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## Elderly patient with community-acquired pneumonia. Does the problem exist?

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### Abstract

Elderly patients are a special category of patients in whom poly-morbid pathology is often observed. Combination of cardio-vascular diseases and community-acquired pneumonia (CAP) is the most prevalent condition, occurring in patients aged over 60 years. Such comorbidity is associated with difficulties not only at the stage of diagnosing, but also in administering therapy, taking into account the necessity of simultaneous administering both of anti-bacterial therapy and that of cardio-vascular pathology diseases, physiologic changes of an elderly organism and complicated inter-drug interactions.

**Keywords:** pneumonia, elderly patient, cardio-vascular pathology, comorbidity, drug interaction, anti-bacterial therapy.

### 1. Introduction

Progressing aging of the population is one of the most topical problems of the present time. Today there are about 650 million of elderly persons in the world [7]. In this category of patients pneumonias acquire specific significance. The annual incidence of pneumonia increases together with the age: from 1-11, 6 of cases per thousands of young and middle aged people to 20-44 persons per 1000 in elderly [23, 36]. Community-acquired pneumonia (CAP) is one of the most frequent reasons, which requires hospitalization to therapeutic unit. Lethality in CAP in persons without concomitant diseases ranges about 1-3%, while in elderly patients groups with background comorbidities it achieves 30%. In the same time mortality of CAP in elderly patients occupy the 1-st place in the structure of mortality from infectious diseases and being on the 4-th in elderly persons, leaving IHD, strokes and malignant neoplasms behind it [6, 15].

It is well-known, that elderly patients usually suffer from poly-morbid pathology. In 80-90% of elderly patients the most often revealed cardio-vascular diseases (CVD) are: arterial hypertension, ischemic heart disease, multi-focal atherosclerosis as well as diabetes mellitus, which require permanent therapy.

In the present work peculiarities of etiology, pathogenesis, clinical manifestations and treatment of CAP in elderly patients are discussed.

### 2. Etiology

In a whole, bacterial pathogens that cause CAP in elderly aged groups does not differ from that of in patients of young and middle age. Up to today *S. pneumoniae* (30-50% of cases) remains the single most common organism identified in hospitalized elderly patients with CAP [5, 6]. CAP caused by Gram-negative bacteria are often related to comorbid illnesses, thus elderly patients are more likely to succumb to these organisms (*H. Influenzae* (to 20%), *E. coli*, *Potusspp Kl. Pneumonia*) [6, 15]. In elderly patients, hospitalized because of CAP, may be revealed combined, so called co-infection, nonetheless such bacterial pathogens as *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* (up to 5%) are revealed much rare than in young patients [27]. A higher risk of aspiration in elderly and senile age patients and pulmonary circulation congestion, results to increasing of the role of oropharyngeal flora in this category of patients.

### 3. Pathogenesis

There are a number of peculiarities about pneumonia development in elderly patients, linked first of all with age-related anatomic and functional changes of pulmonary tissue and cardio-vascular system, known as a conception of a "senile lung". Main pathogenetic factors contributing to development of inflammatory process in the lung are [5, 6, 8, 25, 40]:

- decrease of the number of elastic fibers in the pulmonary tissues;
- decrease of anti-oxidant defense and enforcement of peroxide oxidation;
- reduction of alveolar-capillary surface, which causes decrease of diffusion ability of the lungs with development of arterial hypoxemia;
- decrease of surfactant activity, phagocytic activity of alveolar macrophages and neutrophils;
- decrease of mucociliary clearance.

At the same time age-related depression of cough reflex, caused by reduction in sensitivity of bronchial mucous membrane, leads to disturbance of trachea-bronchial tree clearing and aggravates disturbance of pulmonary ventilation. Mentioned factors contribute to increase of microbe colonization of mucous membrane of the respiratory tract and development of broncho-pulmonary infection development. Suppression of immune response at the respiratory tract, caused by disorder of drainage function of the lungs and activation of microbe microflora in the presence of background pathology leads to slow resolution of inflammatory process. Decrease of cardiac output in elderly people leads to a chronic decrease of arterial blood oxygenation. Age-related changes of arterial vessels (sclerotic induration of intima, decrease of aorta and pulmonary artery elasticity) cause the deflection in dilatation and contraction which lead to decrease of adaptation abilities both in systemic and pulmonary circulation<sup>[10]</sup>.

