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EC DIABETES AND METABOLIC RESEARCH

Review Article

Infectious Diseases and Vaccination in Patients with Diabetes

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Abstract

Hyperglycemia and other complications associated with metabolic imbalance of diabetes constitute nontrivial risk of infections. Some of them occur more frequently in patients with diabetes, have different clinical course or are caused by microorganisms which are rarely observed amongst healthy population. The aim of prevention is to provide good education, systematic control of glycemia, metabolic balance and hygienic care. The use of immunization is one of most important factors in preventing infections. Vaccination is not prohibited in diabetic patients, there can only appear some transient contraindications due to, for instance, a significant metabolic deregulation of diabetes. Presented review spotlights most frequent and most unique infections affecting population of diabetic patients and emphasizes the role of vaccination in diabetology.

Keywords: *Typical Infections in Diabetes Mellitus; Predisposing Factors; Complement System; Prevention of Infections; Vaccination*

Abbreviations

AIH: Autoimmune Hepatitis; HCV: Hepatitis C Virus; HBV: Hepatitis B Virus

Introduction

Serious infections trigger insulin resistance among all people, through increased secretion of hormones with antagonistic profile of action versus insulin. These hormones are glucagon, epinephrine and cortisol. In response, secretion of insulin rises, which allows to maintain metabolic balance. Patients with diabetes, due to inability to escalate insulin release, present bigger release of glucose from the liver, which together with decrease in its peripheral tissue uptake, leads to hyperglycemia. Disturbances in insulin sensitivity of the tissues are escalated by cytokine activity.

In defensive reactions against infection, essential role is played by non-specific immunity, which is dependent on cells capable of absorbing and destroying bacteria or other xenoparticles. Mechanisms of specific immunity are based on lymphocytes T and B activity. Lymphocytes T release lymphokines while lymphocytes B secrete antibodies [1,2]. Hyperglycemia plays role in disorders of non-specific immunity mechanisms, duration of diabetes is also essential. The compound of great importance in immunity mechanisms is complement system C3 [3]. Future studies are necessary to assess the impact of hyperglycemia on immune mechanisms in diabetes [4]. Many authors spotlight potential role of enteroviruses in the development of type 1 diabetes. A lot of evidence indicates their involvement in β cells destruction [5]. Researches on using enterovirus vaccines for the prevention of type 1 diabetes development are appealing [6].

Infections commonly associated with diabetes- factors predisposing to infection

Some disorders which usually occur rarely- affect patients with diabetes more often than those without such metabolic condition. The risk of infection onset is most pronounced whilst metabolic imbalance, hyperglycemia and ketoacidosis.

Among risk factors there should be mentioned:

- Long duration of illness;
- Chronic complications of diabetes- insufficient blood supply, microangiopathy, pain and sensory disturbances due to diabetic neuropathy- all these become the cause of necrotic lesions, which secondarily get infected;
- Ketoacidosis- it was indicated that whilst ketoacidosis- polymorphonuclear leukocytes functioning, chemotaxis, phagocytosis and intracellular destruction of microorganisms are impaired;
- Immunity disorder- hyperglycemia is the cause of non-specific immunity disturbances in both - cellular and humoral aspects.

Infections commonly associated with diabetes

Mucormycosis (zygomycosis)

Infection caused by zygomycetes is a very aggressive fungal disease. It is mainly reported in patients with decompensated diabetes in the state of ketoacidosis. The most common manifestations are pulmonary and invasive rhinocerebral infections [7,8].

Mucormycosis rhinocerebralis

The condition is usually dramatic. Such infection usually develops in the paranasal sinuses, where it spreads to the orbits and then to the brain. Its complication may be cavernous sinus thrombosis or internal carotid thrombosis**.** This syndrome is characterized by high mortality, although cases, in which intensive treatment allows saving the patient's life, are described [7].

Pathological lesions in oral cavity

In diabetes, inflammations of periodontium occur relatively often, also the rate of dental caries is higher. Such conditions are favoured by microangiopathy complications [9-11].

Skin and subcutaneous tissue

Patients with diabetes experience skin infections more often than others. Hyperglycemia significantly increases the risk of soft tissue infection and it is usually caused by *Streptococcus* group A and B [12-14].

Diabetic foot

Occurrence of ulcerations on the surface of toes is favored by undertreated athlete's foot or injury. Essential role is played by peripheral neuropathy and vascular lesions with micro and macroangiopathy characteristic. The discussed condition usually affects the elderly, but it may also occur amongst younger patients suffering from type 1 diabetes, mainly if chronically imbalanced [15,16].

Helicobacter pylori infection

One cause of symptoms from gastrointestinal tract is undoubtedly *Helicobacter pylori* infection. This state plays crucial role in pathogenesis of upper gastrological tract disorders. It is claimed that patients with diabetes, mainly if type 1, are especially prone to such infection. It is also relatively often recognized among the youth [17-21]. Some interesting researches show that *H. pylori* infection in patients with autoimmunological diabetes may be connected with simultaneous thyroid disorder on autoimmunological basis [22].

