the best practice. Actually, patients were subdivided in 2 sub-groups: i) patients treated with standard therapy plus Broncalt® (active group), and ii) patients treated with standard therapy alone (control group).

Patients were suffering from acute illness, including chronic rhinosinusitis, chronic rhinopharyngitis, chronic pharyngitis, chronic tonsillitis and chronic laryngitis.

All patients signed an informed consent. All the procedures were conducted in a real-world setting.

The treatment course lasted 2 weeks. The medical device Broncalt® (Aurora Biofarma, Milan, Italy) was taken following the specific indications, such as two tablets/daily. Patients were visited at baseline (T0), after 1-week treatment (T1), and after 2-week treatment (T2).

Clinical examination and fiber-endoscopy were evaluated in all patients at all visits.

All clinical data were inserted in an internet-platform that guaranteed the patients' anonymity and the findings' recording accuracy.

The following clinical parameters were evaluatated: nasal obstruction, mucosal edema, hyperemia, earache, swelling, sore throat, dysphagia, dysphonia, and cough. These issues were considered both as the quote of patients having them and their perceived severity. Symptom severity was assessed by a visual analogue scale (VAS). VAS is a psychometric test widely used to measure the patient's perception of symptom severity, emotions, pain, etc. Currently, VAS is a reliable and valid tool to assess the perception of symptoms and signs (14). The VAS consisted of one ruler asking for signs and symptoms severity perception. In this study, the VAS was a 10-cm horizontal line on which 0 implied the absence of sing or symptom, while 10 corresponded to maximal severity. VAS is considered a routine and validated parameter to assess disease severity in clinical practice and inflammatory markers are closely related with nasal obstruction perception (5).

In addition, the symptom disappearance duration was also considered, such as 3 period were established for symptom receding: by 3 days, between 4-7 days, and beyond 7 days.

Doctors also evaluated: the effectiveness (scored as very effective, effective, scarcely effective, and ineffective), the tolerability (scored as very good, quite

good, poorly good, no good), and the compliance (very good, good, scarcely good, and no good).

Safety was measured by reporting the occurrence of adverse events.

The paired T-test was used. Statistical significance was set at $p < 0.05$. Data are expressed as medians and 1th and 3rd quartiles. The analysis was performed using STATA, College Station, Texas, USA.

Results

Globally, 1,817 (958 males, mean age 49 years) patients were visited and completed the treatment course.

The demographic characteristics and type of chronic respiratory disease are reported in Table 1.

In particular, the two subgroups were similar concerning the gender, but the age was higher in patients not-treated with Broncalt. The distribution of chronic respiratory diseases was significantly different about some types, i.e. patients not-treated with Broncalt had more frequently recurrent otitis an chronic tonsillitis, whereas Broncalt-treated patients suffered more commonly from chronic pharyngitis. Subgroup treated with Broncalt took significantly less antibiotics and anti-inflammatory drugs than the other subgroup; interestingly Broncalt-treated subgroups did not take any medication more frequently (72.8% versus 3%).

Considering the frequency of patients without symptoms or signs after the treatment, Broncalt treatment induced higher percentages of symptomless patients for nasal obstruction, rhinorrhea, post nasal drip, and hyperemia (Table 2).

Considering the severity of symptoms, patients treated with Broncalt showed less severe facial pain, earache, and sore throat than not treated patients (Figure 1).

The percentages of patients treated with or without Broncalt with global symptom disappearance

Table 1. Demographic and clinical characteristics of patients, treated with or without Borncalt

	Broncalt N=1553		No Broncalt N=264		p-value
Characteristic					
Male gender, n (%)	826	53.2%	132	50.0%	0.338
Mean age, (SD)	**48.2**	**21.5**	**54.1**	**19.8**	**<0.001**
Chronic disease					
Recurrent Otitis, n(%)	**260**	**16.7%**	**64**	**24.2%**	**0.003**
Chronic Tonsillitis, n(%)	**56**	**3.6%**	**25**	**9.5%**	**<0.001**
Chronic Laryngitis, n(%)	244	15.7%	39	14.8%	0.697
Chronic Rhinosinusitis, n(%)	6	0.4%	1	0.4%	0.985
Chronic Rhinopharyngitis, n(%)	**408**	**26.3%**	**32**	**12.1%**	**<0.001**
Chronic Pharyngitis, n(%)	234	15.1%	28	10.6%	0.056
Dysphonia, n(%)	165	10.6%	26	9.9%	0.704
Concomitant treatments					
Antibiotics	**65**	**4.2%**	**44**	**16.7%**	
Cefalosporins	44	2.8%	26	9.8%	
Chinolones	8	0.5%	7	2.7%	
Macrolides	4	0.3%	8	3.0%	
Other	9	0.6%	3	1.1%	
Anti-inflammatory drugs	**308**	**19.8%**	**130**	**49.2%**	
Antipyretics	3	0.2%	3	1.1%	
Corticosteroids	248	16.0%	92	34.8%	
FANS	20	1.3%	20	7.6%	
Other	37	2.4%	19	7.2%	
Anti-inflammatory+antibiotic	**50**	**3.2%**	**82**	**31.1%**	
No drug	**1130**	**72.8%**	**8**	**3.0%**	

