

EFFICACY OF HERBAL MEDICINES IN TREATMENT OF RESPIRATORY INFECTIONS

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Abstract

Introduction. Herbal medicine forms the basis of modern pharmacy, and hence, it has much to offer to patients suffering from common, acute bronchitis and flu.

The aim of this study was to investigate the efficacy of the herbal medicines Broncho Protect and Andrographis Extract as dietary supplements against standard medical treatment in patients with proven acute upper and/or lower respiratory tract infection.

This prospective, double-blind, randomization study was conducted at the PHI University Clinic for Pulmonology and Allergology in Skopje. Forty patients with clinical symptoms of acute upper and/or lower respiratory tract infection were included. Patients were randomized into two groups; the first group received standard therapy without restrictions plus placebo and the second group which, in addition to standard therapy, received Bronho Protect and Andrographis extract.

The results of patients' self-assessment of their health status indicated a statistically significant improvement in both groups, but no difference in the final outcome. The results of the assessment of patients' health status by the doctors indicated that in the group that received herbal medicines all patients got better. Also, auscultation findings were significantly better in patients who were treated with herbal medicines.

Herbal medicines are effective in treatment and prevention of respiratory infections and provide a much-needed alternative to ineffective antibiotics, whereby patients feel they are receiving beneficial therapy, thus reducing their tendency to use antibiotics.

Keywords: herbal medicines, respiratory infections

Introduction

Respiratory infections, especially viral ones, are the most common type of diseases that occur in humans, and according to the place of origin, they are divided into upper and lower respiratory tract infections. Rhinitis and pharyngitis are most common in the upper respiratory tract, while the most common infection in the lower tract is bronchitis [1].

The number one reason for the occurrence of these infections are viruses, followed by bacterial, fungal infections and allergic reactions [2,3].

There are a number of other morbid conditions that result in an acute infection of the upper and lower respiratory tract. Conventional cold and flu treatments only mask the symptoms, and are often ineffective (as in the case of non-steroidal anti-inflammatory drugs) [4]. Conventional treatments that directly target these viruses are few (oseltamivir, zanamivir) and the efficiency is low and the side effects are significant [5,6].

Influenza vaccines are available and recommended for use every year, but unfortunately only a small proportion of the population is vaccinated and they have variable efficacy (depending on the degree of accuracy of strain selection, viral mutation and other factors) [7].

Also, this vaccine has no effect on other viruses. On the other hand, the incorrect prescribing and abuse of antibiotic therapy is clearly described in almost all countries in the world, and Macedonia is no exception [8]. Herbal medicine is as old as humanity and represents the basis of modern pharmacy, and is on the rise in Western medicine, while in the Far East, herbal and modern pharmaceutical treatments are on the same level [9]. Therefore, herbal medicine has a lot to offer to patients with common cold, viral pharyngitis, acute bronchitis and flu [10].

In general, no single herb is the solution to a respiratory infection, but instead a range of herbs with diverse actions is needed [11]. Research shows that herbs have antimicrobial, anti-inflammatory, antioxidant, mucolytic, antitussive and immunostimulating effects [12-15]. For example, andrographis extract is officially approved by the Ministry of Health of Thailand and China as herbal medicine for treatment of patients with infections caused by SARS COV2 [16,17].

Broncho Protect is a dietary supplement with extracts of Chinese tea tree, curcumin, rosemary, black seed, the medicinal mushroom Reishi and vitamin C and vitamin D. Andrographis Extract, in a package of 30 capsules, is a dietary supplement and is an extract of *Andrographis paniculata*. The motive of this study was to investigate the efficacy and safety of Broncho Protect and Andrographis Extract, as dietary supplements, against standard medical treatment in patients with proven acute upper and/or lower respiratory tract infection.

Material and Methods

This prospective, double-blind, randomization study was carried out at the PHI University Clinic for Pulmonology and Allergology in Skopje. Forty patients with clinical symptoms of acute upper and/or lower respiratory tract infection were included. Patients were anonymously randomized into two groups using an independent Research Randomizer tool.

The first group received standard therapy without restrictions plus placebo and the second group which, in addition to standard therapy, also received Broncho Protect twice a day after meals at 15 mL and Andrographis Extract at one capsule twice a day after meals, for 7 days.

