OCCUPATIONAL EXPOSURE OF HEALTH SERVICE EMPLOYEES TO HIV, HBV, AND HCV INFECTIONS: PRE- AND POSTEXPOSURE PROPHYLAXIS

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Serving in the medical profession, especially in direct contact with human excretions, human secretions, or invasive procedures, is connected with a higher risk of infection. One of the most common health service occupational infections in Poland is hepatitis (types B and C). HIV infections can also be transmitted via the same route; thus, post-exposure prophylaxis encompasses all the above-mentioned diseases.

BIOLOGICAL PROPERTIES OF VIRUSES AND EPIDEMIOLOGY

HIV

HIV – the human immunodeficiency virus is an RNA virus belonging to the Retroviridae family. This virus replicates in cells of the immune system that have the CD4 receptor on their surfaces. HIV most commonly infects T lymphocytes and other immunological system cells, especially during the late stage of inflammation. This selective infection leads to deregulation of the immune system, immune system deficiency, and eventually Acquired Immunodeficiency Syndrome (AIDS) as a final effect. During the course of AIDS, one may observe different opportunistic infections and neoplasms. Currently, there is no possibility for complete recovery from an HIV infection. In the middle of the last decade, highly active retroviral therapy was initiated (HAART). Since then, HIV/AIDS infection has changed from a mortal to a chronic disease. According to data obtained from a large multicenter trial (CHORUS-Collaborations in HIV Outcomes Research - United States), the expected survival time for a 39-year old male patient with more than 200 CD4 lymphocytes c/mcl exceeds 32 years. When the patient is not subjected to therapy, death usually occurs after an average of ten years.

According to World Health Organization data, there are more than 42 million people worldwide infected with HIV. In Poland, 11,131 infections have been diagnosed since the introduction of HIV screening (1985-08.2007). However, it is estimated that more than 50,000 residents are HIV positive. Nearly half of the diagnosed infections are due to intravenous use of intoxicating agents. These patients often undergo screening because they are aware of the risks. Thus, there is a significant use of prophylaxis in the above mentioned group. A second group of patients acquires HIV by means of heterosexual contact. Low awareness or dismissal of the risk of infection causes a delay in diagnosis, which is usually made during the symptomatic phase.

Quantity of virus sufficient for enable infection can be found in blood, sperm, genitourinary tract secretions, breast milk, and systemic fluids (cerebrospinal, peritoneal, pleural, pericardial, amniotic, and synovial fluids). Exposure to urine, nasal secretions, saliva,
sweat, and tears is not connected with a risk of infection as long as these secretions are not contaminated by blood.

Infection is possible by means of blood contact, sexual contact, and the vertical route. In case of occupational exposure, the patient is usually infected either percutaneously (injection, scratch, or cut) or following mucous membrane contact with an infected material.

HIV is very sensitive to physical and chemical factors, including standard disinfection and sterilization agents. The virus rapidly dies in external conditions.

HBV

HBV is a DNA virus belonging to the Hepadnaviridae family, and it is exceptionally resistant to physical and chemical conditions. The virus can remain active in a dried material for several weeks or even months. Investigations have demonstrated that the virus does not die in blood maintained at a temperature of either +30°C for 6 months or -20°C for 15 years. The virus is highly infectious. Just 40 nl of blood is sufficient for infection in the case of a patient with type B acute hepatitis (high viremia). The risk of infection in cases of healthy adults with a functional immune system is estimated at 1:4. Infection is possible by blood contact, sexual contact, and (least often) the vertical route (10%).

A significant feature of HBV is its ability to trigger chronic infections, which can lead to liver cirrhosis and primary hepatocellular carcinoma (HCC). HBV is primarily oncogenic. The risk for developing a chronic process depends on the patient’s age. Children infected during the perinatal period do not eliminate the virus in 90% of cases. For adults, the risk of developing a chronic infection ranges between 5-10%; roughly 20% of these cases develop liver cirrhosis (1, 2, 3). Additionally, the risk of hepatocellular carcinoma (HCC, one of the most common carcinomas in the world) in patients with chronic HBV infections is 100-fold greater than that in the healthy population; roughly 80% of patients with HCC are infected with HBC (4, 5).