Table 2. Proportion of patients without symptoms and signs after treatment in the two subgroups: treated with or without Broncalt, evaluated at T1

Symptom	Broncalt	No Broncalt	P
Facial pain	20.2%	25.4%	0.054
Nasal Obstruction	**39.9%**	**31.4%**	**0.009**
Rhinorrea	**40.9%**	**34.5%**	**0.049**
Post nasal drip	**27.71%**	**18.9%**	**0.003**
Earache	16.6%	18.6%	0.435
Nose swelling	29.6%	26.9%	0.379
Sore throat	21.1%	25.4%	0.121
Dysphonia	24.9%	21.2%	0.202
Cough	33.6%	32.6%	0.741
Hyperaemia	**50.1%**	**40.5%**	**0.004**
Edema	24.3%	23.9%	0.885

within 3 days, and over 7 days were significantly different between groups (Figure 2). In particular, 51.4% of Broncalt-treated patients and 42.4% of patients without Broncalt treatment had no more symptoms within 3 days (p=0.007). On the contrary, 24.5% of patients without Broncalt treatment and 36.4% of Broncalt-treated patients still present symptoms over one week (p<0.001).

In patients treated with Broncalt, the perception of efficacy was very good in 77.8% and good in 19.5% (Figure 3A); the tolerability was very good in 87.8% and good in 11.9% (Figure 3B); the compliance was very good in 85.5% and good in 13% (Figure 3C).

The treatment was well tolerated by all patients and no relevant adverse event was reported.

