

Selective immunisation strategy to protect newborns at risk for transmission of hepatitis B: retrospective audit of vaccine uptake

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Summary

Background: 90% of newborns infected perinatally will develop chronic hepatitis B infection with the risk of liver cirrhosis or hepatocellular carcinoma. In Switzerland, screening of all pregnant women for hepatitis B virus (HBV) has been recommended since 1983. Neonates at risk for perinatally acquired HBV are passively and actively immunised immediately after birth as well as at 1 and 6 months of age. The objective of this study was to evaluate the proportion of newborns immunised in accordance with the proposed vaccination schedule.

Methods: Patient records of 3997 mothers who gave birth to a liveborn infant during a two-year period at Zürich University Hospital were screened by computer. 128 women were identified as HBsAg positive or anti-HBc alone positive. Of 133 infants born to these mothers, complete data were available for 94 (71%).

Results: Immunisation was started in 88 infants (94%), but only in 78 (83%) within the first

24 hours of life. 85 (90%) received the 2nd immunisation but only 72 (77%) within the given time limit. 80 (85%) of the infants received the 3rd immunisation but only 69 (73%) within the correct time limit. In summary, only 51 (54%) of the infants at risk for HBV infection were immunised correctly (immunoglobulin within 24 hours and active prophylaxis at 0, 1 and 6 months).

Conclusions: The success of the immunisation strategy following maternal screening and selective immunisation of newborns at risk for HBV infection is limited for various reasons (lack of screening results at birth, problems with correct documentation and communication). To overcome these drawbacks, selective vaccination strategy should be improved and general vaccination strategy, including infants, should be reconsidered.

Key words: hepatitis B; antenatal screening; newborn vaccination; selective immunisation; compliance

Introduction

Hepatitis B is an infectious disease with worldwide extension. The hepatitis B virus (HBV) is transmitted primarily through blood, sexual contact and perinatally from mother to child. The risk of an infant acquiring HBV from an infected mother as a result of perinatal exposure is 70–90% for infants born to mothers who are HBsAg and HBeAg positive; the risk is 5–20% for infants born to HBeAg-negative mothers. More than 90% of infants infected perinatally will develop chronic HBV infection with the subsequent risk of liver cirrhosis or hepatocellular carcinoma. However, only 5–10% of infected adults become chronically infected [1, 2].

Highly effective vaccines against hepatitis B produced by recombinant DNA technology are available. More than 90% of vaccinated adults develop adequate immunity. In vaccinated infants

and newborns the vaccine is effective in nearly 100% [3].

In 1997 the Swiss Federal Health Office (Bundesamt für Gesundheit) published the following recommendations for hepatitis B vaccination: 1) Universal vaccination of all adolescents at age 11–15 years. 2) Vaccination of all persons exposed to a specific risk for hepatitis B infection. 3) Systematic prenatal screening and vaccination of infants born to HBsAg-positive women [4]. A national working group recently refined the recommendations to prevent mother-to-child transmission of hepatitis B [5]. At Zürich University Hospital neonates born to mothers positive for anti-HBc alone are also vaccinated, since this constellation has been shown to be associated with the presence of HBV-DNA, a low but not completely negligible risk of an ongoing infection [6].

The primary objective of this study was to evaluate the number of neonates who had been immunised in accordance with the proposed vac-

ination schedule. A secondary objective was to compare actual vaccination compliance with that of a previous study done ten years earlier.

Methods

The starting-point of the study were all births at Zürich University Hospital Department of Obstetrics and Gynaecology between 1.1.2000 and 31.12.2001. During this period 3997 women gave birth to 4193 newborns.

These women were routinely screened for anti-HBc. If found to be positive they were also tested for HBsAg and anti-HBs. The majority of women were tested in Zürich University Hospital Immunology Laboratory, while for the remainder we used test results from external laboratories. All results available in the computer-based clinic information system were searched. In addition the IC-10 codes, B16 and B18 were used to find additional cases. The following serological constellations were defined as infectious:

- HBsAg positive, anti-HBs negative
- HBsAg positive, anti-HBc positive, anti-HBs negative
- Anti-HBc positive, anti-HBs negative (anti-HBc alone positive)

The limit of detection for anti-HBs was 10 IU/l.

In the 24-month period of observation 144 pregnant women (3.6%) were found to be infectious for hepatitis B. 16 of these women had either an abortion or a stillbirth. 128 women gave birth to 133 liveborn infants (124 singletons, three pairs of twins and one set of triplets). These

133 infants should have been vaccinated and were included in the study group.

In a first step, the time and mode of vaccination were collected from the electronic and paper documentation of all 133 infants.

