IJCMCR Open Access

ISSN 2692-5877
DOI: 10.46998/IJCMCR.2020.04.000097

International Journal of
Clinical Studies & Medical Case Reports

Opinion

Why can't be Special Medications for Pneumonia?

Igor K*

Dana Children's Hospital, Sourasky Medical Center, Aviv Sourasky Medical Center, Russia

***Corresponding author:** Igor Klepikov, Dana Children's Hospital, Sourasky Medical Center, Aviv Sourasky Medical Center, Russia. Tel: +972-3-697-3426; E-mail: igor.klepikov@yahoo.com

Received: August 13, 2020 Published: September 18, 2020

Introduction to the Problem

Each disease known to modern medicine has its own causes (etiology) and mechanisms of development (pathogenesis). Acute Pneumonia (AP) is no exception to this rule. The causes of this disease are known, and among them the most common are bacteria, viruses and fungi. At the same time, for a long period, the leading role was played by the bacterial factor, while viruses were mainly considered as precursors of subsequent microbial aggression, and fungi did not have much epidemiological significance.

Not every disease has methods of treating its causes (etiotropic treatment), but for a long time this possibility existed in the AP due to the presence of antibiotics. This type of drug treatment, which can affect bacterial pathogens, had not only positive but also negative consequences, in particular, the development of antibiotic-resistant strains and the impact on the human microbiome with an increase in the number of viral lung lesions. These trends have become particularly noticeable in the past two decades. In addition, the long-term use of antimicrobial drugs has formed an exclusively etiotropic concept of AP, leaving the basics of its pathogenesis without due attention. Attempts to study mechanisms of disease at the cellular and molecular level, To study the effect of pathogens on body tissues, overlooked features of functional disorders of the damaged organ, which distorts the principles of pathogenetic treatment.

The development of the COVID-19 pandemic not only unexpectedly disrupted the normal rhythm of our life, dramatically changing its routine, habitual norms and patterns, but also significantly affected the work of medical care systems. Contagiousness and rapid spread of infection require strict compliance with epidemiological measures and are accompanied by a significant increase in hospitalization of patients with changes in hospital contingents and profiles of many departments. The high probability of infection and lack of confidence in the favorable outcome of treatment create the basis for depressive and even panic moods among various segments of the population, including medical personnel.

The main reason for the severe course of the disease and critical conditions in these patients are lung lesions, and the reasons for negative emotions and anxious moods are quite justified. On the one hand, mortality among patients with coronavirus is significantly higher compared to other forms of acute respiratory inflammation. On the other hand, to date, there is no evidence that any therapy can reduce mortality in this disease [1].

However, it is known that fear and panic in extreme situations do not help in finding the right solutions, but rather interfere with logical and rational thinking. Therefore, it makes sense to try to look at the facts of the current state of this problem from different points of view, leaving aside emotions and unproven assumptions.

The basis of modern medical care for patients with coronavirus lung disease is drugs that have been tested for other viral infections, as well as immunomodulatory drugs, but evidence of the undoubted benefit of such therapy has not yet been received [2-4]. Due to the unreliability of primary medical care for patients with coronavirus pneumonia, the strategy of their support is based on monitoring in order to determine the optimal time for intubation and transfer to artificial ventilation [5]. During this observation, patients receive infusion therapy to compensate for water losses, oxygen insufflation, symptomatic and syndromic agents (anti-inflammatory, hormonal, anticoagulants, vasopressors, etc.). Due to the large number of patients who need artificial ventilation, specialists are forced to calculate the need for such equipment and call for an increase in its production [6,7].

In this situation, the search for tools and techniques that would help in the treatment of patients with viral pneumonia begins. For example, to increase the oxygen supply to the patient, A. Vianello et al. [8] suggested using a special cannula. Other researchers place patients with severe hypoxemia on their stomach during oxygen insufflation (prone positioning), which, according to the researchers, gives the best effect and allows for many observations to avoid subsequent intubation [9,10]. Of course, any technique that benefits the patient should be used if necessary, but it is a pity that these examples are only about palliative care. From my point of view, the effect of the latter method has a simpler explanation than the long list of suspected pathophysiological changes given by D. Koeckerling et al. [9].

