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IMPACT OF VACCINATION AGAINST HBV ON HEPATITIS B INCIDENCE IN OPOLSKIE PROVINCE IN 2007 - 2011

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ABSTRACT

OBJECTIVE. This article aimed at evaluating the impact of HBV vaccination in population included and not listed in the National Immunization Programme (NIP) on hepatitis B incidence in Opolskie province in 2007 – 2011.
MATERIAL AND METHODS. Analysis was based on data provided by the Sanitary and Epidemiological Inspection under epidemiological surveillance conducted, i.e. MZ-56, MZ-57 reports (reports on cases of infectious diseases), MZ-54 reports (reports on vaccinations) and 'Questionnaires on hepatitis type B and C'. A total of 446 records of detected and confirmed hepatitis B cases, registered in 2007-2011 in district sanitary and epidemiological stations, were subject to analysis.
RESULTS. In 2007–2011, hepatitis B incidence in Opolskie province was higher compared to the average incidence in Poland and was increasing in the successive years (5.8; 6.6; 7.9; 11.8; 11.0 per 100,000 population). An increase of incidence resulted from increasing number of patients with chronic hepatitis B (chronic HBV), i.e. from 47 in 2007 to 119 in 2010 and 110 in 2011 compared to decreasing number of acute infections (acute HBV). In the analyzed period, no new infections were reported in the following age group 0–9 years in Opolskie province. Only 3 cases (chronic stage) were noted in the age group 10–14 years. Of 446 patients, diagnosed with hepatitis B, 309 (69.3%) were not vaccinated. The remaining cases of acute or chronic hepatitis B were vaccinated, including 124 (27.8%) and 13 individuals with complete and incomplete vaccination, respectively.
CONCLUSIONS. This analysis suggests an important role of HBV vaccination in the prevention of HBV infections. In case of individuals at the age older than that specified in the NIP, especially adults, it is recommended to perform diagnostic tests for HBV infection prior to vaccination. Furthermore, it is required to undertake activities aimed at promoting HBV vaccination in populations which are not included in the NIP.

Key words: *hepatitis B, HBV infection, HBV, chronic hepatitis B, acute hepatitis B, vaccination*

INTRODUCTION

Currently, hepatitis B is one of the most serious public health problems globally due to its incidence, HBV integration into the host genome, potentially irreversible health-related consequences (cirrhosis of the liver, accompanied by sequelae and complications and hepatocellullar carcinoma), as well as socio-economic effects. Number of HCV-infected individuals, actively replicating virus, is estimated at approximately 400 million and 320,000 in the world and Poland, respectively. In the last 20 years, there was a considerable improvement of epidemiological situation of hepatitis B in Poland (number of infections and incidence decreased by more than 90% between 1979 and 2004). Undoubtedly, such decrease resulted from: improvement of life conditions, enhancement of standards of medical procedures associated with tissue breakdown, implementation of modern sterilization methods and autoclaving of medical devices, prevalent use of disposable devices, and, above all, introduction of obligatory HBV vaccination to vaccination programme (1,2,3).

Vaccination against HBV was commenced in 1982, using a first generation plasma-derived vaccine, in which hepatitis B surface antigen (HBsAg) was vaccine antigen. In 1986, a second generation vaccine was launched. It was produced, using yeast cells in recombinant DNA technology, where plasmid carrying coding sequences for HBsAg was inserted. Third generation vaccines are also administered globally. They are ap-

plied in the majority of countries, however, in Poland they have not been even registered (4,5,6).

Second generation vaccines against HBV may be monovalent and combined vaccines. Currently, monovalent vaccines in doses for adults and children are registered: Engerix B (GSK), HBVaxPro (MSD), Hepavax Gene TF (CRUCELL), Euvax (LG Life Sciences) and combined vaccines, in which HBsAg co-occurs with vaccine antigens, i.e.: Twinrix Junior and Twinrix Adult (GSK) – against infections with HBV and HAV and Infanrix Hexa (GSK) – against hepatitis B, diphtheria, tetanus, pertussis, poliomyelitis, Haemophilus influenzae type B in doses for children aged up to 3 years (5,7).