The number of viral copies is a direct marker for the risk of HCC development. Irrespective of cirrhosis, viremia >10 000 copies/ml is a significant factor that affects the development of primary hepatocellular carcinoma. Even in cases of patients with positive markers of past HBV infection and undetectable viremia, however, the risk of developing HCC is greater than that in the undetectable population. It is important to remember that concomitant HCV infections enhance the risk of occurrence of the above-mentioned complications.

The World Health Organization states that nearly 2 billion people have had contact with the HBV virus, and more than 350 million people suffer from chronic type B hepatitis. Every year, there are 60 000 deaths connected with the above-mentioned infection (6). The incidence of infection varies according to geographical region. According to the WHO guidelines, Poland is recognized as a region with a low prevalence of hepatitis type B. The HBs antigen is diagnosed in 1.5% of the population (7). However, numerous epidemiological investigations have demonstrated that 7.5 to 40% of investigated subjects have had contact with HBV (i.e., exhibited the presence of anti-HBc antibodies).

The introduction of widespread vaccinations and disposable equipment led to a reduction in the number of HBV infections in Poland. The incidence of hepatitis type B infections was reduced to 1.33 per hundred thousand inhabitants in 2006; for comparison, this rate was approximately 42-45 per hundred thousand inhabitants during the 1980s (8). According to PZH, (Polish Higiene Institute) the presence of the HBs antigen is diagnosed in 1-1.5% of the population and accounts for 380 000-500 000 infected subjects. Vaccinations do not eliminate the requirement for equipment sterilization, because other infections like HCV are also transmitted via the same route. The standard cycle of inoculations against HBV does not always guarantee sufficient immunity.

Health care employees (especially those performing surgical, hemodialysis, laboratory, and intensive care unit procedures) constitute a group of people with an increased risk (4-6 times) for HBV infection.

HCV

HCV is RNA virus belonging to the Flaviviridae family. It is mainly transmitted by means of blood, although vertical (<5%) and sexual (rarely) transmission are also possible. HCV infections are usually asymptomatic, and only 25-35% of patients present with disease symptoms. In just 15% of patients, it is possible to observe the spontaneous elimination of
the virus. The remaining patients develop a chronic infection that can lead to liver cirrhosis and HCC. Contrary to HBV, HCV is a primarily oncogenic virus; HCC develops only during the course of liver cirrhosis.

According to the World Health Organization, nearly 3% of the global population (170 million inhabitants) is infected with the HCV virus. Some authors suggest that this figure approaches 300 million. The asymptomatic course of the disease is responsible for the inaccurate epidemiological data.

Poland belongs to the group of countries with a low prevalence of infected patients. According to the National Department of Hygiene at the Institute of Hematology and Transfusiology, 1.4% of the Polish population is HCV positive.

The actual incidence of this disease remains unknown due to the occult course of the disease. This disease is frequently diagnosed accidentally or during the symptomatic stage (liver cirrhosis/primary hepatocellular carcinoma) of infection. There are, on average, 3,000-5,000 new infections every year, and most of these have a chronic character. Acute cases are rarely diagnosed, and most often these diagnoses are accidental. Health care employees have a high risk for infection. Their risk of HCV infection is estimated to be 0.3-10%. During the 1990s, it was estimated that 0.3-0.7% of health service employees in the USA and Europe were infected with the virus. The most common cause of infection was attributed to injections since injection results in exposure to the largest amount of infected material.

Pre-exposure prophylaxis of health service employees

Due to the consequences of HIV, HBV, and HCV infection, pre-exposure prophylaxis seems to be the most effective method for treating patients. This method is based on both the use of personal protective agents and conforming to safety employment rules.

Exposure is possible by means of the following routes:

- percutaneous – injections or cuts by infected instruments
- mucosal contact with infected material
- prolonged contact of injured skin with infected material

High quality latex gloves are the basic means of protection. However, one should not forget to wash and disinfect the hands. Latex gloves should always be used when the risk of contact with a potentially infected material exists. For procedures with the possibility of mucosal contact with infected material, masks, protective glasses, and lead rubber aprons should be used.

Used and infected material should be stored in special containers, and sharp instruments should be stored in solid boxes. It is unacceptable to replace needles into removable holders, because there is a high risk of pricking one’s finger. Additionally, the maximum suggested volume of stored needles should not be exceeded. Overfilled containers are subjected to damage during closure, and their contents constitute potential infectious material.