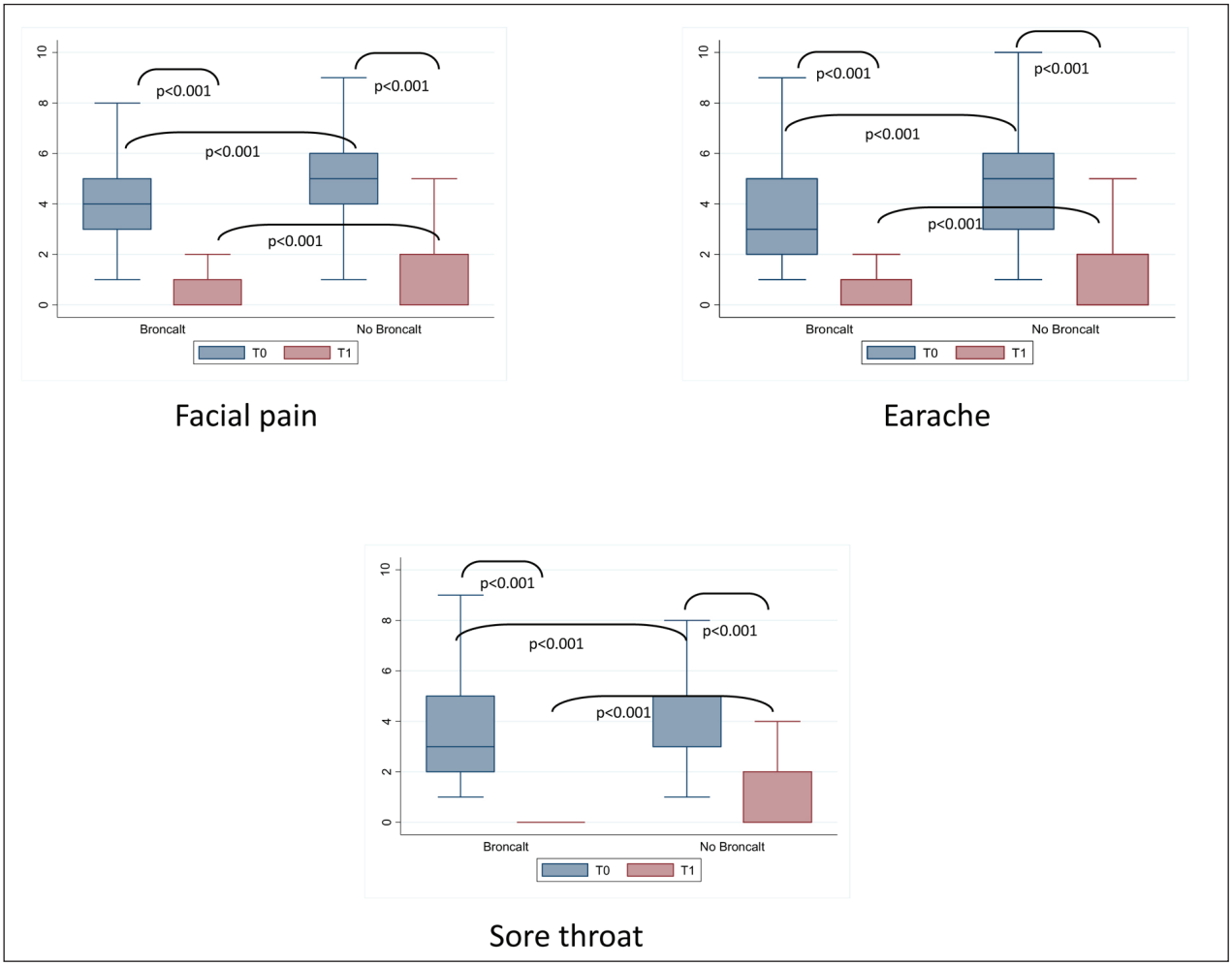

Figure 1. Visual Analogue Scale scores at T0 and T1 in patients treated with or without Broncalt concerning facial pain, earache, and sore throat

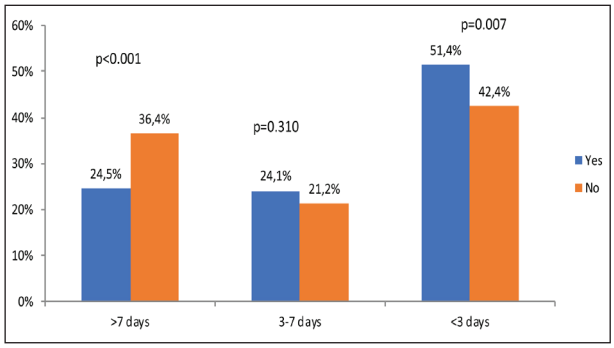

Figure 2. Percentages of patients treated with or without Broncalt with symptom disappearance within 3 days, between 3 and 7 days, and over 7 days

Discussion

At present, there is great interest in the complementary medicine to improve human diseases, including inflammatory/infectious diseases.

Chronic inflammation entails the accumulation of cells and exudates in involved tissues. Inflammation has been studied since thousands of years with the aim of contrasting its effects on the body. In AD 30, Celsius described the 4 classic signs of inflammation (*rubor, calor, dolor,* and *tumor*) and used extracts of willow leaves to relieve them. For many years, salicylate-containing plants were applied therapeutically and lead to the production of a major anti-inflammatory