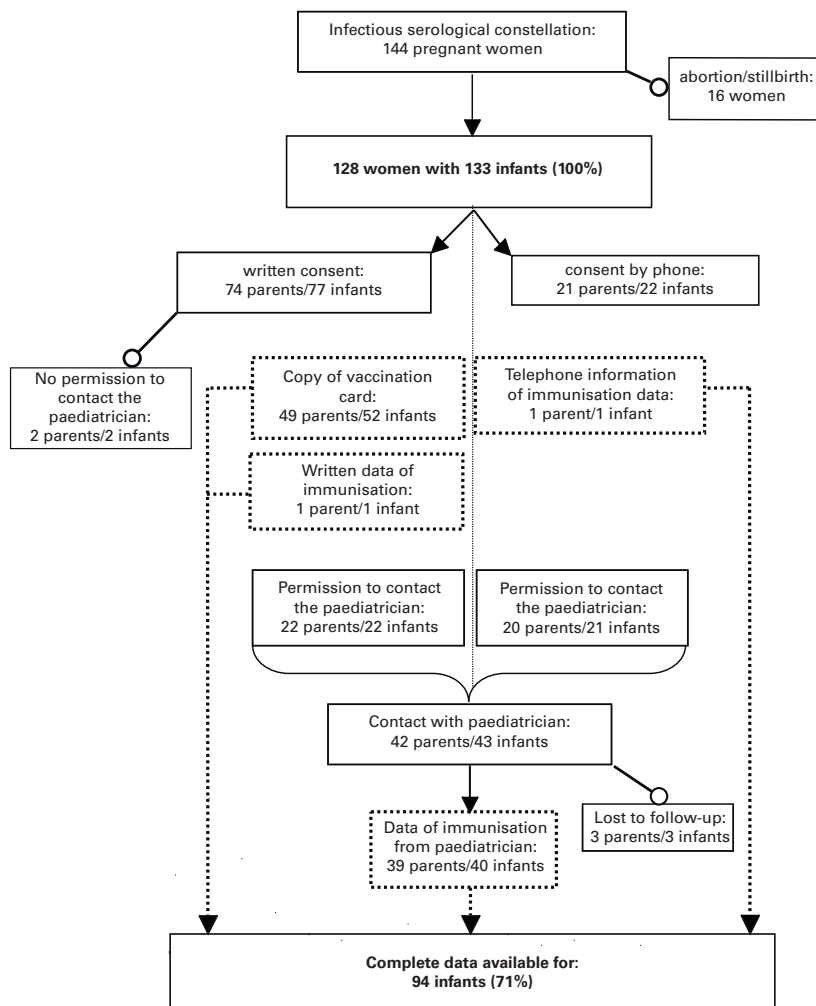
In a second step a letter was sent to the parents of these infants. They were briefed on the study and asked for a copy of the child's certificate of vaccination or for consent to our contacting the paediatrician. The parents of 77 infants (58%) responded within 4 weeks and 53 sent a copy of the vaccination certificate. 22 gave us permission to contact the paediatrician and 2 denied permission.

In a third step, non-responding parents were contacted by telephone. In this way information on the vaccination status of another 22 infants could be obtained. In spite of intensive investigations 33 parents (34 infants) could not be reached, the majority having moved away.

In a fourth step, the paediatricians of 43 infants were contacted. They were able to provide information on the vaccination status of 40 infants. In the case of 3 infants the paediatrician was unable to give the requested information either because the parents had changed paediatrician or because the information was not documented.

Finally, complete documentation on all vaccinations for hepatitis B was available for 94 infants (71%) (fig. 1).

Figure 1
Patients flow chart.



For the analysis of correct timing the following limits were set:

- 1st vaccination (active and passive) within 24 hours
- 2nd vaccination: 21–60 days after 1st vaccination (recommendation 30 days).
- 3rd vaccination: 60–300 days after 2nd vaccination (recommendation 150 days)

For the vaccination to be effective the timing of the first and third vaccination is critical. The first passive and

active vaccination should be carried out immediately after birth, ideally within 12 hours. We chose a 24-hour time interval because in some cases the exact time of vaccination was not available. The interval between the 1st and 2nd vaccination has little effect on the efficacy of the vaccination. However, a minimum interval of 2 months is required between the 2nd and 3rd vaccination. If this interval is 2 months or less, a 4th dose is needed at 12 months [4, 7].

These data were compared with data obtained from a similar study in infants born at this hospital in 1991.

Results

Complete data from 94 infants were available. These were defined as the study cohort. Of these, 67 newborns (71%) received the recommended immunoglobulins (passive immunisation) and the first active immunisation within 24 hours after birth. 11 (12%) received the active immunisation only. In three infants' documents it was noted that passive vaccination was not possible because of "non-availability of hepatitis B immunoglobulin".