It is known that the main muscle that provides ventilation is the diaphragm. In addition, each muscle of the body has its own antagonist, which ensures its more effective function. For the diaphragm, such an antagonist is the abdominal wall muscles. It is no secret that most people's abdominal muscles do not have sufficient training and tone, and the tendency to severe inflammatory processes in the lungs distinguishes people with overweight and older age groups. In the supine position, such

patients suddenly get a strong and stable anterior abdominal wall, which helps to increase the movements of the diaphragm and improve lung ventilation. This method, from my point of view, has no other effect on the current disease. Therefore, it should be considered as a palliative, and published assumptions about possible other effects [9] require objective evidence, not simple statements.

Thus, the main efforts in the treatment of patients with coronavirus pneumonia are aimed at attempts to suppress the pathogen, correct immune protection and maintain adequate gas exchange. In this triad of medical interventions, special hopes are expressed for the development of effective antiviral drugs with the expectation of radical changes in the results of treatment. In this regard, it is quite reasonable to raise questions that still need to be answered today. First, no one can predict when such drugs will be created and how effective they will be, and real help for such patients is needed right now. Secondly, this direction is exclusively etiotropic treatment and the experience of recent decades on the example of antibacterial therapy allows us to see the narrow focus and insufficiency of this approach.

In order to understand the illusory hopes for the absolute effect of etiotropic treatment of inflammation in the lungs, it is necessary to take into account the known standards. Any etiotropic drug (antibacterial, antiviral, antifungal, etc.) can only affect the pathogen of the process, without directly affecting the consequences of its pathological activity in the tissues and structures of the body, is not it? At the same time, the diagnosis of pneumonia is based on clinical and radiological data that are the result of the development of an inflammatory reaction. The bacterial pathogen itself remains unknown in the vast majority of cases and is usually referred to in the diagnosis as an assumption. Using exclusively etiotropic (mainly empirical) treatment, we strive to eliminate one of the causes of inflammation and actually leave the body with the task of stopping the development and eliminating the existing inflammatory transformation of tissues on its own.

The paradox of this situation is that the treatment is directed against the pathogen, and the effectiveness of such assistance is evaluated by eliminating the consequences caused by it. At the same time, it is known that the further development of initial inflammation can continue in the absence of microorganisms, and the inflammatory process develops according to standard biological patterns. The most striking example of this development of the disease are cases of so-called sterile empyema of the pleura. However, in General, the dominant etiotropic approach to treatment explains the fact that, regardless of the nature of clinical and radiological manifestations of the disease, their presence remains the main criterion for the duration of antibacterial therapy. In other words, the crucial role in the diagnosis of acute pneumonia and the duration of antibacterial therapy is played by the effects of pathogenetic mechanisms of inflammation, and not the presence of a virulent pathogen, is not it?

In order to understand the origins of the described paradoxes, it is necessary to recall the history of the use of antibiotics. In the initial period of penicillin use, the effectiveness was so high that the inflammatory process in the tissues did not have time to reach later stages, and several injections of the drug were quite enough for the patient's body to eliminate the already formed focus. However, over the years, the effectiveness of such therapy began to fall due to increased resistance of the microflora. It was necessary to create more and more new medicines. Efforts of researchers and practitioners are increasingly focused on etiotropic treatment, leaving without due attention the unique features of pathogenesis and pathogenetic therapy of Acute Pneumonia (AP). At the same time, the mechanism of development of the disease and its associated disorders in the body of patients did not depend on the etiology of the bacterial process and convincing evidence of a cardinal difference between AP and its pathogen was not presented for a long period of research.Periods of etiological diagnosis of AP according to clinical and radiological data have been preserved in the history of this disease as declarative attempts.

The long-term didactics of the etiotropic approach to solving this problem is deeply rooted in medical science and practice and continues to determine the main directions of medical care for this group of patients at the present stage. For example, based on the materials of T. M. Rawson et al. [11], 72% of patients with coronavirus infection were prescribed antibiotics, but bacterial or fungal co-infection was detected in only 8% of them.According to D. Kim and others [12], 71% of patients with viral infection received antibiotics during the current pandemic. A synthesis of data from 82 hospitals in 23 countries showed that in 82.9% of cases, the administration of antibiotics was consistent with the principles of their use in community-acquired pneumonia and was empirical [13].

These data reflect a strong desire to use the etiotropic treatment pathway, despite the lack of logic and specific drugs. Such materials are only one of the evidences of a narrow understanding of the nature of acute inflammatory lung disease and the absence of any attempts to apply pathogenetic approaches to help patients.