Mentioned changes lead to depression of respiratory center response and peripheral chemoreceptors to hypoxia and hypercapnia, thus changing the exercise tolerance. It is important to remember, that pneumonia also develops, when virulence of pathogen exceeds the ability of immune response. Such situation may occur against the background of insufficient immune response caused by concomitant diseases, such as diabetes mellitus, congestive heart failure.

#### 4. Peculiarities of CAP's clinical presentation in elderly people

Late diagnostics of pneumonias is one of the causes of a high lethality. Namely, in the group of patients over 60 years old the frequency of CAP misdiagnosis at pre-hospitalization stage is two times higher than in other age-related groups. So, hypodiagnostics of pulmonary diseases occupies one of the leading places among other pathologies and makes up 11,76%. The main role of misdiagnosis (up to 86%) possess subjective factors, such as imperfect examination of a patient, incorrect rendering of clinical findings<sup>[4, 5, 34]</sup>. While observing such patients one should always remember that on one side such a patient most commonly has clinical features of pneumonia, and on the other side – suffers at the same time from two diseases as minimum (comorbidity!). That is why there are several important directions in front of internist, dealing with an elderly patient with a suspected CAP. First of all, it is a confirmation of diagnosis and an adequate evaluation of pneumonia severity for defining indications to treatment in conditions of resuscitation and intensive therapy unit and for administering adequate therapy. Contrariwise, it is necessary to reveal concomitant CVD, as such diseases in the decompensation stage may be mistakenly taken for pathology of broncho-pulmonary system or aggravate pneumonia course.

CAP diagnosis is considered to be established in roentgenologically confirmed infiltration of pulmonary tissue

and presence of at least 2 clinical signs: acute disease onset with body temperature higher than 38 °C, physical signs (deadened or dull percussion sound, diminished or rough bronchial breath sounds, focus of ringing fine moist rales and/or crepitation), leukocytosis of more than 10 x10<sup>9</sup>/l and/or stab neutrophils shift of more than 10%.

One of the important peculiarities of CAP's clinical symptoms in elderly patients is the absence of acute onset or slightly marked temperature reaction. Only in 75-80% of elderly and senile age patients with pneumonia fever is observed<sup>[20, 31, 36]</sup>. The disease course, compared with younger patients, is often characterized by normal or even decreased temperature, which is prognostically less favourable. Leukocytosis which is characteristic for pneumonia may be absent in one third of patients, being also unfavorable prognosis sign, especially in presence of neutrophil shift. Such classical signs as dullness of percussion sound and crepitation may be not defined due to dehydration of tissues caused by diuretics taking; fine moist rales may be the consequence of pulmonary edema developing, dry rales – of pneumo-sclerosis manifestation.

Diagnostic value of such a symptom as cough in elderly patients may be underestimated due to depression of cough reflex in patients with the anamnesis of stroke. Breathlessness in elderly patients with CAP may be linked with the presence of obesity, decompensation of heart failure and anemia. Exacerbation and decompensation of concomitant diseases (aggravation or appearance of heart failure signs, heart rhythm disorders, decompensation of diabetes mellitus, signs of respiratory insufficiency, various neurologic symptomatic) may come to the fore in elderly patients with CAP.

False rendering of clinical data may be the cause of hyper- or hypodiagnostics of pneumonia of elderly patients and thus inadequate management strategy. Data presented above reflect complexity of CAP diagnostics in elderly patients with concomitant cardiac pathology.

Chest X-ray examination in frontal anterior and lateral projections is the optimal method of diagnostics, which makes it possible to confirm or rule out pneumonia or its complications as well as to assess dynamics of the chosen treatment. X-ray picture of CAP does not have interrelation with pneumonia etiology, severity of disease course and doesn't give the opportunity to give diseases prognosis<sup>[26]</sup>.

To evaluate degree of pneumonia severity, risk of lethal outcome and adequate choice of management strategy of patients with CAP, score scale PORT, CURB- 65, SMRT-CO are used. Application of prognostic scales gives a great help for the physician in choosing adequate management strategy for patients with CAP. One of the most accessible score scale for practical work is simplified scale CRB – 65, without considering the urea level findings, which gives the possibility for general practitioners already at pre-hospitalization stage to define clinical group of pneumonia and decide where to treat patient<sup>[26, 28, 29, 30]</sup>.