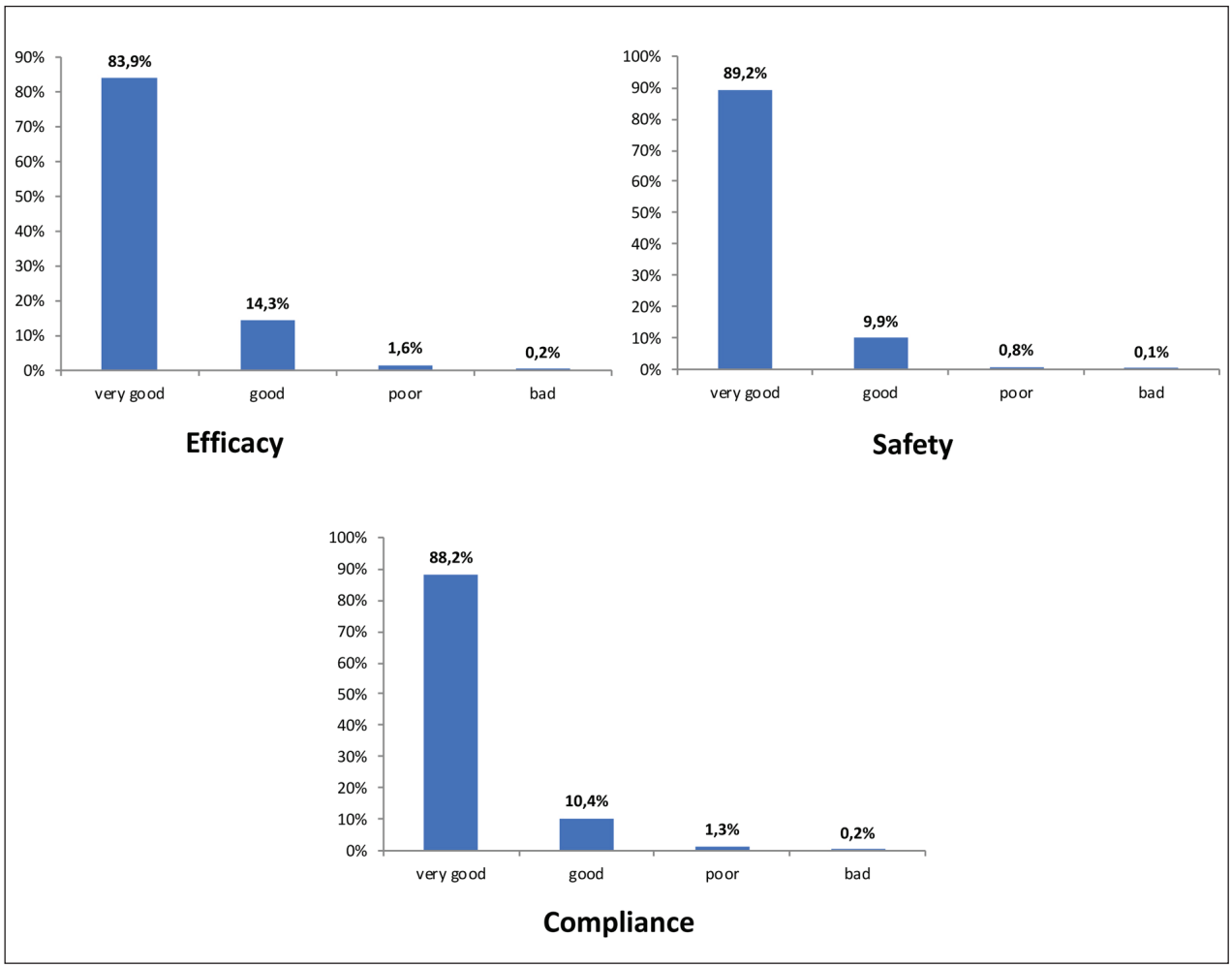

Figure 3. A= Patients' perception of Broncalt efficacy; B= Patients' perception of Broncalt tolerability; C= Patients' perception of Broncalt Compliance

drug (acetylsalicylate). Acetylsalicylate, an agent with anti-inflammatory activity, is derived from natural sources, and is used extensively in current clinical practice. It represents the paradigmatic example of the use of plant-derived compounds in medicine. Many other salicylate-like drugs are now available including the non-steroid anti-inflammatory drugs (NSAIDs). However, a long-lasting use of these compounds may commonly induce adverse events, even severe.

Natural products with anti-inflammatory activity have long been used as a folk remedy for inflammatory conditions such as fevers, pain, migraine and arthritis. As the inflammatory basis of disease becomes clear, anti-inflammatory food products become of greater interest. In this regard, the medical device Broncalt® contains extracts of grapefruit, HA, and thermal water of Medesano.

Currently, the mechanisms of action of these molecules have been identified and examined in depth, thus, their clinical use is no longer empirical but based also on solid scientific grounds. In particular, Broncalt® may exert a relevant anti-inflammatory-antimicrobial activity.

The current survey demonstrated that Broncalt® significantly improved the clinical feature in chronic respiratory ORL disorders in clinical practice. Interestingly, the effectiveness was quick as many symptoms disappeared in Broncalt-treated patients within 3 days. Moreover, it has to be noted that most of Broncalt-treated patients did not take any other medication, and in any case took less antibiotics and anti-inflammatory drugs.

The present findings are consistent with a previous study that explored the therapeutic effects of similar multi-component nutraceuticals in the treatment of chronic ORL diseases (6).

Therefore, the present survey confirms that Broncalt® was able to significantly reduce clinical features in patients with chronic ORL disorders characterized by an inflammatory reaction. However, the current experience has some limitations, mainly concerning the open design and the lack of objective functional data. On the other hand, the strength of this survey is the high number of enrolled patients and the real-world setting, so the findings may mirror what occurs in the daily practice.

In conclusion, the present survey evidenced that Broncalt® may induce a safe and quick control of respiratory complaints in chronic ORL disorders.

The current article was supported by Aurora Biofarma, Italy

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Received: 27 May 2019
Accepted: 27 June 2019
Correspondence:
Giorgio Ciprandi
Via P. Boselli 5 - 16146 Genoa, Italy
E-mail: gio.cip@libero.it