10 neonates (11%) received active immunisation later than 24 hours after birth, 6 of them at the age of 2–8 days, the other 4 at the age of 4 weeks to 12 months. A total of 88 infants (94%) received at least one immunisation. 6 neonates (6%) received no immunisation.

85 infants (90%) received a 2nd immunisation, 72 (77%) within the required time interval (21 to

60 days after the 1st immunisation), 12 (13%) too late and one too early (fig. 2). Three infants (3%) who were given the first immunisation received no further immunisation.

80 infants (85%) received a third immunisation dose, 69 (73%) of them within the required time interval (60–300 days after the 2nd immunisation). Of four infants vaccinated at less than 60 days following the 2nd vaccination, only one received a 4th booster at 12 months and was therefore appropriately immunised. Thus the three infants without a 4th vaccine dose received an incomplete schedule. 7 infants (7%) received the 3rd immunisation more than 300 days after the 2nd immunisation (fig. 3). 5 infants (5%) who had received the first and second vaccinations did not receive the third dose.

Figure 2
Interval between first and second vaccination.

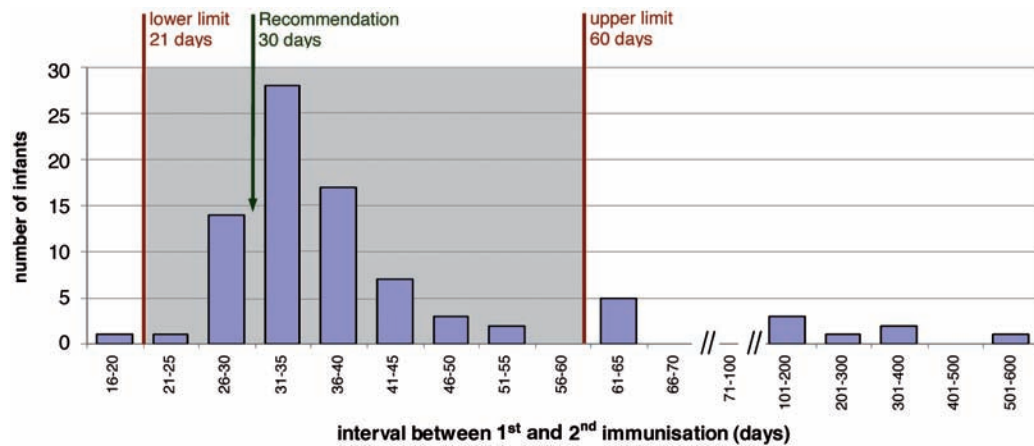


Figure 3
Interval between second and third vaccination.

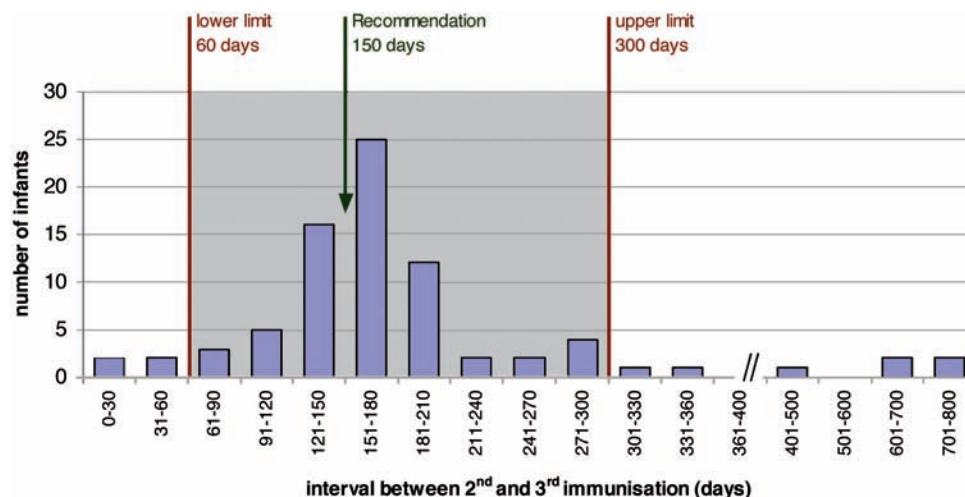


Figure 4
Timing and completeness of immunisation 2000/01.