In Poland, obligatory vaccination against HBV was introduced to the National Immunization Programme (NIP) in 1989. Newborns and infants born to HBV-infected mothers were vaccinated at that time (4,6). In the successive years, obligatory vaccination was gradually becoming available for other groups:

- 1990 – health care workers, students of medical universities and pupils of medical schools;
- 1993 – individuals prior to planned surgeries (vaccination was available free of charge until 2001), those with chronic diseases and having close contact with HBV-infected cases;
- 1994 - 1996 – all newborns (vaccination is available in Opolskie province since 1996);
- 2000 – adolescents aged 14 years (the first and last were individuals born in 1986 and 1995, respectively);
- 2003 – dialyzed patients or those subject to surgeries under extracorporeal circulation – this group was excluded in 2012 (6,8,9,10).

Furthermore, the National Immunization Programme stipulates that vaccination against HBV is recommended for individuals exposed to the risk of HBV infection resulting from: lifestyle, occupation, health status, planned surgeries, travelling to the countries of high hepatitis B endemicity. In such cases, vaccination is not obligatory, but it is payable (8,10,11).

Probably, vaccine-induced and natural immunity are long-term, providing life-long protection. Immunity against HBV is measured by the concentration of anti-HBs antibodies in blood. Protective level against HBV was determined at ≥ 10 mIU/mL. In case of 96% of healthy individuals who received vaccination, immunity response is very good and anti-HBs antibodies are of high titres. Few individuals, i.e. approximately 4%, are not to respond to vaccine and anti-HBs are not detectable or very low, not exceeding the protective level. Poorer response or its lack is usually reported in older individuals, those with immunodeficiencies, chronic diseases and cancers. Such individuals are recommended to receive additional dose of vaccine, i.e. booster dose. Provided they still do not respond to vaccination, it is recommended to undergo revaccination with double-dose of vaccine. Non-response to revaccination with double-dose of vaccine should be considered as sustained non-response to vaccination and it should not be repeated (1,4,5,9,13).

MATERIAL AND METHODS

Impact of HBV vaccination on hepatitis B incidence in Opolskie province in 2007-2011 was evaluated based on data retrieved from MZ-56 reports – 'Biweekly, quarterly and annual reports on cases of infectious diseases and poisonings in Poland', MZ-57 reports – 'Annual report on cases of selected infectious diseases by gender, age, place of residence and its seasonality", MZ-54 reports – 'Annual reports on vaccinations' and 'Questionnaires on hepatitis type B and C', collected by DSES workers under epidemiologic investigation.

Epidemiological analysis was based on 446 records of individuals with detected and confirmed hepatitis B, who were notified and registered between 1st January 2007 and 31st December 2011 by district sanitary and epidemiological stations in Opolskie province, competent with regard to the place of residence of patients.

RESULTS

Impact of HBV vaccination on hepatitis B incidence was analyzed, using data on: number of cases, stage of infection (acute, chronic), age of patients (patients were classified into 15 age groups) and vaccination coverage against HBV.

Analysis of epidemiological situation as of 2007 – 2011 suggests that hepatitis B incidence in Opolskie province was statistically significantly higher compared to the average incidence in Poland. Furthermore, it was continually increasing in the successive years – from 5.8 in 2007 to 11.0 in 2011 (Tab.I).

Table I. Hepatitis B* in Opolskie province and Poland, number of cases and incidence per 100,000 population in 2007 - 2011

Year	Opolskie province		Poland	
	number of cases	incidence	number of cases	incidence
2007	60	5.8	1454	3.81
2008	68	6.6	1337	3.51
2009	82	7.9	1475	3.87
2010	122	11.8	1633	4.28
2011	114	11.0	1584	4.15

*including HBV/HCV co-infections

Having analyzed hepatitis B cases by the stage of infection, i.e. acute and chronic, an increasing number of patients with chronic hepatitis B was demonstrated (from 47 in 2007 to 119 in 2010 and 110 in 2011), compared to decreasing number of acute hepatitis B cases. In total, the percentage of chronic and acute hepatitis B cases in the analyzed five years amounted to 91.3% and 8.7%, respectively (Tab.II).