On the first and seventh days, patients underwent a physical examination with auscultation, a standard blood count was taken, and patient's health status was assessed with a visual analog scale (VAS) and a bronchitis symptom severity score (BSS) by a doctor. The patient filled out a diary daily for 7 days consisting of a visual analog scale on which the patient noted how he felt, and responded to the BSS.

Statistical analysis was performed with IBM SPSS Statistics, version 26 software.

Results

Characteristics of the study group

A total of 40 patients were recruited into the study, who met the study's already established inclusion and exclusion criteria. The first group of 22 (55%) patients were treated with standard treatment, Standard of care (SC) and Broncho Protect (BP) + Andrographis Extract (AE) as dietary supplement (SC&BP&AE group). The second group of 18 (45%) patients received standard treatment and placebo (SC&P). There were no significant differences between groups (SC&BP&AE/SC&P) in baseline demographic and clinical characteristics. All patients appeared at V2 (visit to a doctor) and all patient diaries were submitted within the proposed time frame.

Related to auscultation findings, doctors' assessment registered a significant improvement from V1 to V2 only in the SC&BP&AE group ($p=0.0001$), as well as a significant improvement in the finding of crackles ($p=0.031$) (Table1).

Table 1. Intragroup and intergroup comparison of selective clinical parameters in V1 and V2

Parameters	V 1			V 2			¹ p
	No	Yes	p	No	Yes	p	
Auscultation findings							
SC& BP& AE	8 (36.36%)	14 (63.64%)	² p=0.385	20 (90.91%)	2 (9.09%)	² p=0.122	0.0001*
SC&P	9 (50%)	9 (50%)		13 (72.22%)	5 (27.78%)		0,125
Prolonged expirium							
SC& BP& AE	19 (86.36%)	3 (13.64%)	³ p=0.789	21 (95.45%)	1 (4.55%)	³ p=0.884	0.500
SC&P	15 (83.33%)	3 (16.67%)		17 (94.44%)	1 (5.56%)		0.500
Wheezing							
SC& BP& AE	21 (95.45%)	1 (4.55%)	³ p=0.884	22 (100%)	0 (0%)	NA	-
SC&P	17 (94.44%)	1 (5.56%)		18 (100%)	0 (0%)		-
Crackles on auscultation							
SC& BP& AE	13 (72.22%)	5 (27.785)	³ p=0.564	15 (83.33%)	3 (16.67%)	³ p=0.324	0.031*
SC&P	14 (63.64%)	8 (36.36%)		20 (90.91%)	2 (9.09%)		0.498
Rhonchi							
SC& BP& AE	19 (86.36%)	3 (13.64%)	³ p=0.789	21 (95.45%)	1 (4.55%)	³ p=0.884	0.625
SC&P	15 (83.33%)	3 (16.67%)		17 (94.44%)	1 (5.56%)		0.625
Poor health condition - patient's assessment							
SC& BP& AE	2 (9.09%)	20 (90.91%)	³ p=0.856	21 (95.45%)	1 (4.55%)	³ p=0.857	0.0001*
SC&P	1 (5.56%)	17 (94.44%)		16 (88.89%)	2 (11.11%)		0.0001*
Poor health condition - physicians' assessment							
SC& BP& AE	5 (22.73%)	17 (77.27%)	² p=0.445	22 (100%)	0 (0%)	NA	-
SC&P	7 (38.89%)	11 (61.11%)		16 (88.89%)	2 (11.11%)		0.004*
V1 = Visit 1; V2 = Visit 2; NA = Not applicable SC&BP&AE =Standard of care +Broncho Protect +Andogaphis Extract; SC&P=Standard of care +Placebo ¹ p=McNemar test; ² p=Pearson's Chi Square Test; ³ p=Fisher exact test for p<0.05							
*significant							

At V1 and V2, patients rated their health status as poor in 90.1% vs. 4.5% in the SC&BP&AE group and in 94.4% vs. 11.1% in the SC&P group, respectively. From V1 to V2 patient-rated poor health status decreased by 86.4% in the SC&BP&AE group and by 83.33% in the SC&P group.

