Are medical students sufficiently vaccinated?¹⁾

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Abstract

Medical students are exposed to infectious diseases during the course of their clinical training. Unfortunately, vaccination rates among medical students remain insufficient. However, immunizations against vaccine-preventable diseases should be carried out before the students enter clinical courses. This is vital in order to prevent nosocomial infections. We screened 366 medical students in their first clinical year for hospital-related viral diseases. Serum samples were collected between April and May 2007. Antibody testing was carried out using commercial ELISA systems against measles, mumps, rubella, varicella, hepatitis B (HBV), hepatitis C (HCV), and human immunodeficiency virus (HIV). Overall, 63.9% (n=234) of the students were sufficiently vaccinated against HBV. In contrast, 31.7% (n=116) had not received any HBV vaccine dosage, and 4.4% (n=16) had not completed the full vaccine cycle (<3 dosage). Remarkably, two students showed serological markers of resolved HBV infection. In addition, one student was HCV-positive and one was HIV-positive, respectively. The following seronegative rates were found: measles (7.9%), mumps (17.5%), rubella (6.5%), and varicella (2.2%). Further work is needed to identify optimal strategies for improving vaccination rates among medical students. It is imperative to identify and limit possible disparities in immunity of vaccine-preventable diseases before initial patient contact. With regard to the primary diagnosis of

serious virus diseases including HBV, HCV and HIV, medical students should be screened for these blood borne pathogens.

Keywords: blood borne infection; medical students; vaccine uptake rates.

Introduction

Through direct contact with patients and patient material (blood, saliva, etc.) the risk of infection is higher for healthcare workers (HCWs) than for other occupations. Additionally, medical personnel can be a source of infection, particularly for non-immunocompetent patients [1, 2].

Although both effective and well-tolerated vaccines against many (viral) infections are available and appropriate vaccinations are recommended to these occupationally exposed groups, the vaccination status of HCWs and of medical students is insufficient [3–7].

However, adequate vaccine protection or immune status of medical students is important not only to protect students from nosocomial infections, but also to avoid any iatrogenic transmission to the patients. Pediatric wards and isolation wards in particular contain a variety of infection risks [8, 9]. Furthermore, HCWs should know whether they are HIV- or hepatitis C (HCV)-positive and whether they are immune to hepatitis B (HBV), measles, mumps, rubella (MMR), varicella (VZV) and pertussis.

The aim of this study was to determine the immune status of medical students in the first clinical semester at the Johann Wolfgang Goethe-University Frankfurt. For this purpose, we performed serological analyses:

1. Viral diseases, preventable through vaccination (HBV, MMR, VZV).
2. Viral, blood-transmitted diseases (HBV, HCV, HIV).

These data were to provide information on the current immune status of the students, on necessary vaccinations and on further measures in cases of potentially infectious students.

Materials and methods

During April and May 2007 we examined a total of 366 serum samples from medical students in their first clinical semester at

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Johann Wolfgang Goethe-University Frankfurt. Included were 228 females (62.3%) and 138 males (37.7%). The average age of the students was 24.4 years (range 19.8–48.2 years). For clarification of the immune status we performed antibody tests for MMR, VZV, HBV and HCV in serum. Altogether 345 (94.3%) of the medical students voluntarily agreed to be examined for HIV.

The samples were analyzed at the Institute for Medical Virology of the University hospital Frankfurt. If an analysis could not be performed promptly following blood collection, the serum samples were stored at -20°C .

The detection of the above named virus-specific IgG antibodies was achieved via commercially available test kits, which were processed according to the manufacturer's instructions.

Rubella-specific IgG antibodies were tested by means of Liaison Rubella IgG (DiaSorin Deutschland GmbH, Dietzenbach, Germany). Where a test result did not clearly prove immunity, we additionally performed the hemagglutination-inhibition assay (HHT) (Siemens/Dade Behring, Marburg, Germany). Values higher than 1: ≥ 32 (HHT) or ELISA values ≥ 35 IU/L were defined as sufficient rubella immunity, whereas ELISA values between 15 and 34 IU/L or an HHT titer of 1:16 were classified as low level immunity.

Anti-measles IgG, anti-mumps IgG, and anti-VZV IgG were performed with Enzygnost test kits: (Siemens/Dade Behring, Marburg, Germany) and tested by means of a Behring ELISA processor BEP 2000. Clearly positive test results were classified as "sufficient immunity".

In order to evaluate the immunity situation we established the following categories:

- immune
- "low-level"/borderline: no evidence of certain immunity
- not immune: seronegative test results.