Table II. Number of cases and incidence of acute and chronic hepatitis B* in Opolskie province compared to Poland

Hepatitis B							
Year	Total	acute			chronic		
		number of cases	%	incidence	number of cases	%	incidence
2007	60	13	21.7	1.3	47	78.3	4.5
2008	68	10	14.7	1.0	58	85.3	5.6
2009	82	9	11.0	0.9	73	89.0	7.1
2010	122	3	2.5	0.29	119	97.5	11.55
2011	114	4	3.5	0.39	110	96.5	10.69
Total	446	39	8.7	0.77	407	91.3	7.89

* including HBV/HCV co-infections

To evaluate the impact of HBV vaccination on the incidence of hepatitis B, the total number of cases was grouped by age into the following 15 age groups: from 0-4; 5-9 to 65-74 and 75+. It was determined that no infections were reported for age groups: 0-4 and 5-9 years while only 3 cases occurred in individuals aged 10–14 years (exclusively chronic cases). The highest number of cases was noted in the following age groups - 15-19 and 20-24 years with 70 (including only one acute HBV infection) and 71 infections (including 3 acute HBV infections), respectively. In the age groups 15-19 and 20-24 years, a marked increasing tendency of infections between 2009 and 2011 was reported, irrespective of the fact that this population was subject to vaccination under the National Immunization Programme at the age of 0 and 14 years (Tab.III).

Table III. Hepatitis B* in Opolskie province, number of cases by age group

Age group	Total	Number of HBV cases by years:				
		2007	2008	2009	2010	2011
0–4	0	0	0	0	0	0
5–9	0	0	0	0	0	0
10–14	3	0	2	1	0	0
15–19	70	9	8	15	17	21
20–24	71	7	5	13	24	22
25–29	44	8	6	11	10	9
30–34	49	7	7	12	10	13
35–39	50	4	8	9	20	9
40–44	26	2	7	1	6	10
45–49	28	4	7	6	7	4
50–54	27	4	8	1	4	10
55–59	18	5	1	3	5	4
60–64	15	1	3	4	4	3
65–74	26	5	2	5	8	6
75+	19	4	4	1	7	3
Total	446	60	68	82	122	114

* including HBV/HCV co-infections

VACCINATION AGAINST HBV

Based on reports on vaccination coverage, it was demonstrated that introduction of vaccination for all newborns since 1996 and adolescents aged 14 years since 2000 in Opolskie province, provided protection for children and adolescents in the analyzed period to a very high extent, i.e.:

- up to 2007, 80.8% of persons aged 0-21 years were vaccinated against HBV (only 46.6% of 12-year-olds, i.e. those born in 1995 were vaccinated as they were not included in the NIP);
- up to 2008, the percentage of vaccinated individuals aged 0-22 years increased to 98.3%;
- up to 2009, the percentage of vaccinated individuals aged 0-23 years increased to 98.9%;
- up to 2010, the percentage of vaccinated individuals aged 0-24 years increased to 99.0%;
- up to 2011, the percentage of vaccinated individuals aged 0-25 years increased to 99.1% (14,15).

From the data transpires that since 2007, the number of individuals vaccinated against HBV was gradually increasing within the execution of the NIP. Therefore, after 2011, individuals aged more than 25 years were not vaccinated.

Analysis of data retrieved from epidemiological questionnaires, collected by the workers of sanitary and epidemiological stations, suggests that out of 446 hepatitis B cases registered in Opolskie province in 2007 - 2011, 309 individuals did not receive HBV vaccination (69.3%). Among the remaining individuals vaccinated, 124 (27.8%) underwent complete vaccination (3 doses) and 13 received incomplete vaccination (10 and 3 individuals were vaccinated with 2 doses and 1 dose, respectively) (Fig.1).

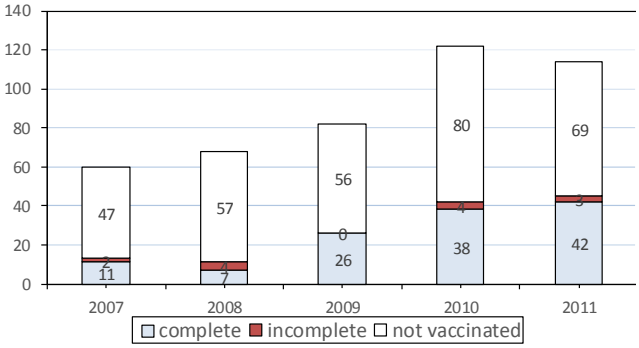

Fig. 1. Vaccination coverage against HBV in hepatitis B cases in Opolskie province in 2007 – 2011

DISCUSSION

Compared to Poland, epidemiological situation of hepatitis B in Opolskie province in 2007-2011 differed considerably. In Poland, HBV incidence rates generally remained stable, while in Opolskie province they were on the increase from year to year, exceeding more than twofold the average for country. It should be highlighted, however, that an increase of registered cases in Opolskie province could be associated not only with increased incidence, but also with improved detection and registration of cases, e.g. due to testing for HBV performed by a part of laboratories or a range of informative, educational activities and prophylactic programmes (Yellow Week (Żółty Tydzień), Yellow Decade (Żółta Dekada), STOP! HCV).