Comparisons and parallels between bacterial and viral, in particular coronavirus, forms of pulmonary inflammation, which are partially presented above, are not only appropriate, but also necessary on the basis of the following facts. First of all, in patients with coronavirus infection, we are talking about acute inflammation of the lung tissue, which is reflected in many publications on this topic. At the same time, M. Lipman et al. [2] emphasize the identity of not only clinical, but also laboratory data and distinguish this type of inflammation by the separate term "pneumonia COVID-19 ", suggesting that differential diagnostics with community-acquired pneumonia should be performed. In acute inflammation of any etiology, the affected organ partially or completely loses its function, does it not? This classic sign that accompanies the inflammatory transformation of certain body structures was described by Galen many centuries ago and is widely known. For example, if there is an acute inflammation of the finger, we lose the ability to fully use it for a certain period. If acute otitis media occurs, then for some time the hearing acuity decreases. And so on.

Of course, viral lung inflammation has certain histological differences from bacterial processes. However, both forms of pneumonia involve the same structures of lung tissue [14-16], which is indirect evidence of the occurrence of identical functional disorders. For a particular patient, it does not matter in principle, as a result of which infection he loses lung function. These features of the disease are necessary for treating physicians to provide etiotropic care in addition to the General principles of treatment. If the issue of treating a single nosology, which is called acute inflammation of the lung tissue, is on the agenda, then the treatment strategy cannot have different interpretations, since regardless of the etiology, one organ and its functional potency suffer, right?

DOI: *10.46998/IJCMCR.2020.04.000097*

However, modern reality does not coincide with the logic of such reasoning. The main goal of modern AP treatment strategy is determined by the etiology of the disease, and in practice, the correctness of this characteristic is often assumed and has no real evidence. Features of the pathogen that are important for the emergence of the inflammatory process continue to be considered as the main factors of the disease, while the assessment of the severity of the condition of patients and treatment efforts are determined by the nature of pathological tissue transformation and its impact on functional shifts. Today, the attending doctor, having prescribed an anti-bacterial or antiviral drugsto a patient with AP, expects the success of treatment by destroying the pathogen. But if the disease continues to progress and there is a need for additional help, the pathogen acts more as a symbol of the process, and the actual assessment of the patient's condition and the necessary correction are carried out based on the dynamics of the focus of inflammation in the lung and its pathogenetic effect on vital functions, is not it?
In this regard, it should be recalled that the lungs, playing a complex role in the life support of the body, provide not only gas exchange, but also perform a number of non-respiratory functions, among which the most important is the regulation of blood circulation. Anatomically, the vessels of the small circle of blood circulation are inextricably linked with the systemic circulation, but functionally they are its antagonist. Unfortunately, these indisputable and long-known scientific facts are not taken into account when providing medical care to patients with AP. Treatment that gives a positive effect in inflammatory processes in the large circle of blood circulation can give the opposite result in AP.
Therefore, understanding the pathogenesis of the disease and the chain of functional shifts is important for developing the principles of pathogenetic care for such patients. This is especially important in the absence of effective etiotropic treatment and the use of General Therapeutic, rather than specific methods of auxiliary support. In this case, we are talking primarily about the possibility of maladaptive action of intravenous infusions and vasopressors, which are widely used in this category of patients with a progressive course of the disease.

The pathogenesis of AP cannot be an abstract judgment for a Clinician. Understanding the sequence of operating mechanisms and clearly defining what is the cause and what is the effect is fundamental to the targeted application of therapeutic methods. Currently, the best option in this direction is considered to be the detection of the pathogen in the first days of hospitalization and the possibility of conducting etiotropic therapy. If this set of instructions is feasible, this option is considered a great success regardless of subsequent results.
However, everyone knows how such a treatment plan is practically implemented. First, in many patients, the pathogen remains unrecognized or the accuracy of its diagnosis is very doubtful. Secondly, the verification of the pathogen, even if it is determined, lags behind in time from the beginning of medical care, so these drugs are initially prescribed empirically. Third, the necessary etiotropic drugs may simply not be available, which has been observed in recent years with an increase in cases of viral pneumonia. Fourth, the negative dynamics of the disease against the background of ongoing treatment is usually explained by the characteristics and virulence of the pathogen, although many experts have already noticed that in the current pandemic, an identical pathogen can cause an infinite number of clinical variants of the disease [17]. Finally, the most casuistic is the fact that monitoring the condition of patients and the necessary medical correction are based on signs of inflammation of the lung tissue and its functional disorders at the same time, the etiological factor in the complex of further treatment does not really determine the choice of means of assistance.
In addition to the above, we should add the General opinion of experts from more than 20 countries who justify the reasons for empirically prescribing antibiotics for coronavirus infection only by signs of the inflammatory process [13]. In this case, the most important importance is attached to the clinical picture of the disease, followed by laboratory markers of inflammation and radiological data. But at the end of the day, these diagnostic tests are completely consistent with a diagnosis like viral pneumonia, which is a viral inflammation (!) of the lung tissue, isn't it?
At present, the dynamics of the inflammatory process in the lungs are usually evaluated based on the results of repeated radiological studies, and the main criteria for evaluating the condition of patients and the necessary therapeutic correction are the characteristics of such vital functions as breathing and blood circulation, to which the lungs are most directly related. The appointment of additional medical care is not related to the etiology of AP. In other words, the pathogen of the process affects only the choice of etiotropic treatment, and then remains a kind of brand of the disease. All further actions of medical personnel are dictated by a biological process called "inflammation" and its consequences.