Biological contamination should be rapidly removed using disinfectant agents. HBV is resistant to physical and chemical factors, whereas HIV rather susceptible. Disinfection and sterilization methods covering the spectrum of all viruses should be applied. Instruments contaminated with biological material should be sterilized in an autoclave for a period of at least 20 minutes at a temperature of 120°C. Ethylene oxide is recommended for devices sensitive to heat. Agents containing chlorine and 2% glutaraldehyde are recommended for disinfection.

In cases of HBV infection, vaccinations make specific prophylaxis possible. In Poland, second generation recombinant vaccines containing protein S HBV are currently used. In Europe, third generation vaccines containing pre-S1 and pre-S2 proteins are available. The above-mentioned vaccines are recommended for subjects who do not develop a proper post-inoculation response following standard vaccinations (anti-HBs antibody titer >10 IU/ml).

These vaccines are considered safe for both pregnant and breast-feeding women. They are characterized by high immunogenicity, and more than 95% of subjects vaccinated with three doses produce a protective titer of antibodies. The basic scheme for inoculation is comprised of three doses administered at 0, 1, and 6 months. Booster doses are no longer necessary due to lifetime cellular immunity. Health service employees and students are provided with inoculations through the national prophylactic vaccination program.

However, one should bear in mind that vaccinations do not protect against other hepatotropic viral infections.
No effective prophylactic vaccine against HCV infection is presently available. Advanced investigations are under way, however, and it is estimated that the first vaccine will be available in 2015.

Post-exposure prophylaxis (PEP)

Contrary to pre-exposure prophylaxis, post-exposure management is aimed at 1) minimizing the risk of viral transmission after contact with an infected material and 2) preventing the development of a permanent chronic infection. Non-specific management reduces the risk of HIV, HBV, and HCV infections. Specific management is only possible in cases of HIV and HBV infections.

Non-specific management

In case of an incision or cut wound, the flow of blood should not be inhibited. The “squeezing” of blood is not recommended due to possible hypotension that can, in turn, aspirate the biological material. The wound should immediately be cleansed of the infected material under running water with the use of soap. Disinfection with agents capable of protein denaturation is not recommended. In case of mucosal contact with an infected material, lavage should be initiated.

If possible, a single dose of 250-300 mg of zidovudine (Retrovir, AZT) should be administered as an element of HIV infection prophylaxis during the first two hours after exposure. Superiors should be informed of the exposure, and advice from regional specialty centers specializing in post-exposure prophylaxis should be sought. These specialty centers are typically infectious disease departments or clinics.

In post-exposure prophylaxis, both the exposed person and the source of the exposure are subjected to serological examinations if possible.

THE SOURCE OF EXPOSURE: HBsAg, (anti-HBc), anti-HCV, and anti-HIV results are necessary. In selected cases, infectious disease specialists may decide to subject patients to molecular examinations. One should bear in mind that examinations concerning the source of exposure are supplemental, since one can obtain false-negative results in cases of recent exposure. When exposure is considered as highly risky, post-exposure prophylaxis is initiated. Nevertheless, one should immediately determine the serological status of the source of exposure. In some countries, examinations concerning the source of exposure for health service employees require patient consent. In the European Union, such consent is mandatory.

THE EXPOSED PERSON

- As soon as possible after exposure, levels of anti-HIV, anti-HCV, anti-HBc, and HBsAg should be measured in non-vaccinated subjects. The anti-HBs titer should be measured in inoculated patients.
- If exposure was connected with the risk of transmission, anti-HIV and anti-HCV levels should be measured after 6 weeks, 3 months, and 6 months; anti-HCV levels should be measured after 12 months.

Evaluation of the risk of infection

Both the initiation and type of post-exposure prophylaxis are decided upon by the infectious disease specialist based on the predicted risk of exposure. Increased risk of transmission is influenced by many factors, such as frequent and deep cuts, incisions by means of instruments containing a large amount of blood (e.g. injection needles), the absence of protective gear (latex gloves), significant viremia in the source, and a lack of post-exposure prophylaxis initiation despite evident indications. Thus, all data concerning the source and character of the exposure are quite important. For secondary personnel without access to medical documentation, data obtained from the attending or on-duty physician may qualify the source independently of the type of exposure to high or low risk of infection.