Irrespective of higher HBV incidence rates in Opolskie province compared to other provinces, a positive impact of vaccination on restricting the number of HBV infections was observed. In the analyzed period, a decreasing incidence of acute hepatitis B was reported (from 1.3 in 2007 to 0.39 in 2011), while no acute HBV infections were registered in 0-14 age group and only sporadic cases were observed in individuals aged 15-19 and 20-24 years. Undoubtedly, it is associated with obligatory vaccination against HBV which was introduced in 1996 as well as active-passive management of newborns born to HBV-infected mothers.

Having analyzed hepatitis B cases by the stage of infection, registered in Opolskie province, it was stated that chronic stage predominated over acute stage. Since 2007, an increasing tendency of chronic compared to acute stages was reported in the successive years. Such predominance of chronic stages of infection seems to result mainly from the improvement of sanitary standards in health care units as well as HBV vaccination.

Analysis of data from epidemiological questionnaires suggests that out of 446 individuals, who were diagnosed with hepatitis B in the analyzed period, 309 (69.3%) did not receive HBV vaccination, while 13 (2.9%) individuals did not undergo complete vaccination. The fact that 72.2% of patients, who were not vaccinated against HBV or underwent incomplete vaccination, contracted hepatitis B (out of all hepatitis B cases), underscores an important role of vaccination in the prevention of HBV infections.

Irrespective of data from epidemiological questionnaires, suggesting complete HBV vaccination, a total of 124 (27.8%) individuals were diagnosed with hepatitis B. Such situation should raise concerns. It cannot be, however, entirely explained as serologic status of these individuals prior to vaccination was not known. It should be presumed that individuals previously infected with HBV were present in that group and thus, they were unnecessarily vaccinated under obligatory (mainly as 14-year-olds) or recommended vaccination. It seems to be highly probable as the highest number of infections was reported in the following age groups: 15-19 and 20–24 years, who were immunized in nearly 100% (70 and 71 cases, respectively). Furthermore, the highest number of infections was registered in 2010 and 2011, i.e. years in which individuals aged up to 25 and 26 years were subject to vaccination. Moreover, having analyzed HBV infections by acute and chronic stage of infection in the aforesaid age groups, i.e. 15-19 and 20–24 years, it was declared that the majority of cases had chronic hepatitis B (69 and 68 cases, respectively). It may be also indicative of contracting HBV infection prior to vaccination in the majority of such patients.

There is also a possibility that infections in vaccinated individuals were with regard to those that underwent incomplete vaccination and did not provide that information or neither humoral nor cell-mediated immunity was achieved following complete vaccination. Available studies suggest that HBV vaccine results in protective response in approximately 96% of healthy vaccinated individuals, while the remaining 4% are those who do not respond to vaccination or vaccine-induced immunity is not sufficient enough, with antibody titres not exceeding the protective level, i.e. below 10 IU (4,6) .

CONCLUSIONS

Evaluation of HBV vaccination impact on hepatitis B incidence in Opolskie province showed an important role of vaccination in the prevention of HBV infections. From the analysis transpires that HBV vaccination is not always justified, e.g. in situations where no diagnostics was performed to verify past/active HBV infection prior to vaccination – testing for total anti-HBc is a required minimum (excluding newborns covered by the NIP). It seems to be advisable to verify the effectiveness of vaccinations performed by determining anti-HBs titres, especially in case of individuals at higher risk of HBV infection, i.a. health care workers, dialyzed patients, those with immunosuppression, having close contact with chronic HBV cases and subject to planned surgeries.

Lack of awareness in vaccinated individuals on the probable past history of HBV infection and lack of evaluation of HBV vaccination effectiveness may negatively influence the course of HBV infection due to delayed diagnosis and treatment. Moreover, it poses an epidemiological threat as hepatitis B virus may be further transmitted in the population.

To improve the epidemiological situation of HBV infections, it is required to conduct planned, systematic actions aimed at promoting HBV vaccination, especially

in individuals who are at increased odds of contracting HBV infection and are not included in the NIP.

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