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Original article

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

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Summary. Inflammation is a common pathogenic mechanism involved in many otorhinolaryngological (ORL) disorders. Broncalt® is a class II Medical Device containing: thermal water (Medesano, PR, Italy), hyaluronic acid, and grapefruit seed extract. It has been reported that it exerted 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 acute upper airways disease. The 3,533 (1,797 males, mean age 43.5 years) patients were evaluated at baseline (T0) and after a 2-week treatment (T1) with or without Broncalt®. Signs and symptoms severity were measured by visual analogue scale. Broncalt® significantly and safely diminished the clinical features in all sub-groups ($p<0.001$ for all). Interestingly, Broncalt® significantly induced a faster symptom relief already within 3 days after the start of the treatment. In conclusion, Broncalt® is a class II Medical Device able to exert a safe and effective activity in patients with acute ORL disorders. (www.actabiomedica.it)

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

Introduction

In clinical otorhinolaryngological (ORL) practice, the airways disorders represent the most frequent cause of visit. From a clinical point of view, the respiratory ORL diseases may be subdivided in 3 categories: i) acute illness, including common cold, acute rhinosinusitis, acute rhinopharyngitis, acute pharyngitis, acute otitis, bacterial tonsillitis, acute laryngitis and acute laryngotracheitis; ii) chronic illness, includ-

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ing chronic rhinosinusitis, chronic rhinopharyngitis, chronic pharyngitis, chronic tonsillitis and chronic laryngitis; and iii) acute-chronic illness, i.e. the chronic disease when exacerbates.

Common cold is the most frequent respiratory disease and involves entirely the upper respiratory tract, it is usually self-limiting (1). The best pragmatic approach for rhinosinusitis management has been recently pointed out in clinical practice (2, 3). Alike, pharyngitis, laryngitis, and tracheitis are very common and are usually managed as proposed by *ad hoc* guidelines (4-7).

Acute ORL diseases may be commonly caused by bacterial, viral or fungal aetiology, even though non-infectious acute disease may also exist. However, infectious illness is the most frequent acute ORL disorders, apart allergic and non-allergic rhinitis. The acute infectious diseases share a common pathogenic mechanism: the inflammation. Therefore, the treatment of acute airways diseases is targeted to fight both infection and inflammation, usually using antibiotics and anti-inflammatory medications (8-10). These medications are effective, but antibiotics may be associated with bacterial resistance and anti-inflammatory drugs may induce serious adverse events. Therefore, the option of complementary medicine has having even more interest by doctors and also patients (11).

In this regard, 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%.

Salso-bromo-iodine thermal water may exert some relevant therapeutic effects, including enhancing the mucociliary clearance, anti-edema activity, and washing effect (12). HA is a fundamental component of the connective tissue. HA is able to modulate inflammatory response, cellular proliferation, and remodeling of extracellular matrix (13). Grapefruit seed extract exerts an antimicrobial activity (14).

Recently, it has been reported that Broncalt® was effective in the treatment of postnasal drip-related cough in children with upper respiratory tract infections (15).

On the basis of this background, an Italian survey explored the pragmatic approach of a group of otolaryngologists in the management of acute 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 acute 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 acute respiratory ORL disease.

Patients were consecutively recruited during the specialist visit. The inclusion criteria were: to have a diagnosis of acute 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 personal best practice. Actually, patients were subdivided in 2 subgroups: 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 common cold, acute rhinosinusitis, acute rhinopharyngitis, acute pharyngitis, acute otitis, bacterial tonsillitis, acute laryngitis or acute laryngotracheitis.

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 evaluated: nasal obstruction, mucosal edema, hyperemia, earache, nose swelling, sore throat, 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 (16). 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 (17).

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, 3,533 (1,797 males, mean age 43.5 years) patients were visited and completed the treatment course. The demographic characteristics and type of acute respiratory disease are reported in Table 1.