According to clinical observations data, pulse-oximetry is accessible and simple screening method in patients with CAP. Decrease in arterial oxygen saturation (SaO<sub>2</sub> <90%) is an important criterion, making it possible to specify indications for patient's hospitalization, despite absence of obvious signs of CAP and hypoxemia<sup>[31, 38]</sup>.

#### 5. Treatment

Antibacterial therapy is an initial and defining step in CAP treatment. Principles of antibacterial therapy management are stated in appropriate international and national clinical

protocols [12, 24, 35, 37, 41, 43, 44]. In the presented work discussing not even the details of the proper and adequate choice of medicine, but peculiarities of anti-bacterial therapy, when it is necessary to prolong taking cardiologic medicines.

Principles of antibiotics administration:

- wide spectrum of drug action, considering poly-etiological character of pneumonia in persons over 60;
- timely initiation of antibacterial therapy (first 4 hours after established diagnosis);
- proved clinical effectiveness;
- adequacy of dosing, route of taking and term of usage;
- awareness about presence of resistance to antibiotics in the hospital unit;
- considering pneumonia degree severity;
- considering functional state of liver and kidneys;
- considering possible side effects of medications and avoiding administering those ones which may cause side effects and course of the background and concomitant diseases;
- decreasing risk of antagonist interaction of anti-bacterial agents, unwanted interactions with other medicinal agents, risk of allergic reactions development by means of administering single-drug therapy;
- administration of medications with various routes of introduction using regimen of «step-by-step» therapy [14, 16, 19, 21, 22].

One of the causes of inadequate clinical and bacteriological efficacy of antibiotics in elderly persons is changes of pharmacokinetics of medicinal agents, which lead to the change of pharmacodynamic effects [1, 13, 5]. Age-related decrease of the number of functioning hepatocytes, hepatic blood flow and correspondingly activity of microsomal ferments, first of all of cytochrome P-450, leads to retardation of inactivation and elimination of medicinal agents in the liver and growth of antibiotics concentration, metabolized by the liver [24]. A lot of medical remedies, used in cardiologic practice, subjected to oxidations which undergo biotransformation with the involvement of this enzyme system. Specifically, klopidogrel, calcium channels blockers, amiodaron, varfarin, sildenafil, statins, as well as some antibiotics of wide spectrum of action are metabolized with the involvement of the same isoenzymes of cytochrome P450 (CYP2C9, CYP2C19, CYP3A4) [3].

In such a way, simultaneous taking of verapamil, erythromycin and statins can lead to increase their concentration in the blood up to 3 times [2, 3, 11]. It is important to remember, that if a medication has a low bioavailability when taken orally, then simultaneous administration of medications being its inductors or inhibitors may substantially change its bioavailability. For example, inhibitors of isoenzyme CYP3A4, may sharply increase bioavailability of medicinal agent, period of its half-life, thereby to increase its concentration in the blood and enhance effect, what may be considered as an acute overdose. Statins (simvastatin, atorvastatin) which are characterized by low indices of bioavailability on the background of simultaneous taking inhibitors CYP3A4 (clarithromycin, erythromycin), may lead to the increase of their concentration in the blood, causing diffuse myalgia, growth of creatine phosphokinase level and acute renal insufficiency [2, 17]. Due to this, it is necessary either diminish statin dose or use medications which may be an alternative one in patients receiving inhibitors CYP3A4, e.g. rosuvastatin metabolized by CYP2C9. It is proved by population cohort investigation of Canadian scientists who

have studied incidence of development of statins toxic effects in patients over 65 years of age taking these medicines for a prolonged period of time after combined usage with clarithromycin (n=72591) or erythromycin (n=3267) as compared with azithromycin (n=68478) [17, 39]. According to the published data, combined administration of statins with clarithromycin or erythromycin led to increase of risk of hospitalization in connection of rhabdomyolysis, comparing with azithromycin taking only. Increase of absolute risk made up 0,02% and relative risk made up 2,17. Risk of development of acute renal lesion and overall mortality to all causes increases as well – increase of absolute risk being 1, 26% and 0,25% respectively. On the other side, risk of similar interaction is much less in medications with a high bioavailability, as even in usual conditions their concentration in the blood is close to maximal. Only intravenous administration of medicinal agent provides 100% bioavailability.

