COMBINED TREATMENT OF BRONCHOOBSTRUCTIVE DISEASES

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The difficulties of therapeutic choice in patients with broncho-obstructive states are due to complex pathogenesis of disease as well as to prevalence of one or another pathogenetic mechanism during single stages of its evolution (atopia, infectious-allergic component, dysbalance of bronchial autonomic regulation, glucocorticosteroid deficit, etc.). Recently, no new in principle discoveries in the field of bronchial obstruction treatment have occurred, indeed. However, previous solutions are optimized to a considerable extent (1, 2, 5). Indications and schedules for application of bronchoselective $ß_2$-adrenergic agonists for inhalatory, peroral and parenteral use, anticholinergic medicaments, inhibitors of mediator release, corticosteroids for local application are already specified. Medicamentous forms of theophyllin derivatives are improved. Despite of undoubted successes achieved in mastering of reversible bronchial obstruction it presents a serious therapeutic problem in single cases and at different stages till now. Besides moddern bronchorelaxing means are not free of side effects. That is why renewal of our therapeutic possibilities has a definite practical importance (3, 4, 8, 9).

The purpose of the present communication is to evaluate comparatively the clinical effectiveness of some contemporary therapeutic schemes of bronchoobstructive diseases.

Material and Methods

During the period 1980–1986 a total of 195 bronchial obstruction patients (i.e. with infectious-allergic form of bronchial asthma and chronic obstructive bronchoobstructive disease) were followed-up in the Clinic of Pulmology and ambulatorily (in the allergological and polyclinical consulting rooms of Hospital, Varna). Varna). Patients with approximately equally expressed bronchial obstruction evaluated according to physical and spirographic examination were selected. Patients were divided into 7 groups as followed: 1st – 30 patients treated with prolonged xanthine preparations (Phyllocontin or Bulgarian preparation "Theotard") at dosage of 300 mg twice daily; 2nd – 30 patients treated with Novphyllin at dosages 200 mg thrice daily; 3rd – 30 patients treated with selective $ß_2$-agonists; Salbutamol or Partusisten (Fenoterol); 4th – 30 patients treated with cholinolytic preparation – Atrovent for inhalatory use at dosage of 0.2 mg thrice daily; 5th – 30 patients treated with inhalatory corticosteroid preparation – Beclomethasondipropionat (Beclomet) at dosage of 100 mg 4 times daily; 6th – 15 patients treated with calcium agonist – Isoptin in an acute experiment used in patients with contraindications to xanthine preparations and ß-agonists, and 7th – 30 patients treated with soidum chromoglycate (Intal) at dosage of 20 mg four times daily or with Ketodiphen (Zaditen) at dosage of 1 mg twice daily. Patients were followed-up for three months. At the beginning of treatment as well as at the end of every month a functional examination of respiration was carried out by using of "Pneumoscreen" apparatus and alveolo-diffusion test of the firm "Jaeger". Therapeutic effect was evaluated according to clinical and spirographic criteria. Presence of favourable effect was considered when paroxysmal bronchial obstruction disappeared or at least reduced, accompanying cough and physically manifested bronchial spasm decreased and spiro-

graphic parameters, especially FEV_1, increased by more than 15 per cent. Data obtained were processed by the methods of non-parametric and variation analyses.

Results and Discussion

The results from our study are shown on table 1.

Monotherapy with xanthine derivatives – a rapidly acting and prolonged theophyllin preparations influences favourably upon more than the half of the patients. However, patients with good therapeutic effect prevail. Significant side unfavourable phenomena during the therapeutic

Table 1

Clinical effectiveness of different therapeutic methods

Group No	Therapy applied	Patient No	Favourable effect	
			n	%
Ist	prolonged xanthine preparation	30	17	56.7
IInd	Novphyllin	30	20	66.7
IIIrd	selective ß$_2$-agonist	30	18	60.0
IVth	cholinolytic (Atrovent)	30	19	63.3
Vth	inhalatory corticosteroid preparation (Beclomet)	30	7	33.3
VIth	calcium antagonist (Isoptin)	15	12	80.0
VIIth	prophylactic means (Intal, Zaditen)	30	24	80.0