In particular, the two subgroups were similar concerning the age and the gender. The distribution

Table 1. Clinical characteristics in patients with acute respiratory disease and treated with or without Broncalt

	Broncalt N=2784		No Broncalt N=749		p-value
Demografic characteristics					
Males, n(%)	1406	50.5%	391	52.2%	0.409
Mean age, years, (SD)	43.6	20.9	43.4	18.4	0.432
Disease					
Otitis, n(%)	**408**	**14.7%**	**137**	**18.3%**	**0.014**
Tubaritis, n(%)	359	12.9%	79	10.6%	0.084
Rinosinusitis, n(%)	**604**	**21.7%**	**129**	**17.2%**	**0.007**
Rinopharyngitis, n(%)	**652**	**23.4%**	**107**	**14.3%**	**<0.001**
Bacterial Tonsillitis, n(%)	**165**	**5.9%**	**108**	**14.4%**	**<0.001**
Pharingytis, n(%)	**365**	**13.1%**	**144**	**19.2%**	**<0.001**
Laryngitis, n(%)	338	12.1%	102	13.6%	0.277
Laryngotracheitis, n(%)	196	7.0%	49	6.5%	0.634
Concomitant Tretaments					
Antibiotics	**280**	**10.0%**	**199**	**26.6%**	
Cefalosporins	197	7.1%	119	15.9%	
Chinolones	26	0.9%	31	4.1%	
Macrolides	26	0.9%	30	4.0%	
Other	31	1.1%	19	2.5%	
Anti-inflammatory drugs	**484**	**17.4%**	**221**	**29.5%**	
Antipyretics	11	0.4%	10	1.3%	
Corticosteroids	368	13.2%	101	13.5%	
FANS	44	1.6%	76	10.1%	
Other	61	2.2%	34	4.5%	
Anti-inflammatory+antibiotic	**212**	**7.6%**	**312**	**43.3%**	
No drug	**1808**	**64.9%**	**17**	**2.2%**	

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

Symptom	Broncalt	No Broncalt	P
Nasal Obstruction	**48.4%**	**28.8%**	**<0.001**
Rhinorrea	**44.3%**	**28.3%**	**<0.001**
Post nasal drip	**32.7%**	**19.4%**	**<0.001**
Earache	26.2%	24.6%	0.369
Nose swelling	**33.3%**	**23.1%**	**<0.001**
Sore throat	27.1%	33.1%	0.001
Dysphonia	22.5%	21.8%	0.688
Cough	**39.9%**	**34.5%**	**0.006**
Hyperaemia	**55.2%**	**50.3%**	**0.017**
Edema	25.3%	32.7%	<0.001

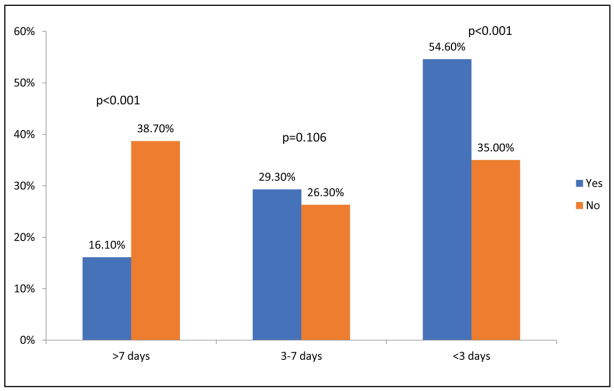

Figure 2. Percentages of patients treated with or without Broncalt with symptom disappearance within 3 days, between 3 and 7 days, and over 7 days

of acute respiratory diseases was different about some types. Subgroup treated with Broncalt took less antibiotics and anti-inflammatory drugs than the other subgroup; interestingly Broncalt-treated subgroups did not take any medication more frequently.

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, nose swelling, cough, and hyperemia (Table 2). On the contrary, a larger percentage of patients not treated with Broncalt had no more sore throat and edema.

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

The percentages of patients treated with or without Broncalt with global symptom disappearance within 3 days, and over 7 days were significantly different between groups (Figure 2). In particular, 54.6% of Broncalt-treated patients and 35% of patients without Broncalt treatment had no more symptoms within 3 days (p<0.001). On the contrary, 38.7% of patients without Broncalt treatment and 16.1% of Broncalt-treated patients still present symptoms over one week (p<0.001).