The first reduction in poor health status (improvement in health) was reported starting from the 3rd day in patients treated with SC&BP&AE, and on day 4 in patients treated with SC&P.

However, the first significant improvement in health was registered starting from the 4th day in both groups of patients ($p=0.008$ vs. $p=0.031$ respectively). According to self-assessment report, patients from both groups had a significant improvement in their health status from V1 to V2 ($p=0.0001$) (Table 1).

Doctors' assessments of the same patients at V1 and V2 showed poor health status in 77.2% versus 0% of patients in the SC&BP&AE group and in 61.1% versus 11.1% of patients in the SC&P group, respectively.

According to doctors' assessments, a significant improvement in the health condition of patients from V1 to V2 was observed in both groups. Specifically, at V2, no patient with poor health status was registered in the SC&BP&AE group, and 2 patients with poor health status were in the SC&P group ($p=0.004$) (Table 1).

Doctors' assessments of improvement in the Bronchitis Symptom Severity Score (BSS) showed that the BSS total score and the individual symptom scores of cough, sputum, auscultation of crackles, chest pain on coughing, and dyspnea decreased significantly in both groups from V1 to V2 ($p < 0.05$) (Table 2).

Table 2. Analysis of BSS symptom scores and their reduction from V1 to V2 (as assessed by doctors)

Parameters	Treatment	BSS – Bronchitis severity score				
		V1	V2	V1 → V2	Reduction score V1 → V2	
		Mean± SD	Mean± SD	¹ p	Mean± SD	² p
BSS	SC& BP& AE	6.23±3.65	0.82±1.22	p=0.00004*	5.41±3.44	p=0.946
	SC&P	6.44±4.45	1.61±1.22	p=0.0002*	4.83±2.64	
Cough	SC& BP& AE	2.41±0.91	0.41±0.59	p=0.00006*	2.00±1.02	p=0.775
	SC&P	2.55±1.09	0.67±0.84	p=0.0003*	1.89±0.90	
Sputum	SC& BP& AE	1.68±1.13	0.27±0.45	p=0.0003*	1.21±1.05	p=0.859
	SC&P	1.94±1.26	0.50±0.79	p=0.0004*	1.44±0.78	
Crackles on auscultation	SC& BP& AE	0.82±1.18	0.09±0.29	p=0.012*	0.73±1.12	p=0.463
	SC&P	0.72±1.23	0.39±0.78	p=0.043*	0.33±0.59	
Chest pain when coughing	SC& BP& AE	0.59±0.73	0.00±0.00	p=0.005*	0.59±0.73	p=0.881
	SC&P	0.61±0.69	0.00±0.00	p=0.008*	0.61±0.69	
Dyspnea	SC& BP& AE	0.72±0.70	0.04±0.21	p=0.001*	0.68±0.65	p=0.455
	SC&P	0.61±0.85	0.05±0.23	p=0.018*	0.55±0.78	
V1 = Visit 1; V2 = Visit 2; SC& BP&AE =Standard of care +Broncho Protect +Andographis Extract; SC&P=Standard of care +Placebo ¹ Wilcoxon Signed-ranks test ² Mann Whitney U test *significant for p<0.05						

Comparison of mean difference (V1 → V2) between groups (SC&BP&AE / SC&P) related to BSS scores was not significant ($p > 0.05$) (Table 2). However, the mean difference between V1 and V2 was slightly larger (greater improvement) in the SC&BP&AE group than in the SC&P group for the BSS total score (5.41±3.44 vs. 4.83±2.64), for cough symptoms (2.00±1.02 vs. 1.89±0.90), crackles on auscultation (0.73±1.12 vs. 0.33±0.59) and dyspnea (0.68±0.65 vs. 0.55±0.78). For the symptoms of sputum (1.21±1.05 vs. 1.44±0.78) and chest pain when coughing (0.59±0.73 vs. 0.61±0.69), the mean difference between V1 and V2 was found slightly higher (greater improvement) in the SC&P group than in the SC&BP&AE group (Table 2).

The symptoms of cough, sputum, and crackles in patients treated with SC&BP&AE improved earlier than those of patients treated with SC&P.

A significant decrease in the total score of the BSS was registered in both groups on day 3. No significant decrease in the score was registered in either of the two groups related to the finding of rhonchi (Table 3).