In the case of students without a history of hepatitis B vaccination we examined anti-HBc. In the case of students with complete hepatitis B vaccination we examined anti-HBs. In the case of negative anti-HBs post vaccination we also determined anti-HBc. In the case of positive anti-HBc we determined anti-HBs and HBsAg.

Hepatitis B and hepatitis C parameters were established by means of an Architect (CMEIA) or AxSYM MEIA test in accordance with manufacturer's instructions (Abbott, Wiesbaden, Germany) (anti-HBc: AxSYM core; anti-HBs: Architect anti-HBs; HBsAg: Architect HBsAg).

Hepatitis C-specific antibodies were determined by means of EIA in the Vitros ECI Automat (Ortho Clinical Diagnostics, Neckargemünd, Germany). Reactive samples were examined in the Line Immunoblot Assay (INNOLIA™ Score; Fa. Innogenetics/Bayer Corporation, Wuppertal, Germany). A reactive HCV immunoblot prompted a polymerase chain reaction (PCR) (Cobas Taqman, Fa. Roche Molecular Diagnostics; Mannheim, Germany) and, if necessary, a genotype analysis (Versant HCV Genotype 2.0 Assay; Bayer Corporation, Wuppertal, Germany).

Screening for anti-HIV occurred by means of the AxSYM HIV 1/2 gO MEIA test (Abbott) and in the HIV Ag/Ab Combo Assay, Architect (Abbott).

Results

A total of 63.9% ($n=234/366$) of medical students had received a complete hepatitis B basic immunization

(three vaccinations) and were anti-HBs seropositive. Of these vaccinated students, 70.9% ($n=166/234$) showed an anti-HBs >100 IU/L and 68 students (29%) an anti-HBs of 10–100 IU/L (Figure 1).

At the time of the study a total of 116 students (31.7%) had not yet been vaccinated against HBV and 16 students (4.4%) had received an incomplete HBV vaccination of one or two doses of vaccine.

Two students had suffered an HBV infection, serologically verified with positive anti-HBc and anti-HBs (HBs antigen negative).

One female student was diagnosed with a Hepatitis C infection. A quantitative polymerase chain reaction (PCR) showed a virus load of 2.8 Million IU/mL and a genotype 1. This student received antiviral therapy, consisting of pegylated interferon- α -2a in combination with ribavirin for 24 weeks and the HCV protease inhibitor telaprevir for 12 weeks. Fortunately, no HCV-RNA was detectable in serum at 6 and 12 months after the termination of therapy, so that it may be assumed that this therapy was of lasting success.

One of the 345 students, who agreed to an HIV test (94.3%), was anti-HIV seropositive. Virus load was around 51.700 copies/mL. A phylogenetic analysis of the pol region identified the subtype G. CD4+ cells were at 372 cells/ μL and CD8+ cells at 929 cells/ μL , which did not indicate anti-retroviral therapy at the time of the diagnosis.

The results of mumps serology showed that 64 students (17.5%) had no specific mumps anti-bodies, whereas 302 (82.5%) of the students were seropositive. A total of 261 students (71.3%) demonstrated sufficient immunity and 41 students (11.2%) showed no certain immune protection (Figure 2).

IgG antibodies specific to measles were found in 338 (92.2%) of the students we examined, of which 11.1% ($n=41$) showed borderline immunity. A total of 7.9% of students ($n=29$) were seronegative (Figure 2).

Figure 1 Hepatitis B vaccination status of medical students in the first clinical semester ($n=366$).

Of completely vaccinated students ($n=234/63.9\%$) 70.9% ($n=166$) showed an anti-HBs >100 IU/L; 29% ($n=68$) showed an anti-HBs between 10 and 100 IU/L.

Figure 2 Prevalence of measles, mumps, rubella and varicella antibodies in the examined medical students (n=366).

Remarkably, 6.5% (n=24) of students also had no rubella-specific antibodies. A total of 93.5% (n=342) of the specimens we examined were seropositive, of which, however, only 262 (71.6%) exhibited sufficient immunity (Figure 2).

Only 2.2% of the students we examined were seronegative in regard to varicella (n=8). A total of 358 (97.8%) students had VZV-specific antibodies, of which 347 (94.8%) showed sufficient varicella immunity and 11 (3%) showed borderline immunity (Figure 2).

Discussion

In comparison to other professional groups HCWs have a higher risk of infection. Nevertheless, national as well as international studies have provided proof of insufficient immunity protection and a lack of booster vaccinations for HCWs as well as medical students [2, 5, 6, 9–11]. The implementation of existing vaccination recommendations is insufficient [3, 4].

However, in order to avoid outbreaks of nosocomial infections, HCWs should be adequately vaccinated at the very beginning of their medical training [9].