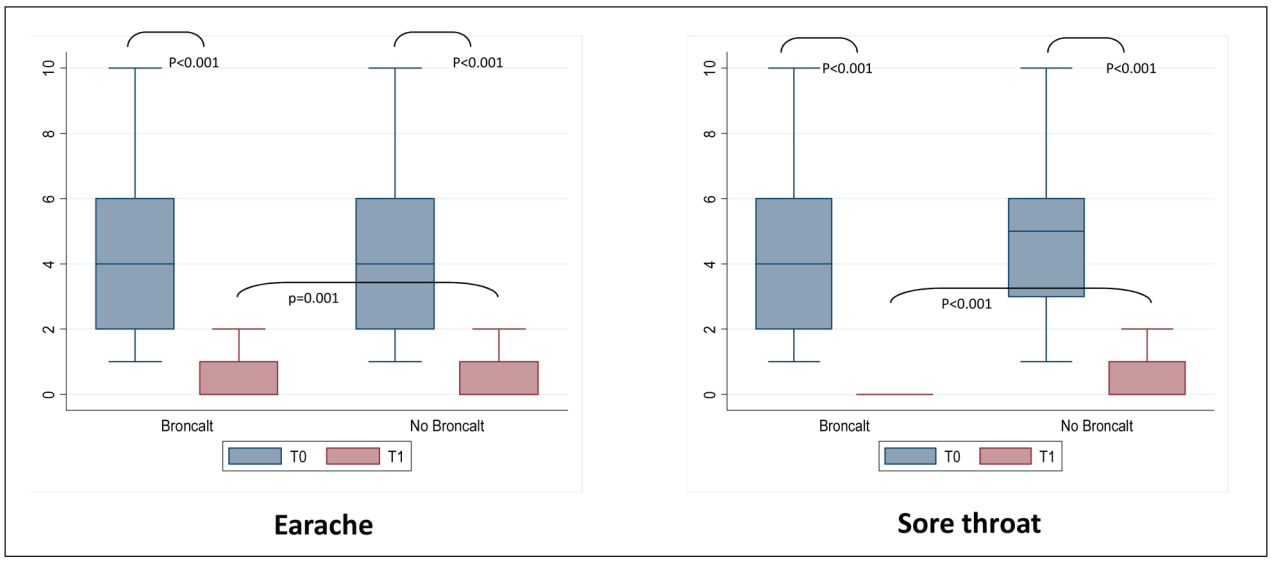

Figure 1. Visual Analogue Scale scores at T0 and T1 in patients treated with or without Broncalt for Earache and Sore throat

