Effect of Hepatitis A vaccination programs for migrant children on the incidence of Hepatitis A in the Netherlands

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Background: Since 1998 Municipal Public Health Services (MPHSs) in the Netherlands carried out Hepatitis A (HAV) vaccination programs for Turkish and Moroccan children to reduce import and secondary HAV infections. The aim of this study was to assess the effects of the programs on HAV incidence. Methods: MPHSs were questioned about HAV vaccination programs for migrant children. Notification data of HAV over the period 1995–2006 were analysed. Results: Since 1998, 19 MPHSs (58%) organized vaccination programs for Turkish and Moroccan children. A large variation in the range of activities in HAV vaccination programs was observed. In the Netherlands, HAV incidence declined, from 6.5 per 100 000 inhabitants in 1995 to 1.3 in 2005. HAV incidence in children of Turkish and Moroccan decent declined from 70.3 per 100 000 in 2000 to 13.5 per 100 000 in 2005. Regions where MPHSs organized vaccination campaigns had the steepest decline in HAV incidence. Conclusion: The decline in HAV incidence in the Netherlands coincided with that observed for the rest of Europe. Therefore, also other causes than the enhanced vaccination programs could have contributed to this effect. At present, low priority is placed on continuing these HAV vaccination programs, as in areas without enhanced programs the incidence also declined to very low levels. Because HAV is still endemic in Morocco and Turkey, it remains important that all travellers to these countries are vaccinated against HAV, regardless of their country of origin.

Keywords: Hepatitis A, vaccination, child, incidence, risk factors.

Introduction

Hepatitis A (HAV) is considered a benign, often asymptomatic childhood infection but when a HAV infection occurs in older children and adults, infection typically is symptomatic, with jaundice occurring in >70% of patients¹ (Lednar, 1985 #51). As a result of improved sanitation and hygienic conditions the prevalence of anti-HAV antibodies in the general Dutch population declined after 1950 to 33.8% in 1995.² In the Netherlands, HAV shows a seasonal peak incidence in autumn due to import of HAV by young immigrant travellers returning from family visits in Turkey and Morocco and secondary cases among siblings and schoolmates. This is followed later in the year by an increase in notifications of adults who are infected in the Netherlands.³,⁴ Notification data over the period 1993–2002 revealed that 64.4, 6.5 and 11.5% of the HAV cases were contracted in the Netherlands, Turkey and Morocco, respectively.³

Despite frequent travel (on average once every 3 years) and many HAV infections, only 21% of the Turkish children and 41% of the Moroccan children who live in The Netherlands are immune against HAV.⁵ Another study showed that in second-generation immigrants, born in the Netherlands, the seroprevalence does not differ from that of adults of Western origin.⁶ In 2000, more than half of Turkish and Moroccan children in Amsterdam travelling to Turkey or Morocco were not vaccinated against HAV.⁷ Starting 1998, 19 of 33 Municipal Public Health Services (MPHSs) initiated annual programs to vaccinate children of Turkish and Moroccan decent who plan summer travel to their country of origin.⁸–¹⁰ The influence of these programs on the HAV-incidence is unknown.

Only the Amsterdam-MPHS evaluated their HAV-vaccination program. They concluded that their program reduced both import and secondary HAV cases in Amsterdam.¹¹ However, in other MPHS regions without vaccination programs, a similar incidence reduction was seen. It is possible that this is partly due to a declining incidence in the countries visited. We therefore compared areas with these enhanced programs with areas without such programs to assess whether the enhanced programs reduced the HAV incidence in the Netherlands.

Methods

We conducted a retrospective observational comparative study into the effect of enhanced vaccination programs on HAV incidence.

MPHSs

Clinicians are legally required to report a patient with HAV to the MPHS. The MPHSs take appropriate public health measures (contact tracing, vaccination and education). MPHSs report patient characteristics, including the most likely source
of infection to the Dutch Centre for Infectious Disease Control (Cib) of the RIVM (National Institute for Public Health and the Environment in the Netherlands).

**Questionnaires**

All 33 MPHSs were contacted by telephone. If vaccination initiatives for programs targeted at immigrant children were confirmed, a questionnaire was sent by email to assess the content of the program. The questionnaire contained the following topics: the reason for starting a vaccination program, the period in which the vaccination initiatives were held, recruitment and vaccination strategy, whether vaccines were for free or had to be paid for, how many Turkish and Moroccan children were reached for a first and second vaccination, the number of inhabitants and the number of Turkish and Moroccan children in the region.