The presented inconsistencies between existing views and actual reality are the cause of distorted perceptions and stagnation in solving this problem. The process of inflammation with its inherent dynamics and stages, its impact on the work of the lungs, including the violation of their non-respiratory functions, are not taken into account properly when forming ideas about the pathogenesis of AP and determining methods of medical care. Of course, any medical effort that can improve a patient's condition is commendable. However, attempts to solve this problem by expanding palliative measures, such as prone positioning for oxygen inhalation or increasing the availability of artificial ventilation devices, are inherently not capable of leading to radical changes.Even when these measures are implemented, the mortality rate among COVID-19 patients admitted to intensive care units reaches 40-50% [18].

The development and use of a coronavirus vaccine can significantly reduce the burden of the pandemic, although experts have already noted a trend towards mutations and modifications of this pathogen. This trend can be seriously reinforced if effective antiviral drugs are created. Many years of experience in antibacterial therapy and its current results provide a full basis for such a conclusion about the upcoming consequences of the predicted etiotropic therapy of viral infections. High expectations and hopes for a radical change in results after the development of antiviral drugs should also take into account the possible consequences, and not just our wishes. After all, such drugs, acting on pathogenic microorganisms, will gradually lead to the appearance of resistant strains, and most importantly, will not affect the inflammatory process itself. Therefore, there is always a group of patients who cannot do without pathogenetic treatment.

Dreams and plans for the future are only possible prospects that have yet to be realized. Modern literature and the mass media are currently filled with similar appeals and hopes. However, these General wishes are presented instead of real solutions to the problem, as the disease strategy remains stubbornly focused on the leading role of pathogens and their suppression. Anti-epidemic measures and prevention of infections, such as coronavirus, are extremely important and do not cause even a shadow of doubt. Rational and accurate implementation of these efforts can significantly reduce the spread of infection and overall morbidity. However, when the fact of the disease is already obvious, these measures are necessary for others, but the patient needs adequate medical care not prevention.

Insufficient attention to the process of inflammation, the peculiarities of its localization, as well as the impact on polyfunctional pulmonary insufficiency do not allow us to assess the maladaptive effect of a number of generally accepted General Therapeutic methods of treatment, which are not combined with the exceptional nature of AP pathogenesis. It is only necessary to remember that before the beginning of the era of antibiotics and the formation of the etiotropic concept of the disease, medicine for many centuries used the empirical search and application of various ways to help with acute lung inflammation. Some of the old methods, such as bloodletting, are now a thing of the past due to their danger and non-physiology. Other methods of care, such as cupping therapy or short-term cooling of the patient's body, continue to be used in various areas of mainly alternative medicine, without reaching the group of patients with AP where they could have a noticeable success. Modern medical equipment for monitoring and conducting various studies provides a wide range of opportunities for an objective assessment of the actual effect of specific medical procedures. At present, such possibilities are far superior to the conditions in which the author of these lines conducted his research [19]. It is objective testing of therapeutic activity and trace reactions, as well as potential ways to help with AP, that will allow us to evaluate their true, rather than their intended effectiveness. But to do this, you need to have an idea of the sequence and relationship of existing mechanisms of the disease. A more detailed description of these features of AP pathogenesis, as well as the results of additional studies and first successful clinical trials, can be found in Igor Klepikov's recently published monograph " Acute pneumonia. New doctrine and first results of treatment" - ISBN (978-620-2-67917-6).If necessary, this publication can be found at the following address-https://www.cheapesttextbooks.com/IM/?keyval=ISBN+%28978-620-2-67917-6%29.

