

Comparing the efficacy and safety of high-concentrate (5-7.5:1) ivy leaves extract and Acetylcysteine for treatment of children with acute bronchitis.

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As we know, the hyper secretion of mucus takes the first place in pathogenesis of respiratory airways diseases and leads to obstruction of upper airways and cough [1]. This is why the symptomatic therapy is the major objective during the treatment of infectious diseases of the respiratory tract. It includes prescription of mucolytic agents, expectorants and bronchodilators.

There are a lot of different mucolytic agents at the modern days, and Prospan[®], the herbal expectorant, is one of them. It contains high-concentrated dried ivy leaves extract (drug extract ratio 5-7.5:1) [2], as well as glycosidic saponins, which are the basis of expectorant, spasmolytic and antimicrobial action [3]. Besides that, the product reduces sputum viscosity and increases the mucociliary clearance [4]. The drug is produced in forms of syrup and effervescent tablets, which both have a palatable taste [2]. Prospan[®] can be applied to infant babies, since it has a very good safety profile. Due to the fact that it contains sorbitol as sweetener, the product can be prescribed for children with pancreatic [insular] diabetes, as it does not bring to glucose overload [5–7].

The aim of the study was to compare the efficacy and tolerance of the high-concentrated (5–7.5:1) ivy leaves extract (Prospan[®]) and Acetylcysteine in the treatment of children with acute bronchitis (obstructive and non-obstructive).

Research was conducted from March until September 2004, on the basis of the chair of hospital pediatrics # 2 of Pharmacology Production Society DDMA (in Dnepropetrovsk and Krivoy Rog), chair of hospital pediatrics # 1 of Donetsk Medical University and chair of children's diseases in Ivan-Franko Medical Academy.

Research materials and methods

Research has been done as multicenter, open and controlled study. The participating patients were children from 2 to 10 years old with acute bronchitis (obstructive and non-obstructive, see Fig. 1). Patients with hypersensitive reaction and those who were taking some other expectorants or antitussive drugs were excluded.

Before Prospan[®] or Acetylcysteine were prescribed, all patients were examined for confirmation of clinical diagnosis and concomitant diseases. Primary clinical symptoms such as cough, sputum, short breath and respiratory pain were documented, along with external respiratory parameters. Prospan[®] was prescribed in the following dosage: for children 2–6 year old 5ml 3 times a day, 7–10 year old 10ml 3 times a day (1-st group). Acetylcysteine: for children 2–6 year old 100–200 mg 3 times a day, 7–10 year old 300–400 mg 3 times a day (2-nd group). Treatment duration in both cases was 7–10 days.

Clinical symptoms were evaluated at day 7 and after full treatment (for those who were under clinical care for more than 7 days). External respiratory parameters were evaluated at day 5 and after full treatment.

The efficacy was rated as "very good" when all clinical parameters normalization course was fast, "good" – when course was positive, "moderate" – when several clinical parameters normalization course was positive and "poor" – in the case of negative course or deterioration of symptoms

The tolerance of both drugs was evaluated by means of the occurrence of side effects as well as of patient's compliance etc.

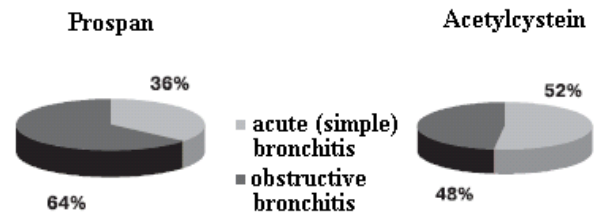


Fig. 1: Comparing the efficacy and safety of Prospan[®] and Acetylcysteine for treatment of children with acute (simple) bronchitis and obstructive bronchitis

Results of research and their discussion

Totally 50 children from 2–10 year old suffering from bronchitis were involved in the study. See Tab. 2 for age, sex and nosology spread-out.

Average duration of the disease (before treatment) was $4,72 \pm 0,6$ days in the 1-st group and $4,52 \pm 0,4$ days in the 2-nd. Along with the tested products 12 children (48%) of the 1-st group and 14 children (56%) of the 2-nd group were taking additional medication (antibiotics, antihistamines, etc.) because of concomitant diseases such as allergy, TT - diseases and also ENT – pathologies.

Tab. 1: Patients involved into research

Parameter	1-st group	2-nd group
Number of patients	25	25
Male	17 (68%)	15 (60%)
Female	8 (32%)	10 (40%)
Age (average)	$6,96 \pm 0,44$	$6,71 \pm 0,55$
Patients with acute bronchitis	16 (64%)	13 (52%)
Patients with obstructive bronchitis	9 (36%)	12 (48%)

As we can see in Tab. 2 and in Fig. 2–4, the main symptoms of disease normalized in both groups practically in the same time (a more rapid normalization in the Prospan® group is statistically not to discover). In that way, both tested products have mucolytic effects.