Reasons for not having initiated any enhanced programmes (low incidence of HAV, few inhabitants of Turkish and Moroccan origin, absence of HAV outbreaks, limited budget and absence of evidence for effectiveness of vaccination programs) were asked in a short questionnaire sent by email.

**Incidence of HAV in the Netherlands**

Notification criteria for HAV were: (i) having symptoms that correspond with a HAV infection in combination with the finding of anti-HAV IgM in the serum and (ii) having HAV-like symptoms with an epidemiological link to serologically confirmed case(s). From the Cib database, data on reported cases were extracted: age, birth country, birth country of the parents, MPHS region in which the patients live, date of onset, date of diagnosis, source of infection, most probable country of infection and men who have sex with men (MSM). The origin of the patient was available as of 1999. Denominator data was obtained from the website of Statistics Netherlands (www.cbs.nl). The number of inhabitants per MPHS region was obtained from the national association of MPHSs.

**Analysis**

We described the HAV vaccination programs targeted at immigrant children in the Netherlands. Ethnicity was determined by the native country of the parents of the children. We also described trends in notifications due to the main risk factors for HAV and calculated HAV incidence for the general population, for Turks and Moroccans younger than 16 years and for Turkish and Moroccan immigrants 16 years and over. Furthermore, the 33 MPHSs were divided into three groups: MPHSs who did not organize vaccination programs (this group is called hereafter: ‘no activity’), MPHSs who organized programs in 2–4 years (called hereafter: ‘low activity’) and MPHSs who organized programs in 5–9 years (called hereafter: ‘high activity’). For calculating HAV incidence rates in the groups ‘no’, ‘low’ and ‘high activity’, the number of inhabitants of the general population and the number of Turkish and Moroccan children of the MPHS region as of 1 January 2007 were used. When comparing HAV incidence in three MPHS groups, MSM were excluded, since a molecular epidemiological study demonstrated that strains found among MSM differ from strains in school children and no transmission was seen between these groups. In Amsterdam, HAV strains among travellers are limited in the extent and season of their spread; HAV among MSM remains endemic and spreads to a large number of individuals without a seasonal pattern.

**Results**

**Hepatitis A vaccination programs**

Nineteen of 33 MPHSs (58%) organized enhanced vaccination programs for Moroccan and Turkish children. Of these, 11 MPHSs were classified in the ‘low activity’ and eight in the ‘high activity’ group. Two MPHSs of the last group served larger cities. Thirteen MPHSs did not organize a hepatitis A vaccination program. One MPHS organized a limited vaccination program in which only 58 children were vaccinated in 1 year. This MPHS was added to the ‘no activity’ group. In MPHSs without vaccination programs three were of a large city. The programs were organized throughout the country with exception of the three northern provinces and Zeeland.

**MPHSs with vaccination programs and reasons for initiating**

All 19 MPHSs with enhanced vaccination programs filled out the questionnaire (response 100%). The median number of years with enhanced programs was four (range: 2–9). In 1998, three MPHSs started to organize vaccination programs. The maximum number of MPHSs that organized such programs was 17 (in 2004), declining to 14 in 2006. Flyers and posters at schools, mosques and community centres, local media and personal invitations were used for recruiting the children in the HAV vaccination programs. The target group eligible for vaccination concerned frequently children in the age of 1–16 years (10 out of 19 MPHSs). For 15 MPHSs the immunization days were in larger cities of the MPHS region, the remaining five MPHSs also vaccinated in smaller cities. Eleven MPHSs (58%) did not register how many children they vaccinated per year. For the remaining eight regions the vaccination coverage ranged from 27% to 80% of the target group. All but four MPHSs gave the parents a reduction of the price of vaccination.

More than one reason could be mentioned for initiating programs. Eight MPHSs started a program after they experienced clusters, six because of the high number of notifications of HAV and six because of the high population size of Turkish and Moroccan children. Six MPHSs with only a few HAV clusters started the program to prevent clusters or an increase in notifications in the future. Three MPHSs wanted to diminish the pressure on the regular consultation hours for travellers. Other reasons mentioned were the death of a teacher due to HAV, the good experiences with the programs by other MPHSs and because prevention is the responsibility of the MPHS.