Decrease of glomerular filtration rate (GFR) in persons over 60 years has also a great importance. As consequence, excretion of many medicinal agents is slowed down in elderly patients, which leads to the growth of their concentration in the blood [32]. Thus, administration of antibacterial agents with kidney elimination pathway require a careful dose correction in elderly patients with renal dysfunction, according to GFR. For example, such «respiratory» fluoroquinolone as levofloxacin should be administered with caution to the patients with creatinine clearance < 50 ml/min, as its half-life period increases by 4–5 times on the background of such renal dysfunction. Protected amoxicillin requires dose correction in creatinine clearance < 30 ml/min. At the same time, another fluoroquinolone – moxifloxacin is excreted predominantly through the digestive tract and its dose regimen in patients with renal insufficiency does not change. Administration of such medications as azithromycin and ceftriaxone does not depend on creatinine clearance too [42]. Sometimes, in case of marked edemas (in case of cardio-vascular decompensation), a standard therapeutic or a little bit raised initial dose may be required, which will make it possible to overcome excessive re-distribution of medication in organism's tissues and achieve bactericide or bacteriostatic concentration in the blood and tissues.

It is also necessary to bear in mind that CAP treatment in elderly persons with concomitant cardiac pathology is linked with additional difficulties. The main reason of it is the necessity of persons over 60 of receiving basic therapy of concomitant diseases. The largest number of inter-drug interactions is observed during simultaneous taking of antibiotics and cardio-vascular medications. Taking of antibacterial medications together with anti-coagulants, thrombolytics, inhibitors of thrombocytes aggregation may lead to increase of bleeding risk. Macrolides may increase plasma concentration of statins (increase of rhabdomyolysis) and digoxin (glycoside intoxication). Mutual taking of fluoroquinolones (levofloxacin, moxifloxacin) and anti-arrhythmic medications may cause lengthening of QT interval – the risk of development of such ventricular arrhythmia as “torsade de pointes”.

However, despite the fact that poly therapy may lead to increase of side effects incidence, it is often impossible to discontinue of anti-aggregant, anti-arrhythmic, anti-hypertensive and some other drugs taking, as it is entailed with great risk of complications development and lethal outcomes because of concomitant disease. Administration of only necessary medications possessing the highest efficacy and the

least number of side effects is, therefore, the main criterion of drug therapy. Polyprogmsy should be assessed as a specific feature of elderly person's treatment, which requires a more thorough and accurate physician's control (ECG, INR, ALT, AST, creatinine, electrolytes, GFR calculation).

One of the most important ways of CAP prevention in elderly persons with concomitant cardiac pathology is vaccination with pneumococci and influenza vaccines. Despite the fact that such means of prevention in elderly people is considered to be moderately effective, this makes it possible to decrease incidence of upper respiratory tract infections, pneumonia, decompensation of CVD<sup>[33]</sup>.

## 6. Conclusion

Elderly patients practically always suffer from polymorbid pathology. CAP most often develops on the background of cardio-vascular diseases, which require continuous therapy of this comorbidity. Mutual influence of diseases, involutive processes of natural aging, action of drug therapy change clinical picture and course of the disease, character and severity of complications, limit or complicate treatment-diagnostic search. Application of pneumonia severity scales CRB-65 and routine determination of SaO<sub>2</sub> can make it possible to define clinical group of pneumonia patients and administer adequate therapy. In order to make treatment of elderly and seniors as much safe as possible, one should always remember about possible ways of medicine's side effects prevention. For example, when it is necessary to administer antibiotics with liver elimination pathway and involvement of isoenzyme cytochromeP450 (CYP3A4) to the patients receiving statins, one should temporally stop taking statins during of antibacterial therapy, to control unwanted medications interactions phenomena or use alternative antibacterial medications which do not interact with statins (azithromycin, fluoroquinolones, cephalosporins, penicillins). It is obligatory to evaluate a renal function (calculation of GFR) in elderly patients for defining optimal individual dose of antibiotics or taking medications with another elimination pathway in case of significant renal insufficiency. In the majority of elderly patients with CAP on the background of cardio-vascular diseases, treatment of CVD does not stop and inter-drug interactions must be taken into account. Polytherapy is, nevertheless, one of the most optimal treatment strategies of elderly patients.

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