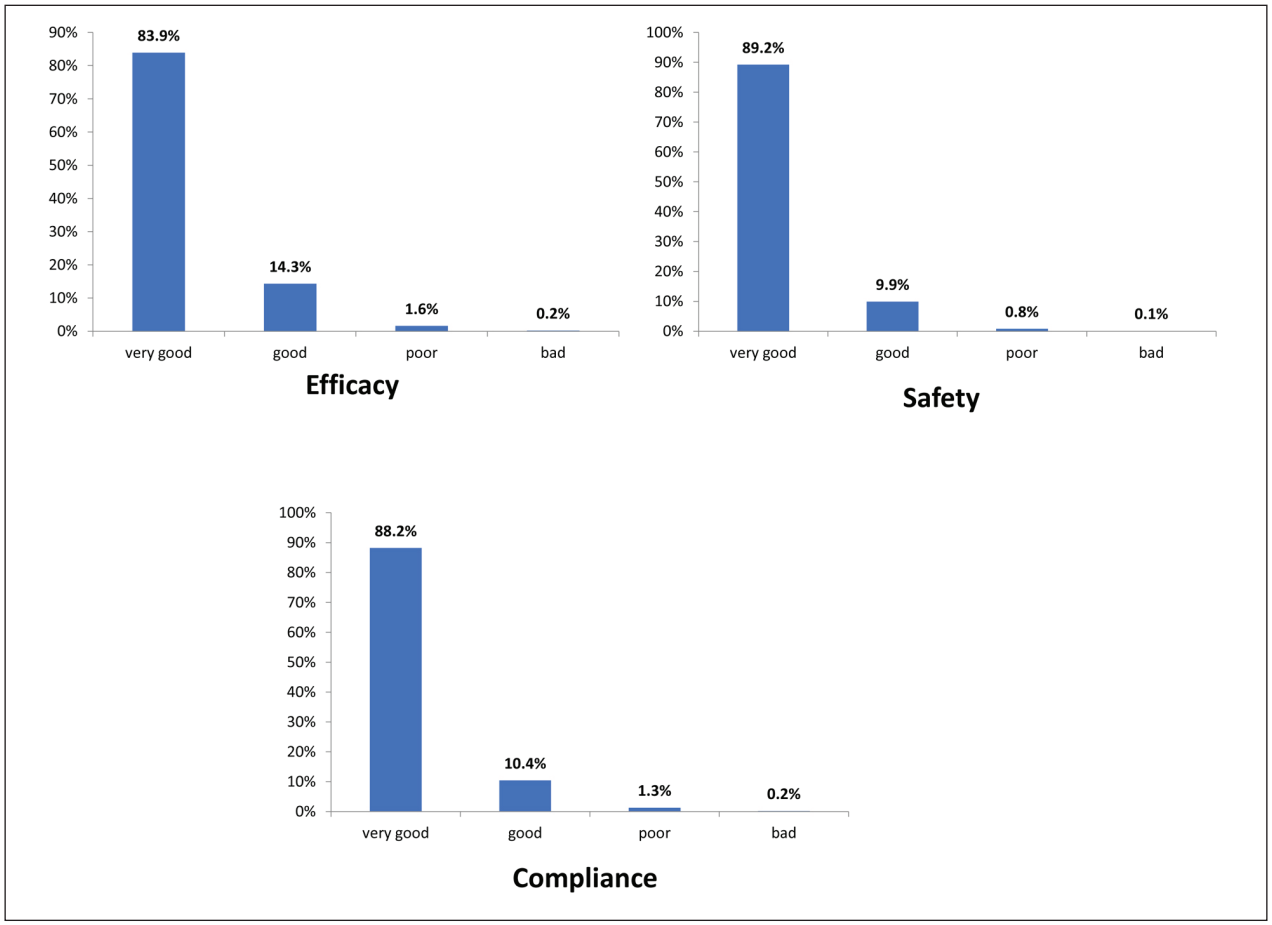

Figure 3. A= Patients' perception of Broncalt efficacy; B= Patients' perception of Broncalt tolerability; C= Patients' perception of Broncalt Compliance.

In patients treated with Broncalt, the perception of efficacy was very good in 88.2% and good in 10.4% (Figure 3A); the tolerability was very good in 89.2% and good in 9.9% (Figure 3B); the compliance was very good in 88.2% and good in 10.4% (Figure 3C).

No clinically relevant adverse event was reported.

Discussion

The role of natural non-pharmacological products as remedies has been respected since ancient times. At present, there is popular and scientific interest in the use of medical device to improve human diseases, so sparing the use of conventional medications. In spite of major scientific and technological progress in combinatorial chemistry, products derived from natural products, including thermal water, still make an enormous contribution to medication discovery today.

Inflammatory reaction is a common pathway in acute infectious ORL disorders. In this regard, the medical device Broncalt® contains 3 main components: salso-bromo-iodine thermal water, HA, and grapefruit seed extract. All of them provide anti-inflammatory, antimicrobial, and washing properties. Consequently, this medical device seems to be indicated in the acute ORL respiratory disorders as recently reported (15).

The current survey demonstrated that Broncalt® treatment significantly improved the clinical feature. In particular, Broncalt significantly reduced the percentage of patients still reporting symptom occurrence after the treatment and the symptom severity. Interest-

ingly, the Broncalt treatment induced a faster disappearance of symptoms as more than 50% of patients had no more symptoms already within 3 days after the start of the treatment.

The present findings are consistent with previous studies that explored the therapeutic effects of similar multi-component nutraceuticals in the treatment of ORL diseases (12-15).

In addition, it has to be mentioned that upper airways are closely linked with lower ones, so, these outcomes could have a clinical relevance if there is a lower respiratory co-morbidity (18, 19).

Therefore, the present survey confirms that Broncalt® may significantly reduce clinical features in acute ORL diseases characterized by an infectious/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 control of respiratory complaints in acute ORL disorders.

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