Table 3. Analysis of BSS symptom scores from day 1 to day 7 (as assessed by patients)

Parameters	BSS score in days - Mean± SD							
	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D1 - D7

BSS

SC& BP& AE	6.27±3.3 7	6.09±3.54	4.54±2.8 1	3.73±2.3 3	2.54±1.7 6	1.95±1.4 6	0.91±1.6 0	5.36±3.0 9
p	Ref.	0,227	0,002*	0,000*	0,000*	0,000*	0,000*	
SC&P	6.33±4.5 2	6.50±4.51	5.44±2.8 1	4.50±3.3 9	3.11±2.1 9	2.44±2.0 9	1.67±2.3 0	4.67±2.7 6
p	Ref.	0,739	0,007*	0,001*	0,001*	0,000*	0,000*	¹ p=0,642

Cough

SC& BP& AE	2.50±0.8 6	2.36±0.73	1.77±0.6 8	1.50±0.6 7	1.14±0.5 6	0.90±0.5 3	0.40±0.6 7	2.09±0.9 2
p	Ref.	0,180	0,000*	0,000*	0,000*	0,000*	0,000*	
SC&P	2.44±1.1 5	2.44±1.04	2.17±0.9 8	1.78±0.8 1	1.44±0.7 0	1.17±0.5 1	0.72±0.8 3	1.71±0.9 6
p	Ref.	1,000	0,059	0,001*	0,002*	0,001*	0,000*	¹ p=0,292

Sputum

SC& BP& AE	1.68±1.1 3	1.72±1.08	1.32±0.8 9	1.27±0.7 7	1.00±0.6 2	0.68±0.5 7	0.32±0.5 7	1.36±1.0 0
p	Ref.	0,705	0,033*	0,013*	0,002*	0,000*	0,000*	
SC&P	2.00±1.2 4	2.00±1.14	1.78±1.1 1	1.50±0.9 2	1.05±0.8 0	0.78±0.8 1	0.50±0.7 8	1.50±0.7 1
p	Ref.	1,000	0,102	0,007*	0,001*	0,000*	0,000*	¹ p=0,624

Crackles

SC& BP& AE	0.82±1.1 8	0.77±1.11	0.64±0.9 0	0.54±0.8 0	0.32±0.4 8	0.32±0.4 8	0.14±0.3 5	0.68±1.0 4
p	Ref.	0,317	0,046*	0,034*	0,015*	0,015*	0,011*	
SC&P	0.72±1.2 2	0.83±1.24	0.72±1.0 7	0.50±0.9 2	0.39±0.6 9	0.44±0.7 8	0.39±0.6 9	0.33±0.5 9
p	Ref.	0,317	1,000	0,046*	0,034*	0,025*	0,034*	¹ p=0,385

Chest pain when coughing

SC& BP& AE	0.54±0.7 4	0.54±0.67	0.36±0.4 9	0.14±0.3 5	0.04±0.2 1	0.00±0.0 0	0.00±0.0 0	0.54±0.7 4
p	Ref.	1,000	0,157	0,014*	0,005*	0,006*	0,006*	
SC&P	0.55±0.7 0	0.55±0.78	0.33±0.6 8	0.33±0.6 8	0.05±0.2 3	0.00±0.0 0	0.00±0.0 0	0.55±0.7 0
p	Ref.	1,000	0,102	0,046*	0,014*	0,008*	0,008*	¹ p=0,902

Dyspnea

SC& BP& AE	0.73±0.7 0	0.68±0.72	0.45±0.5 9	0.27±0.4 5	0.04±0.2 1	0.04±0.2 1	0.04±0.2 1	0.68±0.6 5
p	Ref.	0,705	0,083	0,008*	0,001*	0,001*	0,001*	
SC&P	0.61±0.8 5	0.67±0.91	0.44±0.6 1	0.39±0.6 1	0.17±0.3 8	0.05±0.2 3	0.05±0.2 3	0.55±0.7 8
p	Ref.	0,317	0,082	0,046*	0,024*	0,015*	0,015*	¹ p=0,409

