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A comparative effectiveness of different antibiotics in management of mild community-acquired pneumonia

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Current guidelines for the management of community-acquired pneumonia recommend using different antimicrobial drugs. The purpose of this open randomized parallel group study was to assess efficacy and cost-efficiency of three most commonly used oral antibiotics in patients with mild community-acquired pneumonia. 45 out-patients were randomly distributed into 3 groups to receive oral treatment with either amoxicillin 500 mg thrice daily, or azithromycin 500 mg once daily or levofloxacin 500 mg once daily. In terms of treatment outcomes the efficacy of study drugs was 93,3% (amoxicillin group), 86,7% (azithromycin group) and 100% (levofloxacin group) (p>0,05). The results of pharmacoeconomic analysis revealed a lower cost of treatment with amoxicillin and azithromycin versus levofloxacin.

Keyword: Community-acquired pneumonia, treatment, antibiotics.

1. Introduction

It is widely recognized that antibiotic therapy of patients with community-acquired pneumonia (CAP) is still a challenging problem regardless of abundant scientific information and different international guidelines published worldwide [1]. As generally accepted a strict following of national protocols in administering an empiric antibiotic treatment is a key factor of success in management of these patients [2]. At the same time, certain clinical situations require an individual approach to the therapy and flexibility in choice of medications, especially alternative ones. Moreover, as new data of epidemiology of lower respiratory tract infections become available, novel diagnostic methods and pharmaceutical products are introduced, actual clinical guidelines must be updated every 3–5 years [3]. The recommendations should also consider regional antibiotic resistance data and the results randomized controlled clinical studies of different antimicrobials in CAP patients [4, 5].

2. Materials and methods

An open randomized comparative study of effectiveness of 3 different antibiotics in patients with mild CAP was conducted. 45 patients with mild CAP were enrolled. According to actual clinical guidelines, approved in Ukraine, study population was defined as a cohort of CAP patients, not requiring hospitalization with mild severity of disease, no comorbid conditions, and no previous (within 3 months) use of antibiotics. The diagnosis was made in accordance with Ministry of Health of Ukraine Decree # 128, dated 19.03.2007 after a detailed clinical, radiological and laboratory examination.

Antibiotic therapy was started in all patients immediately after the diagnosis was confirmed. Since the lack of reliable express tests for

identification of causative pathogen, the antibiotics were always administered empirically. The choice of antibiotic was based on natural activity of the agent against major respiratory pathogens and known resistance pattern. The safety and possible drug interaction reasons were also evaluated.
Depending on antibiotics used all patients were randomized in 1:1:1 ratio in 3 groups. An individual number was assigned to each subject. Patients with numbers 1, 4, 7 were allocated into group 1, whereas numbers 2, 5, 8 and 3, 6, 9 — in groups 2 and 3, respectively.

The participants of the study received the following therapy:

- group 1 — oral amoxicillin 500 mg 3 times daily for 7–10 days;
- group 2 — oral azithromycin 500 mg once daily for 3 days;
- group 3 — oral levofloxacin 500 mg ones daily for 7–10 days.

The clinical efficacy was assessed using body temperature, dyspnea, cough, sputum production, crackles in lungs, white blood cells (WBC) count and erythrocyte sedimentation rate (ESR).
Chest radiograms (anterior-posterior and lateral view) were performed twice: before treatment and on day 14.
A pharmacoeconomic analysis was performed in all CAP patients, enrolled into study, regardless of whether antibiotic therapy per protocol was completed or interrupted due to treatment failure. A method of "minimization of cost" was used, which was based on a comparison of a cost of treatment between subgroups.

3. Results and Discussion.

The clinical and laboratory characteristics of study patients are given in Tab 1.

