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Present situation of bacterial neuroinfections across the globe – review

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Abstract

Bacterial meningitis is still life-threatening disease, which cause about 1.2 million cases and it is responsible for over 100 thousand of deaths across the globe. [2] The most common pathogens which cause the disease are *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Listeria monocytogenes*. Morbidity is significantly higher in Africa, than in other regions in the world. Region of the highest frequency of new cases is located in sub-Saharan Africa and called meningitis belt. Vaccination campaigns against bacterial, mostly meningococcal were conducted in some of these regions and the benefits of it were seen [5].

Young children and elderly patients are predisposed to have bacterial meningitis. In pediatric population the disease usually presents as fever, seizures, vomiting, chills, altered mental status and stiff neck. [4] Development of each country have impact on mortality and morbidity among children. [6] Elderly patients, because of their comorbidity are also predisposed to bacterial meningitis. Diseases like diabetes mellitus, alcoholism, cancer, HIV/AIDS or being after splenectomy may make the patients susceptible for bacterial invasion of CNS.

Also, every factor which interrupt blood-brain barrier, like trauma or surgery may cause the infection.

Intracerebral hemorrhage can be consequence of the infection, which cause other complications like impaired consciousness, focal neurological deficit, need of mechanical

ventilation and seizures. It was noticed that in most of cases bacterial meningitis had *S.pneumoniae* etiology.

Key words: bacterial neuroinfections, bacterial meningitis, meningococci, pneumococci, meningitis belt, intracerebral hemorrhage

Introduction and purpose

Meningitis is potentially lethal infection of central nervous system. [1] It may have bacterial, viral, fungal or parasitic etiology [2][8][9]. Bacterial meningitis is seemed to be one of the most life-threatening disease especially in underdeveloped countries. Variety of signs and symptoms, even lack of it, connected with its ability to present in child and adult population is a huge challenge for medics across the globe. There are differences between countries, generally from other continents, based on health care level. Also, character of disease is varied but in general prognosis of even in well treated meningitis can be uncertain. In this article we will present current state of knowledge about bacterial meningitis, its epidemiology, therapy and some consequences and the risks resulting from the disease.

State of knowledge

Bacterial meningitis (BM) is infection of CNS. It is begun by presence of bacteria in blood and after that the pathogens cross blood-CNS barrier (blood-CSF or blood-brain barrier). When bacteria reach the nervous system cells massive and potentially uncontrolled inflammatory response is triggered. Bacteria's multiplying is generally also uncontrolled in CSF because host immune response factors, like complement, are present in very low (100 or even 1000 times) concentration than in serum. This state certainly should not stay without any organism defense response, so that it starts immune system activity like complement cascade. [3]

There are about 1.2 million cases of BM each year and about 135 thousand deaths because of the disease. [2][11] The most common pathogens responsible for BM are *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Listeria monocytogenes*. [3][4][5] In last two decades epidemiology of BM has significantly changed because of introduced vaccinations against *N. meningitidis*, *S. pneumoniae* and *H.influenzae*. [4] In some African countries like Burkina Faso, Niger or Mali about 20 million people aged 1 to 29 years took part in great vaccination campaigns against pathogens like *N.meningitidis* type A, which had caused most of BM. [5][10] In most industrialized countries number of BM caused by *Haemophilus influenzae* b was decreased dramatically because of vaccination programs and now it is not problem for public health. [4]

There are some endemic regions of *N.meningitidis* infections called meningitis belt. It is located in sub-Saharan Africa, where epidemics of BM are noted every 5-12 years. Epidemy of *N.meningitidis* BM is connected with dry season, when winds blowing in Western Africa transport small particles of sand and dust. It irritates respiratory system mucous membrane and in addition to *N.meningitidis* carriage state in this location predispose to BM. Nowadays the meningitis belt is seem to grow because the sporadic, but meaning epidemics were noted in countries originally outside the belt. [5][12][13][14] This phenomenon should justify need of vaccination in territories primary not included to the compaigns.