In the collective of students we studied during the students' first clinical semester mumps was found to have the highest seronegativity rates (17.5%). Similar values were shown by a Swiss study, where 15% of medical students were seronegative [6]. In the past years there have repeatedly been worldwide outbreaks of mumps. For this reason the effectiveness of the mumps component of the trivalent MMR vaccine has been disputed by various authors [12, 13].

Measles-specific antibodies could be identified in 92.2% of the Frankfurt students; 81.1% of the students examined, showed sufficient immunity against measles. Comparable immunity rates were also published in yet another study [14].

A noticeably higher rate of measles-seronegative students was presented in a Swiss study, where 15% of medical students had no measles-specific antibodies [6].

However, against the background of repeated measles outbreaks [15–17] immunity against measles in medical personnel is of greatest importance. In all probability measles will not be eradicated in Europe by 2010 as planned. The reason for not achieving this target of the World Health Organization (WHO) is lacking acceptance of vaccination, predominantly in the countries of Germany, Rumania, Great Britain, Italy and Switzerland. A total of 12132 measles cases were registered in Europe in the years 2006 and 2007, of which seven resulted in death. Altogether 85% of cases occurred in the five countries named above. While the WHO recommends a vaccination rate of at least 95% of a population to eradicate the disease, the vaccination rate in Switzerland, Italy and Great Britain was between 80 and 90% and in Germany it was even less at only 70%. This is problematic also, because Europeans again and again bring measles into countries with poor health systems [18].

A total of 6.5% of the students we studied were seronegative for Rubella, while 93.5% showed rubella-specific antibodies. Similar rates of seronegative medical students were found at the University hospital Basel (8%) [6]. Comparable immunity rates were also found in an Italian university clinic, where 94.5% showed rubella-specific antibodies [8]. Earlier studies by our work group from the year 2005 also proved such similar immunity rates [7, 19]. In contrast, an Australian study presented higher rates for seronegativity: here 33% of medical students in their first clinical year had no immunity against mumps, 26% had no immunity against measles and 13% lacked immunity against rubella [5]. The vaccination status of medical students in Slovenia on the other hand was very good: 96.4% were immune against measles, 97.8% were immune against mumps and 99.3% were immune against rubella [1].

In our cohort 2.2% showed no immunity and 3% showed borderline immunity against varicella. Comparable data have been reported from Italy, where 94.1% of students showed VZV-specific antibodies [8]. In contrast, 10% of the students examined in an Australian study were not immune against varicella [5].

Virus infections like measles and varicella exhibit a high contagiousity index and for non-immune HCWs they represent a relevant, occupational health risk [8, 11]. In order to avoid occupational infections, existing vaccination recommendations should be implemented consistently.

At the same time, when evaluating laboratory-diagnostic detections of virus-specific antibodies, we have to bear in mind that these verify only specific immunity rates and do not inevitably prove individual protection. Individual immunity essentially is secured through specific memory cells, whose verification at this time is not yet routinely available.

To lessen the risk of blood-transmitted virus infections, all HCWs with direct patient contact or with contact to potentially infectious patient materials should be vaccinated against HBV and they should consistently follow standard hygiene precautions. In this connection hand

hygiene as well as wearing appropriate personal protection (e.g., gloves, surgical masks), as well as the use of so-called safe instruments and the proper sterilizing of devices or the adequate disposal of the instruments used play a crucial role.

During the serologic examinations of the Frankfurt medical students a total of nine first-time diagnoses of infectious, blood-transmitted virus infections (HBV, HCV, HIV) were made in the past 5 years. These were two HIV infections, three HCV infections and four HBV infections. Within the framework of our study here introduced we diagnosed a subsided HBV infection in two students (corresponds to 0.5%) of the examined collective and in two others we diagnosed, respectively, one HCV and one active HIV infection (each corresponds to 0.3% of the examined collective). A comparison with the frequency in the German "general population" (HBV/HCV/HIV prevalence: 5%–7%/0.4%/0.07%) shows that the rate of infection of the students with HBV is significantly lower, while their rate of infection with HCV and HIV is within the confidence interval.

Dealing with infectious employees in the health services requires great care and appropriate risk assessment. There should be a balancing of interests between the risk of a nosocomial infection of the patient and the employee's freedom to practice his or her profession (§12 of the German Constitution). Both the interests of employees as well as the interests of the patients in physical safety (§2 of the German Constitution) must be safeguarded [20]. From the perspective of occupational medicine and virology it is desirable that any possible infections are recognized early. This would mean that those involved can receive adequate therapy and that the risk of a nosocomial transmission of an infection can be lowered. For this reason serologic studies of medical students are an important measure to be able to ensure adequate occupational medical care.

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