Table 1: Clinical characteristics of patients with mild CAP before treatment

Characteristic	Group		
	1 (n = 15)	2 (n = 15)	3 (n = 15)
Age, years	35,9 ± 5,1	33,7 ± 5,9	37,2 ± 5,6
Body temperature:			
<37 °C, % of patients	13,4 ± 8,8	20,0 ± 10,3	6,7 ± 6,5
>37 °C ≤ 38 °C, % patients	53,3 ± 12,8	60,0 ± 12,6	66,7 ± 12,2
> 38 °C ≤ 39 °C, % patients	33,3 ± 12,2	20,0 ± 10,3	26,6 ± 11,4
Dyspnea, % of patients	46,7 ± 12,9	40,2 ± 12,7	46,7 ± 12,9
Cough, % of patients	100	100	100
Sputum discharge, % of patients	86,7 ± 8,8	80,0 ± 10,3	80,0 ± 10,3
Crackles, % of patients	93,3 ± 6,5	93,3 ± 6,5	86,7 ± 8,8
WBC count, 10^9 /l	11,3 ± 0,7	11,9 ± 2,2	10,4 ± 0,8
ESR, mm/h	19,5 ± 2,7	16,4 ± 1,9	15,2 ± 2,6

Data of table 1 demonstrate a complete similarity of three groups of comparison by the age of the patients, clinical and radiological signs and laboratory test results.
An equal (p>0,05) improvement of all clinical manifestations of the disease were observed on the third day of treatment in all groups (Tab. 2). At the same time a fever was still present in 1 (6,7%) patient of group 1and 2 (13,3 %) patients of group 2. This was also accompanied by a certain increase of cough, sputum production, leukocytosis and acceleration of ESR.
Minor worsening on chest radiograms made us to classify these cases as clinical failures. The study antibiotic in these occasions was considered ineffective and switched on alternative one (levofloxacin 500 mg once daily for 5 days).

Table 2: Clinical characteristics of patients with mild CAP 72 hours after the start of therapy

Characteristic	Group		
	1 (n = 15)	2 (n = 15)	3 (n = 15)
Body temperature:			
< 37 °C, % of patients	80,0 ± 10,3	66,7 ± 12,2	80,0 ± 10,3
>37 °C ≤ 38 °C, % patients	20,0 ± 10,3	33,3 ± 12,2	20,0 ± 10,3
> 38 °C ≤ 39 °C, % patients	0	0	0
Dyspnea, % of patients	6,7 ± 6,5	13,4 ± 8,8	6,7 ± 6,5
Cough, % of patients	66,7 ± 12,2	80,0 ± 10,3	73,3 ± 11,4
Sputum discharge, % of patients	46,7 ± 12,9	53,3 ± 12,9	40,2 ± 12,7
Crackles, % of patients	40,2 ± 12,7	53,3 ± 12,9	40,2 ± 12,7

Note: no statistically significant differences between groups were revealed (p>0,05).

We observed a significant improvement of clinical symptoms at the end of therapy. A dyspnea disappeared completely, while the cough, sputum discharge, lung crackles decreased but not fully resolved in all subjects (Table 3).

An improvement of clinical condition of the patients was also accompanied by an improvement of blood indices. We registered a statistically significant (p>0,05) decline of WBC count after treatment in patients of group 1to (5,1 ± 0,5) × 10^9/l, group 2— to (5,2 ± 0,6) × 10^9/l, group 3 — to (4,9 ± 0,2) × 10^9/l (Table 3).

The same trend was observed for the ESR as well. After treatment ESR value decreased in all patients: group 1 — to (5,2 ± 0,4) mm/h, group 2 — to (6,3 ± 0,5) mm/h and group 3 — to (5,7 ± 0,7) mm/h (Table 3).

Radiological examination at the end of therapy (day 14) demonstrated a complete resolution of infiltrative lesions in lung in (86,7 ± 8,8)% of patients in group1, (80,0 ± 10,3)% of patients in group 2 and (93,3 ± 6,5)% of patients in group 3 (p>0,05).