According to the Centers for Disease Control (CDC) classification, the average risk of HIV transmission after exposure to a significant risk factor (e.g. needle pricking, direct needle removal from the vein, high source viremia, or direct contact with blood) is estimated to lie between 1:100 and 1:1000. This value is ten times lower for HCV and one hundred times lower for HBV (tab. 1). The use of latex gloves reduces the risk of HIV and HCV transmission, because most of the blood localized on the surface of the needle or scalpel is wiped away during the passage through the latex. On average, skin continuity disruption can be observed once in every 25 procedures. In the United States, models have been established to determine the predicted risk for health service employee contamination. Throughout their medical careers, surgeons have an estimated infection risk that depends on the
Table 1. Comparison of HIV, HBV, and HCV infections

<table>
<thead>
<tr>
<th>Source of infection</th>
<th>Probability of infection</th>
<th>Risk of chronic infection</th>
<th>Efficacy of specific post-exposure prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg(+) / HBeAg(+)</td>
<td>nearly 30% (max. &gt;60%)</td>
<td>&gt;70%</td>
<td>high</td>
</tr>
<tr>
<td>anty-HCV (+) / anti-HCV (+)</td>
<td>nearly 3 %</td>
<td>100%</td>
<td>high</td>
</tr>
<tr>
<td>anty-HIV (+) / anti-HIV (+)</td>
<td>nearly 0.3%</td>
<td>100%</td>
<td>high</td>
</tr>
</tbody>
</table>

Prevalence of HIV; their risk of infection is 0.0015 when the index of infected subjects is lower than 1% and 0.015 when the index exceeds 1%. In Poland, the HIV index is significantly lower than 1%.

HIV prophylactic therapy – specific management:

In order to reduce the probability of a chronic infection after a high risk of HIV infection exposure, patients should receive antiretroviral medication. Therapy should be initiated within the first 72 hours after exposure, although drugs should be administered immediately to avoid the risk of chronic infection. During a period of 28 days, patients must receive at least two therapeutic agents; after high risk exposure, they should receive three.

The therapeutic scheme is established by an infectious disease specialist, and it varies depending on the serological status of the source, history of antiretroviral treatment, risk of exposure, and potential side-effects of the medication. Due to the differences in available therapeutic recommendations and constant changes, we have not mentioned specific preparations in this study. It is essential that the selection of medications considers the possibility of infection with drug-resistant HIV strains. Thus, treatments should differ from the therapeutic agents used to treat the source of the exposure.

It is also important to avoid behaviors that may expose other subjects to infection until serological examination results prove negative.

In cases of confirmed HIV infection after exposure, postexposure prophylaxis (PEP) is not initiated.

Specific management in cases of exposure to HBV infections

Evaluation of the risk of infection is similar to that for HIV. For subjects sensitive to infection, the risk is significantly higher than that for HIV infections and often exceeds 60%.

In addition to its non-specific actions, a significant role is attributed to active or active-passive prophylaxis.

Sensitive subjects who were either not vaccinated or ineffectively vaccinated should receive specific anti-HBs serum followed by a cycle of inoculations. Those subjects effectively vaccinated who have a protective anti-HBs antibody titer (a titer higher than 1:10) require no prophylaxis. Prophylaxis is not needed for subjects with markers of past HBV infections [anti-HBc (+)].

CONCLUSIONS

HBV, HCV, and HIV infections are connected with serious consequences (tab. 1). Thus, a number of questions remain. Should we be afraid of patients? Should we determine hepatotropic virus and HIV infection markers during occupational exposure prophylaxis? Should patients with possible exposure be isolated and subjected to refined methods of management? The answer is NO! In addition to the questionable ethics of such management and eventual stigmatization of the patient, one should bear in mind both the serological window and the limited sensitivity of serological tests that can render false negative results. Moreover, new pathogens requiring specific diagnostic methods may appear in the future. Thus, the most effective course of action is to treat all patients as if they are potentially infected. Using such methods during everyday work will minimize the risk of infection.

Exposure is most often connected with inattention or errors. Thus, simple procedures adapted to the conditions of a given department in addition to adherence to suggested rules significantly reduces the risk of occupational exposure. In model departments, such as the Department of Infectious Diseases, Liver Diseases, and Acquired Immunodeficiency Diseases of the Medical Academy in Wroclaw, risks
of exposure are rarely observed despite frequent contact with infected patients and numerous invasive procedures.

The accumulation and analysis of data concerning the frequency and type of exposure in a given department is highly valuable, because it enables departments to create a prophylaxis strategy and avoid future errors. Thus, close cooperation with the department of hospital infections control is recommended.

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