Research is being carried out on the impact of *H. pylori* infection on the increase in insulin resistance and the development of clinically overt diabetes in patients with pre-diabetes [23,24]. Some other authors also confirm connection between *H. pylori* infection and development of type 2 diabetes and deterioration of metabolic control [25,26].

Liver and bile duct infection

Liver dysfunction may have autoimmunological or inflammatory basis. Due to Japanese authors researches, autoimmune hepatitis (AIH) is a progressive liver disease conditioned by environmental and genetic factors [27]. AIH occurs mainly among young patients with diabetes type 1 [28]. In this group of patients there may also occur inflammatory diseases of liver associated with viral infections-hepatitis virus infection with virus C or B (HCV, HBV) [29-31]. An increased incidence of viral hepatitis is also seen in type 2 diabetes [32-34]. Cholecystitis in patients with diabetes often has a very severe course. In patients with diabetes, more often than in the general population, there occurs severe fulminating infection, especially with gas-forming organisms [35].

Pancreatitis

Among diabetic patients, there is increased risk of acute pancreatitis, which can be particularly severe in type 1 diabetes [36].

Urinary infections

Patients with diabetes suffer from increased risk of infections, mainly in urinary tract. Elevated sensitivity to infections is result of either diabetes itself or its complications. In this increased vulnerability, essential role is played by impaired function of immunological system and also by deficient glycaemic control, dysfunction of urinary bladder voiding due to neuropathy and by diabetes nephropathy. Urinary tract infections may develop from asymptomatic bacteriuria, through pyelonephritis to urosepsis. Diabetic patients are prone to experience emphysematous pyelonephritis, urinary bladder inflammation, renal papillary necrosis or corticomedullary abscesses. Bacterial aetiology of these infections might be really diverse. Fungal infections are relatively common. Incidence of urinary tract infections is promoted by disabled non-specific immunity. Efficient immunological response may be impaired as a result of microangiopathy [37,38].

Genital infections

Most often genital infections in patients with diabetes are fungal infections, that occur mainly in periods of diabetes decompensation. This applies to both type 1 and type 2 diabetes. They are often one of the first symptoms found at the time of diabetes diagnosis [39-41].

The most frequently infecting microorganisms in diabetic patients

In infections of diabetic patients, the spectrum of fungal and yeast bacteria, like in diabetic individuals, may be very diverse. However, there are infectious agents that are particularly common in patients with diabetes. Most frequently isolated bacteria from upper and lower respiratory tract are *S. pneumoniae, H. influenzae* type b, *Moraxella catarrhalis*, less often *S. aureus, S. pyogenes* and Gram-negative rods from the Enterobacteriaceae family - *E. coli, Klebsiella pneumoniae* [42].

Type 1 diabetes is often associated with viral infections, including rubella, mumps, Epstein-Barr and cytomegalovirus. Viral infections often precede the clinical manifestation of type 1 diabetes. The relationship between enterovirus infections and the diabetogenic process remain unclear. Diabetic influenza virus infection may be particularly dangerous in diabetic patients. Complications of influenza, among others bacterial infections, e.g. pneumonia caused by *S. aureus* or *S. pneumoniae*, can lead to death.

There are more and more reports about the inclination of people with diabetes to become infected by herpes zoster virus and varicella zoster virus [43].

This is especially true for patients with type 2 diabetes [44,45].

Vaccinations in diabetic patients

Since diabetes predisposes patients to bacterial and viral infections, and those aggravate the course of the disease, prophylaxis is necessary, including protective vaccinations. Recommendations for carrying out vaccinations are specified by scientific societies [46,47].

Most important recommendations

- Every child with diabetes should undergo all currently recommended vaccinations.
- Annual influenza vaccination is recommended in children > 6 months of age and adults.
- Vaccination against HBV is recommended in all patients with diabetes [48,49].

Suggestions about the relationship between vaccinations and the increase of occurrence of type 1 diabetes have not been confirmed [50]. Each vaccination should be preceded by a physical examination. The vaccination schedule includes mandatory vaccinations, ones people at particular risk of infection and recommended vaccinations. The basic vaccinations recommended for diabetics include influenza, pneumococcal, tetanus and hepatitis B vaccines. Other vaccines are given only after an individual benefit and risk assessment for a diabetic patient [51,52]. Recently, particularly high attention has been paid to vaccination against influenza in diabetic patients. In many clinical centers, studies determine the importance of these vaccinations in various groups of patients with diabetes. However, it is generally believed that these vaccinations are beneficial for all patients with diabetes. Finally, vaccinations are the most effective method of preventing infectious diseases and should be an integral part of the management of risk groups, including those with diabetes [53-57].

Conclusions

At present, it should not raise any doubt that the introduction of preventive vaccination was one of the major achievements of medicine. Thanks to the vaccination, a number of diseases have been largely eliminated. Diabetic patients are particularly susceptible to infections, therefore regular vaccination is very important in this population. There is no evidence that diabetes is a contraindication to vaccination. (http://www.cdc.gov/vaccines/recs/) [58].

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Volume 3 Issue 3 June 2019