Table 3: Clinical characteristics of patients with mild CAP at the end of therapy

Characteristic	Group		
	1 (n = 15)	2 (n = 15)	3 (n = 15)
Body temperature:			
< 37 °C, % of patients	100	93,3 ± 6,5	100
>37 °C ≤ 38 °C, % patients	0	6,7 ± 6,5	0
> 38 °C ≤ 39 °C, % patients	0	0	0
Dyspnea, % of patients	0	0	0
Cough, % of patients	6,7 ± 6,5	13,4 ± 8,8	6,7 ± 6,5
Sputum discharge, % of patients	6,7 ± 6,5	13,4 ± 8,8	0
Crackles, % of patients	0	0	0
WBC count, 109 /l	5,1 ± 0,5	5,2 ± 0,6	4,9 ± 0,2
ESR, mm/h	5,2 ± 0,4	6,3 ± 0,5	5,7 ± 0,7

Note: no statistically significant differences between subgroups were revealed (p>0,05).

There were no differences between groups of comparison in terms of the safety and tolerability of antibiotic therapy. Adverse events were registered in (13,4 ± 6,4)% of patients in group1, (20,0 ± 6,1)% of patients in group 2 and (13,4 ± 6,4)% of patients in group 3 (p>0,05). All these events were mild and didn't require interruption of therapy or modification of study drug dose. A transient increase of ALT was the most often adverse reaction.

The analysis of the clinical, radiological and laboratory data confirmed that antibiotic

monotherapy was equally successful in all three groups of patients. The effectiveness of treatment in group 1 was (93,3 ± 6,5)% (cure — (86,7 ± 8,8)%, improvement — (6,7 ± 6,5)%), group 2 — (86,7 ± 8,8)% (cure —(80,0 ± 10,3)%, improvement — (6,7 ± 6,5)%) and group 3 — 100 % (cure — y (93,3 ± 6,5)%, improvement — y (6,7 ± 6,5)%) (p>0,05).

A pharmacoeconomic analysis demonstrated that the cost of laboratory and other diagnostic tests dominated in the structure of total cost of treatment. The share of this cost in group 1 was 62,5%, whereas the cost of medicines was 33,9% (the cost of antibiotic itself — 16%). Furthermore, the cost of antibiotic made 66,3% the cost of antibacterial therapy, which, in its turn, made 71,1% of total cost of medicinal treatment.

A different distribution of costs we observed in groups 2 and 3 (Table 4). The highest was the cost of antibiotic therapy (47% and 62,9%, respectively). The cost of medicinal therapy in groups 2 and 3 was 55,6% and 68,5%; cost of antibiotic therapy — 35,2% and 62,9%, respectively.

Table 4: Cost of treatment per one patient with mild CAP, UAH

Type of cost	Subgroup		
	1 (n = 15)	2 (n = 15)	3 (n = 15)
Cost of antibiotic	46,7 ± 2,7	142,5 ± 0,2*	356,0 ± 0,4*#+
Cost of antibiotic therapy	70,4 ± 3,2	190,0 ± 2,5*	356,0 ± 0,4*#+
Cost of other medicinal treatment	28,6 ± 5,3	34,8 ± 3,6	31,6 ± 2,9
Cost of laboratory and other diagnostic tests	182,4 ± 6,9	166, 1 ± 5,8	172,5 ± 6,2
Cost of consultation	10,4 ± 3,5	13,5 ± 4,2	15,8 ± 4,9
Total cost of treatment	291,8 ± 10,6	404,4± 9,7*	565,9 ± 8,8*#+

Notes: * — significant difference between groups 1 and 2 (p<0,05); # — significant difference between groups 1 and 3 (p<0,05); + — significant difference between groups 2 and 3 (p<0,05).

It was evident that the cost of antibiotic, antibacterial therapy and total cost of treatment in group 1 was lower than in groups 2 and 3. The same was true for group 2 versus group 3. No statistically significant differences in other costs were identified.

4. Conclusion

The results of the study have clearly proved that in patients with mild CAP, without concomitant conditions and previous (within 3 months) use of antibiotics, oral monotherapy with amoxicillin or azithromycin, or levofloxacin was equally (p>0,05) effective and safe. The results of pharmacoeconomic analysis gave reasons to conclude that in current population of patients oral amoxicillin or azithromycin could be considered first-line therapy, whereas levofloxacin was an alternative choice.

5. References

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