Rhonchi

SC& BP& AE	0.27±0.7 7	0.27±0.77	0.23±0.6 1	0.18±0.5 0	0.09±0.2 9	0.04±0.2 1	0.04±0.2 1	0.23±0.6 1
p	Ref.	1,000	0,317	0,157	0,102	0,102	0,102	
SC&P	0.28±0.8 3	0.28±0.83	0.22±0.7 3	0.17±0.5 1	0.11±0.3 2	0.05±0.2 3	0.00±0.0 0	0.28±0.8 3
p	Ref.	1,000	0,316	0,155	0,180	0,157	0,180	¹ p=0,887

D=Day ; SC&BP&AE =Standard of care +Broncho Protect +Andographis Extract; SC&P=Standard of care +Placebo
 Values are expressed as mean ± SD
 Ref. is D1 which is taken as baseline for comparison with days D2-D7
 Wilcoxon Signed-ranks test¹ Mann Whitney U test *significant for p<0.05

Patient assessments showed that total BSS, as well as symptoms of cough, crackles, and dyspnea improved more in the SC&BP&AE group than in the SC&P group, and that symptoms of sputum, chest pain on coughing, and rhonchi improved more in the SC&P group than in the SC&BP&AE group. However, comparisons of mean difference scores from day 1 to day 7 yielded no significant differences between the two groups related to any of the BSS symptoms ($p > 0.05$) (Table 3).

Discussion

Medicinal plants have been used for centuries, including treatment of respiratory diseases, although their use for these purposes has not always been scientifically supported [18].

Hence, there is a need for reliable phytochemical and pharmacological studies, because their results open the way to the design and development of a truly rational phytotherapeutic practice that would be well established, effective and safe [19].

In our study, we investigated the efficacy of extracts from *Andrographia*, Chinese yarrow, curcumin, rosemary, black seed, and the medicinal mushroom *Reishi*, which have been described in many papers as having a positive effect on the respiratory system.

The results of patients' self-assessment of their health status indicated a statistically significant improvement in both groups, and no difference in the final outcome. But the improvement started a day earlier in the group that took herbal medicine. The results of the assessment of patients' health status by the doctors indicated that in the SC&BP&AE group all patients recovered, while 2 patients in the SC&P group did not get better. A study with 158 adult patients who had a common cold used a standardized dry extract of *A. paniculata* SHA-10 (1200 mg/day) for five days and found that the extract significantly reduced the intensity of symptoms of fatigue, insomnia, sore throat and nasal discharge, starting from the second day of treatment [20].

In a randomized, double-blind, controlled study, Tamlikitikul *et al.* administered *A. paniculata* at a dose of 6 g/day for seven days to 152 adult patients who had pharyngotonsillitis. Efficacy was comparable to acetaminophen in relieving symptoms of fever and sore throat [21].

In our study, there was no statistically significant difference in the reduction of chest pain during coughing in the two groups. Boscabadi *et al.* investigated the antiasthmatic effect of *N. sativa* extract in 29 patients with asthma in a double-blind study lasting 3 months. All asthma symptoms, weekly asthma symptom frequency, wheezing and PFT values were significantly better in the study group receiving *N. sativa* extract ($P < 0.05$ to $P < 0.001$) [22]. In our study, there was no statistical difference in auscultation of wheezing and rhonchi in both groups, but there was an overall improvement in auscultation findings in the group receiving herbal medicines. Hu *et al.* report that the use of *A. paniculata* reduces the duration of cough and sore throat and shortens recovery time compared to standard therapy (23). In our study, however,

there was no significant difference in recovery time between the two groups, but the group receiving SC&BP&AE experienced faster improvement in symptoms.

Conclusion

There are numerous effective medicinal herbs for treatment and prevention of respiratory infections. Many have been proven in clinical trials, although more evidence is still needed for the majority of medicinal herbs. Mechanisms of action include direct inhibition of various viruses and bacteria, improvement of the immune and inflammatory response to infection, and reduction of symptoms.

Herbs provide a much-needed alternative to ineffective antibiotics, whereby patients feel they are receiving beneficial therapy, reducing their tendency to use antibiotics. However, more trials are needed to help guide the adoption of recommendations that will put herbal medicines at the forefront to help reduce the significant burden that respiratory infections place on society

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