**Reasons for not organizing hepatitis A vaccination program**

All 14 MPHSs that did not organize vaccination programs responded (100%). Eleven MPHSs reported that HAV incidences were too low to warrant a vaccination program. Four MPHSs reported that the Turkish and Moroccan population in their region was relatively small. Three MPHSs had a limited budget for organizing vaccination campaigns. Other reasons mentioned: lack of sufficient staff, absence of financial compensation by health insurers and the verdict in 2006 of the Dutch Equal Treatment Commission that reduction in price for a HAV vaccination for children of Turkish and Moroccan origin was discriminatory.

**Incidence of HAV in the Netherlands**

Figure 1 shows the HAV incidence rates between 1995 and 2006 in the general population and between 1999 and 2006 in
Turks and Moroccans older and younger than 16 years of age. The absolute number of HAV notifications declined from 1009 in 1995 to 210 in 2005. This corresponds with a decrease in HAV incidence from 6.5 per 100 000 inhabitants in 1995 to 1.3 in 2005 (in 2006 1.7). In Turks and Moroccans older than 16, HAV incidence was similar to that in the general population; it remained fairly stable and ranged from 2.6 to 5.2 per 100 000. The highest HAV incidence in Turkish and Moroccan children below 16 years was 70.3 per 100 000 in 2000; with the lowest incidence in 2005 (13.5 per 100 000).

The infections (46–90%) among Turkish and Moroccan children were contracted during visits to Turkey and Morocco; the remainder was obtained as secondary infections in the Netherlands.

Risk factors for HAV
The trends of HAV notifications in relation to the main risk factors (country of infection Turkey or Morocco, infection in the Netherlands and in other countries and infection in MSM) are shown in figure 2. After a peak in 1997, infections contracted in Turkey and Morocco were decreased. The number of HAV infections, contracted in other countries, remained stable in the period 1995–2006. The number of HAV infections among MSM was low with exception of 2001 (63 cases) and 2004 (39 cases). In 1998, a peak in HAV infections with source in the Netherlands was seen. Since then, HAV infections declined.

Overall incidence of HAV in relation to HAV vaccination programs
Figure 3 displays the incidences in the three MPHS groups ‘no’, ‘low’ and ‘high activity’. In 1995, (3 years before implementation of the campaigns) the group ‘high activity’ had the highest incidence (8.6 per 100 000) compared to the other groups. In all three groups, a peak in HAV incidence was seen in 1997 and 1998. The group ‘high activity’ had the largest peak in 1997 and 1998 and also the steepest decrease in HAV incidence in later years. MPHSs with ‘low activity’ had a more moderate increase in incidence in 1997 and 1998. After 1998 the incidence gradually decreased to 1.7 in 2006. MPHSs with ‘no activity’ had the smallest increase in 1997 and 1998 and a small decline in HAV incidence afterwards.

Incidence in Turkish and Moroccan children in relation to HAV vaccination programs
The yearly incidence of HAV in children of Turkish or Moroccan origin in the three MPHS vaccination program groups is shown in figure 4. The MPHS group with ‘high’ and ‘no activity’ peaked in 2000; afterwards HAV incidence declined. The group with ‘low activity’ had a peak in 2002, since then HAV incidence decreased.

Discussion
HAV incidence in the Netherlands
As in the rest of Europe, the incidence of HAV in the Netherlands declined in the study period 1995–2006. In 2006, the incidence was 1.7 per 100 000 inhabitants.
Though incidences of Turkish and Moroccan children in the Netherlands also showed a declining trend in the past years, HAV incidence in these children remained higher (19.7 per 100,000 in 2006) than in the general population or in Turkish and Moroccan immigrants older than 16 years.

**HAV vaccination programs**

Since 1998, more than half of the MPHSs in the Netherlands organized HAV vaccination programs for Turkish and Moroccan children. In 2007, some MPHSs had already stopped their activities while others still considered starting a HAV vaccination program. When comparing the three intervention groups, the rise in notifications in the late nineties was higher for MPHSs who subsequently started a vaccination program compared to MPHSs with no vaccination programs. This is in agreement with the most frequently reported reason for MPHSs to start a vaccination program being the high number of notifications and clusters. After the peak in 1998, the number of HAV notifications in the three MPHS groups started to decline. In the regions where MPHSs started the vaccination programs, a sharper decline was observed compared to the MPHSs with no vaccination programs. Since 2002, incidences were approximately at the same level for all three groups. In recent years, an effect of continuing the vaccination program on the incidence of HAV could not be noticed.