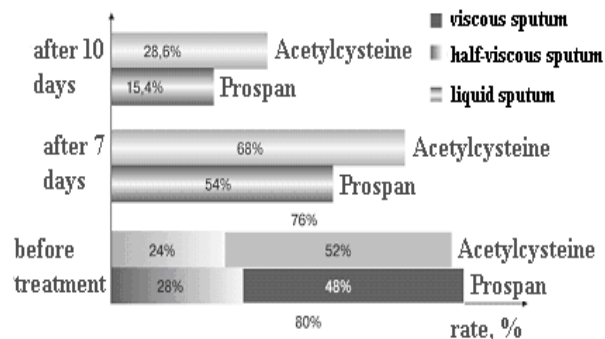


Fig. 3: Clinical symptoms normalization course - sputum expectoration

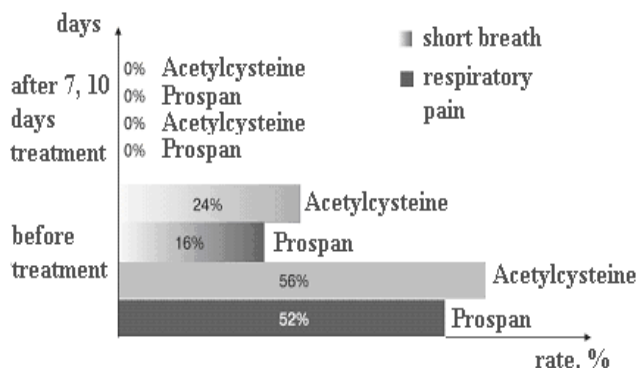


Fig. 4: Clinical symptoms course - short breath, respiratory pain

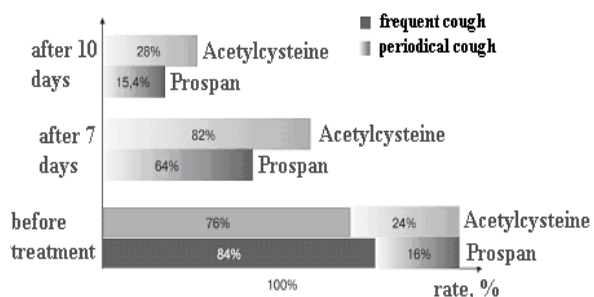


Fig. 2: Cough normalization course during the treatment

Tab. 2: Clinical parameters course, in both groups

Parameter	1-st group			2-nd group		
	Before treatment (%)	In 7 days (%)	In 10 days (%)	Before treatment (%)	In 7 days (%)	In 10 days (%)
Cough	100	64	15,4	100	81	28,6
Frequent	84	0	0	76	0	0
Periodic	16	64	15,4	24	81	28,6
Dry	20	10	0	24	12,5	0
Wet	80	54	15,4	86	68,5	28,6
Sputum						
Liquid	4	54	15,4	0	68,5	28,6
Half-viscous	28	0	0	24	0	0
Viscous	48	0	0	52	0	0
Short breath	52	0	0	56	0	0
Respiratory pain	16	0	0	24	0	0

Tab. 3: External respiration parameters during the treatment (in % from normal)

Parameter	1-st group			2-nd group		
	Before treatment	In 5 days	After treatment	Before treatment	In 5 days	After treatment
FVC	60.5±9.9	73.8±5.4	136.4±19.1*	56±4.3	71.7±7.5	89.4±7.5* **
FEV1	62±8.4	74.5±5.8	129.6±18.4*	63.7±6.9	71.3±7	88.6±8.5* **
PEF	74.5±11	116±25.3	131.4±14.3*	61.4±8	51.1±6.9**	80.8±8.8* **
MEF25	68.3±19	90.6±17.7	125.6±13.8*	60.2±8	49.4±5.3**	83.7±9.9* **
MEF50	64.4±14.1	92.3±10.3	137.1±12.4*	72.5±9.1	63.7±5.1**	106.1±15.3* **
MEF75	84.8±18	86.1±13.7	161.1±21.4*	85.4±10.8	82.5±7.5	125.4±21.1* **
AWSV 25-75	75±5.8	79.7±8.2	152±18.1*	77.6±8.1	69.2±7.2	103.8±15.5**

*- Parameter statistically different from baseline (p<0.05); **- Parameter statistically different from parameters in 1-st group (p<0.05).
 FVC - forced vital lungs volume; FEV₁ - forced exhalation volume within first second; PEF - maximum expiration weight hour space velocity of airflow; MEF₂₅ - maximum inhalation weight hour space velocity within 25% of lungs vital volume; MEF₅₀ - maximum inhalation weight hour space velocity within 50% of lungs vital volume; AWSV - average inhalation weight hour space velocity.