Children are generally one of the predisposed groups to BM. In pediatrics population described in one clinical trial, meningitis is presented with mostly fever (98,3%), seizures (92,5%), vomiting (52,4%), chills (17,5%), altered mental status (10%), stiff neck (9,4%) and coma (3%). In one year or older children headache were seen in 7,4% of cases. Bulging fontanelle were found in 20% of under 18-month-old children. Only 3 children from more

than 350 had positive culture of *Neisseria meningitidis* and 3 children *Streptococcus pneumoniae* in CSF after lumbar puncture. [4] Another clinical study analyzed differences between countries – Finland, Angola and Latin America in BM. In well developed country like Finland there were much less frequent cases of *S. pneumoniae* cases than in other countries from comparison. What is significant mortality were lower in Finland than in Latin America and much lower than in Angola. Also, sequelae of BM like hearing problems, deafness, mild or severe neurological consequences were widely less common or absent in Finland than other countries. [6] Time from the beginning of signs and symptoms to arriving to hospital was, also correlated with the disease outcome. In Angola median time to admission was about 5 days, in Latin America – 3 days, in Finland 24 hours. On the other hand, presence of underweight, anemia, IDS, sickle cell disease, and parasitic infections worsen outcomes, certainly induce higher morbidity and mortality. [6] [18][19]. It shows the connection between status of development of country, also health care quality and positive result of therapy in BM.

Another group predisposed for BM are elderly people. It is important function of immune system decrease in elderly patients and they have comorbid illness which also affect on immune response. Also, there are not clear evidences of vaccination against pneumococci benefits in this age group. In adult population symptoms can be very atypical like headache. Comorbid diseases: diabetes mellitus, alcoholism, cancer, HIV/AIDS also can affect immune system and predispose to BM. Presence of leukemia or lymphoma is quite common in total BM cases because of negative impact of total immune response. The same mechanism makes organ transplant recipients vulnerable to BM, but in this group causative pathogens like *Nocardia* are more common than the other patients. Splenectomy or hyposplenic state also increase probability of BM because of susceptibility for encapsulated bacteria infection. [1][15][16]

What is interesting, there were found correlations between BM and genetic conditions. Higher incidence of meningococcal meningitis, than in general population was described in patients with properdin or complement system deficiency. Also, higher probability of pneumococcal BM was found in patients with some gene variation, but a part of them has rather protective effect. [1][17]

The blood-brain barrier can be called the most important part of defense against BM. Every disease or clinical state which has negative impact on it can potentially cause the disease. Any disruption of the barrier like trauma, surgery, congenital defects, ear or sinus infection may dramatically increase risk of BM. Recurrent episodes of the disease, caused by *S.pneumoniae*, *N. meningitidis*, *S.aureus*, *H. influenzae* can be result of presence of CSF leak. It is important that second episode BM risk is higher than risk of first episode in general population and vaccination are seemed to not been able to reduce it. [1]

There is lot of potential complications in BM and one of them is intracerebral hemorrhage (IH), which is one of the worst. It is probably caused by inflammation in BM connected with vasculitis, which was found in most of patients with IH because the meningitis. The patients with IH were mostly female age 54-77 with endocarditis and 1/5 of them was on anticoagulation therapy. In this group of patients classic BM symptoms and signs like headache, neck stiffness, fever or all of them connected with altered mental status were less common than in group without IH. Slightly increased frequency of altered mental status or coma were seen in patients with IH. What is significant about $\frac{3}{4}$ of patients with IM had BM caused by *S.pneumoniae*. The most common complications in this group were impaired consciousness, focal neurological deficit, need of mechanical ventilation and seizures. More than half of the patients with IH did not survive. [7]

Discussion

Despite development of medicine, vaccines and therapy schemes, bacterial meningitis is still a challenge for medics. Its potential life-treating character can be only changed by global vaccination against each of the most common pathogens and fast diagnose connected with targeted therapy. Maybe this condition is not so problematic in most of Europe and North America countries, but it may be impossible to do in Africa, where medicine is still on the low level. Without active help to regions with the highest morbidity BM will be still one of the biggest health problems.

Also, it is very important to reduce mortality and morbidity rate in predisposed patients groups. It can be made by sharing knowledge about BM and its consequences, encouraging to vaccinate and suspecting BM in all of patients with any of signs and symptoms when clinical diagnose is not clear. In some cases, delay in admission was clue in the disease outcome. This problem is obviously most common in low-developed country, is seemed to be induced by health care system availability and quality. It will be a very difficult to overcome these difficulties without help from countries with well-developed health care systems like USA and EU.

On the other hand, tourist arriving to meningitis belt countries and other with high morbidity should be aware of the infection risk. Need of vaccination in this group is irrefutable, but the vaccination is also limited, because there are only a few types of vaccines against only some bacteria. Also, it is important to remember that meningitis can be cause not only by bacteria and etiology of the disease, which induce therapy is sometimes hard to find.

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