In the present study, the effect of the vaccination program strategy on the attendance of the target group could not be evaluated. We observed a large variation in recruitment and vaccination strategies (data not shown). In addition, there was a lack in registration of HAV vaccinations. Only 11 MPHSs registered the number of vaccinations.

Some MPHSs changed their enhanced vaccination programs for migrant children in so called Mediterranean consultation hours for children of all origins (including Dutch children) and eventually their parents too, who are planning to go to a Mediterranean country, like Turkey, Morocco and Tunisia.

The statement of the Dutch Equal Treatment Commission played an important role in this decision. Since price reduction of the HAV vaccination is prohibited, MPHSs should stop the discount or extend their target group with children of all origins.

**Epidemiology of HAV in Western Europe**

Knowing that also in many other European countries Turkish and Moroccan immigrants live we were interested whether enhanced vaccination programs were conducted in other countries. A similar decline in HAV incidences in Europe occurred but to our knowledge in none of these countries enhanced vaccination activities for Turkish and Moroccan immigrants were conducted. Between 1993 and 2005 HAV incidence showed a 2-year peak in 1996–97 (more than 10 cases per 100,000) and then a steady decline in most European countries. In 2005, the overall incidence rate was 1.7 per 100,000 inhabitants.

**Epidemiology of HAV in Morocco and Turkey**

As the declining incidence of Turkish and Moroccan children might be explained by a reduced level of endemicity in the countries of origin we tried to find reports on HAV prevalence in these countries. There were no recent data available on epidemiology of HAV in Morocco. Due to poor sanitary and hygienic conditions, the WHO considers Morocco as a country with high endemicity of HAV. Turkey is one of the intermediary endemic countries in aspect of HAV infections. In Turkey, HAV seroprevalence is closely related to geographic location, socio-economic level and age. With improvement of sanitation, drinking water supplies and socio-economic status of the population there has been an evident decrease in HAV infection in Turkey. Young people living in the western part of Turkey have declining immunity for HAV. Consequently, the average age of infection is changing from childhood to adolescence.

**Explanations for decline in HAV incidence in the Netherlands**

We conclude that the effort of vaccination programs for immigrant children partly contributed to the decline in HAV incidence in the Netherlands in the late 90s, but that the programs have lost their effect in recent years. There may be other factors that have contributed to the decrease in HAV incidence. First, the decrease in secondary HAV infections (with source in the Netherlands) could be caused by the use of HAV vaccination in infectious disease control; many Dutch travellers and contacts of HAV patients have now received HAV vaccinations making a larger proportion of the population immune. Secondly, Turkish and Moroccan children in MPHS regions without vaccination programs could have been vaccinated by their general practitioner, at regular MPHS consultation hours for travellers or other travellers’ vaccination clinics. These data were not available. Finally, as stated above, the decline in HAV infections in Turkey could have contributed to the decrease in the three groups. However, in Amsterdam, a MPHS region with a vaccination program, a decline was also seen in the Moroccan group. Further investigation with help of genotyping of HAV strains could gain an insight in introduction and transmission patterns of HAV in the Netherlands.

**Conclusion**

In conclusion, a sharp increase in the number of HAV notifications in the late 90s triggered MPHSs to start a vaccination campaign for Moroccan and Turkish children. After the start of the vaccination campaigns, the number of notifications declined. In regions where MPHSs did not start a campaign, the number of notifications declined less sharp. It remains inconclusive to what extend the vaccination programs led to a decline in the HAV notifications after 1998. As after all, HAV is still endemic in many countries, including Morocco and Turkey, it remains important that all travellers to endemic regions are vaccinated against HAV. At present, with regard to reducing HAV incidence, it seems less essential to carry on with special HAV vaccination programs for Turkish and Moroccan children.

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**Conflict of interest**: None declared.

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**Key points**

- As in the rest of Europe, HAV incidence declined in the Netherlands.
- Enhanced vaccination programs for migrant children could have contributed to this effect.
- Continuing these HAV vaccination programs is less essential.
References

14 Gezondheidsdienst maakt verboden onderscheid op grond van ras. Commissie Gelijkbehandeling. (MPHS makes a forbidden distinction because of race. Dutch Equal Treatment Commission); 2006.

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