External respiration research was carried out with 19 children from the 1-st group and 18 children from the 2-nd group (all children more than 5 years old). The results indicated that after 5-day treatment the improvements of parameters concerning the function of upper and middle airways (weight hour space velocity (PEF), MEF₂₅ and MEF₅₀), for certain were greater in the 1-st group than in the 2-nd group.

After 5 days of treatment, positive normalization course (compared to baseline values) of external respiration parameters was found in the 1-st group (more reliable data could be reached by increasing the number of patients under research). In the 2-nd group such course was not found. Besides, after 5 days of treatment, research indicated reliable differences of external respiration velocity parameters (FEV₁, MEF₂₅, MEF₅₀) between the two groups (p<0,05). After treatment, parameters of external respiration in the 1-st group were statistically higher than in the 2-nd group. Results of the research showed that Prospan® exerts an obvious broncholytic action.

The efficacy ratings of Prospan® during the treatment of bronchitis are shown in Tab. 4. Efficacy was rated as "very good" and "good" by most (96%),

children with acute (simple) and obstructive bronchitis involved into the study (see Fig.5).

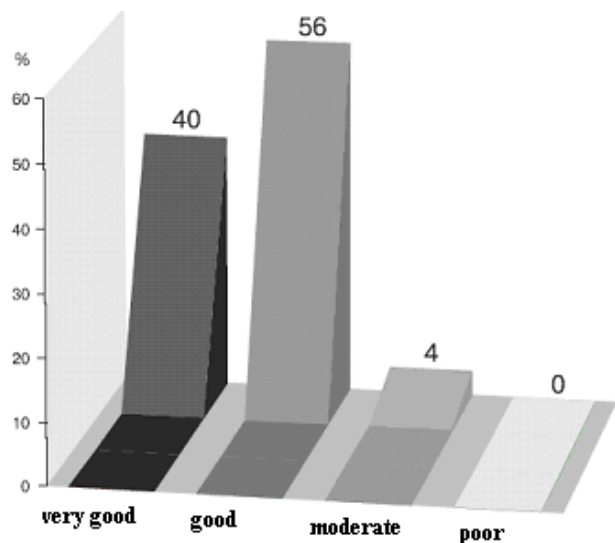


Fig. 5: Efficacy of Prospan® therapy in patients with acute bronchitis

Tab. 4: Efficacy of Prospan® therapy in patients with acute bronchitis

Efficacy	1-st group	2-nd group
Very good	40%	12,5%*
Good	56%	66,7%
Moderate	4%	20,8%

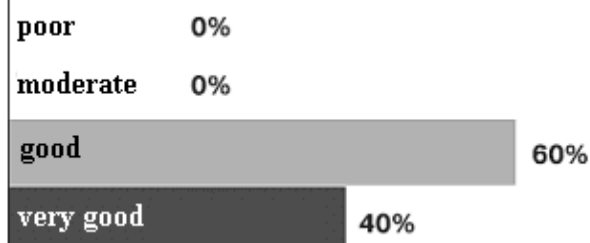
* - $p < 0.05$ – statistically significant

The tolerance of Prospan® was very high. Thus, 40% of doctors rated the tolerability as "very good" and 60% as "good". There was no rating as "moderate" or "poor" (see Tab. 5, Fig. 6).

Tab. 5: Tolerability of Prospan® in patients with acute bronchitis

Tolerability	1-st group	2-nd group
Very good	40%	12%
Good	60%	64%
Moderate	0	20%
Poor	0	4%

* - $p < 0.05$ – statistically significant

**Fig. 6: Tolerability of Prospan®****Summary**

1. The multicenter study indicated, that Prospan® exerts mucolytic action equal to Acetylcysteine but with better tolerability.
2. In 96% of cases the efficacy of Prospan® was rated at least as "good", 100% of the children who were treated with Prospan® tolerated the treatment well.
3. The results of this study confirmed that Prospan® exerts an obvious broncholytic action.
4. Prospan® can be recommended for the treatment of children with acute bronchitis, including the monotherapy of acute (simple) bronchitis and slight forms of obstructive bronchitis.

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