It is very important to note that the new doctrine of disease is based on old, well-known materials of fundamental medical and biological science. Therefore, the novelty of this doctrine lies in the relative concept, which is more applicable to its justification and the sequence of changes occurring in the body, than directly to the actual rules and canons of biological processes. Without these basic materials of medical science, it is impossible to count on the success of comprehensive treatment of the most severe group of patients with AP, who are hospitalized daily around the world and hope for a positive result.

References

1. I Zagury-Orly, RM Schwartzstein. Covid-19 - A Reminder to Reason. N Engl J Med. 2020;383:e12. DOI: 10.1056/NEJMp2009405.
2. Lipman M, Chambers RC, Singer M, et al.SARS-CoV-2 pandemic: clinical picture of COVID-19 and implications for research. Thorax. 2020;75:614-616.
3. JH Beigel, KM Tomashek, LE Dodd et al. Remdesivir for the Treatment of Covid-19— Preliminary Report. NEJM, 2020. DOI: 10.1056/NEJMoa2007764.
4. Correspondence: Remdesivir for the Treatment of Covid-19 - Preliminary Report. NEJM, 2020. DOI: 10.1056/NEJMc2022236.
5. DA Berlin, RM Gulick, FJ Martinez. Severe Covid-19. NEJM, 2020. DOI: 10.1056/NEJMcp2009575.
6. ML Ranney, VGriffeth, AK Jha. Critical Supply Shortages - The Need for Ventilators and Personal Protective Equipment during the Covid-19 Pandemic. N Engl J Med. 2020;382:e41. DOI: 10.1056/NEJMp2006141.
7. Johns Hopkins Center for Health Security. Ventilator stockpiling and availability in the US. 2020. (http://www.centerforhealthsecurity.org/resources/COVID-19/200214-VentilatorAvailability-factsheet.pdf.
8. Vianello A, Arcaro G, Molena B, et al. High-flow nasal cannula oxygen therapy to treat patients with hypoxemic acute respiratory failure consequent to SARS-CoV-2 infection. Thorax. Published Online First: 2020. doi: 10.1136/thoraxjnl-2020-214993.
9. Koeckerling D, Barker J, Mudalige NL, et al. Awake prone positioning in COVID-19. Thorax Published Online First: 2020. doi: 10.1136/thoraxjnl-2020-215133.
10. Thompson AE et al.Prone positioning in awake, nonintubated patients with COVID-19 hypoxemic respiratory failure. JAMA Intern Med 2020; [e-pub]. (https://doi.org/10.1001/jamainternmed.2020.3030).
11. Rawson TM, Moore LSP, Zhu N, et al. Bacterial and fungal co-infection in individuals with coronavirus: A rapid review to support COVID-19 antimicrobial prescribing [published online ahead of print, 2020 May 2]. Clin Infect Dis. 2020;ciaa530. doi:10.1093/cid/ciaa530.
12. Kim D, Quinn J, Pinsky B et al. Rates of co-infection between SARS-CoV-2 and other respiratory pathogens. JAMA 2020; -323:2085-2086.
13. B Beović, M Doušak, J Ferreira-Coimbra et al. Antibiotic use in patients with COVID-19: a 'snapshot' Infectious Diseases International Research Initiative (ID-IRI) survey. Journal of Antimicrobial Chemotherapy, dkaa 326, 2020. https://doi.org/10.1093/jac/dkaa326.
14. Luo W, Yu H, Gou J, et al. Clinical pathology of critical patient with novel coronavirus pneumonia (COVID-19). Pathology & Pathobiology 2020; 2020020407.
15. M Ackermann, SE Verleden, M Kuehnel et al. (2020). Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. 2020. DOI: 10.1056/NEJMoa2015432.
16. L Hariri, CC Hardin. Covid-19, Angiogenesis, and ARDS Endotypes, 2020. DOI: 10.1056/NEJMe2018629.
17. A Sakurai, T Sasaki, S Kato et al. Natural History of Asymptomatic SARS-CoV-2 Infection. NEJM, 2020, DOI: 10.1056/NEJMc2013020.
18. Renato Seligman and Beatriz Graeff Santos Seligman. "Pandemic in the 21st Century. The Challenge of COVID-19". EC Pulmonology and Respiratory Medicine. 2020;9(8):30-31.
19. Igor Klepikov. "First Aid for Aggressive Forms of Acute Pneumonia". EC Pulmonology and Respiratory Medicine (2018);7(2): 34-37.