course are not observed. However, patients' majority (53.3 per cent) showed an exacerbation (bronchial spasm) during the 3-month long follow-up. The relative share of favourably influenced patients after Salbutamol therapy is approximately equal to that of patients after theophyllin preparation therapy when the group of selective ß$_2$-agonists is concerned. However, side unfavourable effects are noted in 24.3 per cent of the cases predominantly of the cardiovascular system. Partusisten (Fenoterol) eliminates bronchospasm still on the 30th min. This favourable effect as well as the increase of spirographic values retain for hours. Sinus tachycardia is observed and electrocardiographically registered in 14 of all the 15 patients causing therapy cessation in 5 of them. Headache is found in two patients but tremor accompanying tachycardia in three ones. The relative share of favourably influenced patients after Atrovent therapy is high (63.3 per cent) although spirographic indexes do not undergo such a favourable dynamics, too, when compared with those of patients from the other groups. Immediately after Atrovent inhalation, tachycardia is registered with 5 patients. It disappeared spontaneously one hour after the procedure.

In patients of the 6th group Isoptin therapy results in favourable influence and spirographic value increase 30 min after application of the drug. Rhythmic disorders preceding therapy are removed. Headache is established only in two patients with accompanying ischemic heart disease. The lowest relative share of favourably influenced patients is in the group of inhalatory corticosteroid treatment. Probably, it is determined by the circumstance that the majority of these patients are corticosteroid-dependent and with considerably manifested durable bronchial obstruction. Corticosteroid dependence is eliminated in 7 of the patients of this group. Patients treated with Intal or Zaditen are also favourably influenced. Most frequently, Intal induces a very good therapeutic effect while Zaditen results in a good one. Ten patients of this group be-

come spastic during the 3-month follow-up. This circumstance can be due to the fact that despite of phosphodiesterase inhibitory effect of these preparations they do not possess a strong direct bronchorelaxation effect similarly to classic phosphodiesterase inhibitors such as theophyllin preparations (6, 7). Clinical effectiveness of their "prophylactic" usage increases by combination with specific hyposensibilization started in remittent periods when bronchial obstruction is neutralized.

The dynamic follow-up reveals differences in clinical effectiveness and spirographic parameters. While theophyllin preparations and ß-agonists influence on diffuse bronchial obstruction (of smaller respiratory tracts, inclusive) objectified by means of capacity measurements with smoller pulmonary volumes cholinolytic medicaments, calcium antagonists and corticosteroids for local use influence predominantly on large respiratory tract obstruction (pulmonary resistance).

We can conclude that as result from our investigations of many years it can be accepted that modern combined treatment of bronchoobstructive diseases should comprise as "basic therapy" some bronchodilatators – theophyllin preparation (recommended is that one with least side effects), ß-mimetics or cholinolytics. When there are cardiovascular contraindications a calcium antagonist is preferred but when corticosteroid dependent and hardly influenced patients are concerned a corticosteroid preparation for local application should be administered. In the remittent period, combination of bronchodilatators and specific hyposensibilization together with prophylactic medicaments – Intal or Zaditen – results in maximally good therapeutic effect.

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КОМБИНИРОВАННОЕ ЛЕЧЕНИЕ БРОНХООБСТРУКТИВНЫХ ЗАБОЛЕВАНИЙ

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РЕЗЮМЕ

Проведено сравнительное исследование клинической эффективности некоторых современных схем лечения бронхообструктивных заболеваний. Больные были распределены на семь групп. В каждой группе проводилось лечение с применением одного из препаратов: новфилин, филоконтин (теогард), сальбутамол (партосистен), атровент, беклomед, изоптин, интал (задитен). У всех больных прослеживались показатели внешнего дыхания и физикального синдрома до и после лечения соответствующими препаратами. В результате исследований, проводимых в течение долгих лет, авторы делают заключение, что современное комбинированное лечение бронхообструктивных заболеваний должно включать в качестве „базисной терапии" препарат теофилина, бетамиметик или холинолитик, а при кортизонзависимых больных – беклomед. Наилучший эффект дает сочетание бронходилататорного лечения со специфической гипосенсибилизацией, которое применяется одновременно с медикаментами, имеющими профилактическое действие – инталом или задитеном.