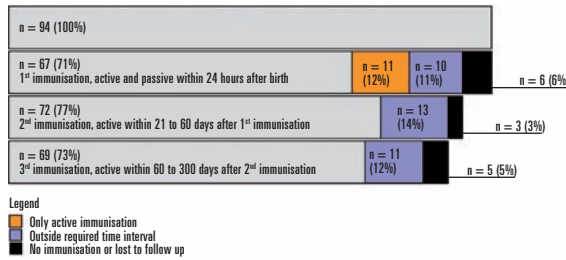
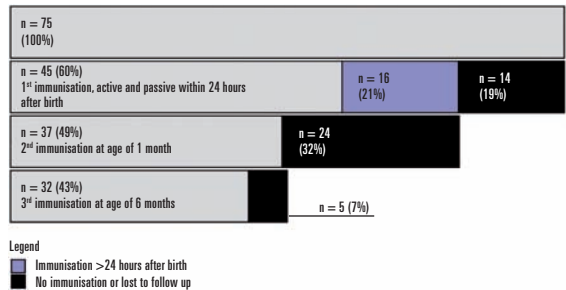


Figure 5
Timing and completeness of immunisation 1991.



In summary, only 51 (54%) of the infants born to maternal carriers of hepatitis B virus were vaccinated according to the recommended vaccination schedule. Six infants (6%) obtained the three immunisation doses within the required time intervals but not the passive vaccination after birth. 32 infants (34%) received 3 immunisation doses but at least one dose outside the required

time interval. A total of 14 infants (15%) did not receive the recommended three doses of hepatitis B vaccine (5 infants received two doses, 3 only one dose and in 6 cases no vaccine at all) (fig. 4).

Serological control of HBsAg and anti-HBs at the age of 9–15 months of life (to exclude chronic infection and to check immunity), as recommended by the Swiss Health Office, was documented in only one child.

In our study 6 preterm newborns with a birthweight below 2000 g were included. In such cases the American Academy of Pediatrics (AAP) recommends four active immunisations at 0, 1, 2–3 and 6–7 months of age. None of the 6 infants received four immunisations.

Data from 1991

75 newborn infants of mothers who were chronic HBV carriers (23 HBsAg positive, 52 anti-HBc alone positive) were included. Only 60% of these infants at risk were immunised actively and passively within 24 hours after birth. 21% received the first vaccination later than 24 hours after birth. Only 43% of the entire cohort received three immunisation doses (fig. 5).

Control of serology revealed that 3 infants (4%) had been infected despite passive immunisation within 4 hours of life.

Discussion

Our retrospective audit shows that only 54% of the infants born to maternal carriers of hepatitis B virus were vaccinated according to the recommended vaccination schedule. This is better than 10 years before, when only 43% of infants were correctly immunised, but still unsatisfactory. 71% versus 60% in the first study received immunoglobulins within 24 hours and 85% versus 43% received three active immunisations.

The main problem revealed by this study is incorrect or incomplete documentation and transmission of information on maternal hepatitis B immune status and about the time and dose of vaccines given. For example, laboratory data from investigations during pregnancy were not available at birth, thereby delaying the first vaccination, or maternal hepatitis serology was wrongly noted in the infants' documents. The most common error was confusion between anti-HBc and hepatitis C antibodies.

Incomplete documentation of the exact time of vaccination, and as to whether both active and passive immunisation were given, was also an obstacle to retrospective analysis. As the exact time of passive immunisation was not available for analysis in some patients' charts, we had to extend the critical time interval to 24 hours rather than the recommended 12 hours after birth. Another cause of confusion was the fact that in the case of a few infants

the entries in the certificate of vaccination did not agree with the data provided by the paediatrician.

These findings demonstrate that hand copying of vaccination data is prone to error. This could be reduced by electronic transmission and/or a patient card with all relevant medical data. One step in this direction is the maternal pass introduced recently at Zürich University Hospital Obstetric Clinic [8].

Another known source of error is the change from one paediatrician to another. This was shown in a study in England where 66% of infants who did not change doctor were vaccinated completely, versus only 34% who changed doctor [9].

How can protection against perinatal transmission of hepatitis B be improved?

Five starting points have to be considered [10, 11]: 1) Improvement of hepatitis B screening during pregnancy, 2) Improved documenting of the time of the first vaccine, 3) Improved information to parents, 4) Improved information to paediatricians on the need for serological monitoring following the third vaccination, 5) Improved general vaccination in newborns and adolescents.

1. Improvement of prenatal screening

In 5% of women delivered at Zürich University Hospital, hepatitis B status was not known at birth. The majority of these women had been

screened during pregnancy but the result was not available. This problem could be solved by a maternal pass as used in many countries.

2. Better documentation and adequate communication following the first vaccination

As the first immunisation is usually done in the hospital where the infant is born, the boosters must be given by the paediatrician doing follow-up. He is kept informed by the certificate of vaccination and a health booklet given to the parents. As the parents may not have presented both to the paediatrician in 2005 we started to mail a discharge summary for the baby direct to the paediatrician in addition to the above documents.

3. Improved information to parents

In our experience a very small number of parents are strictly against vaccination and do not accept the arguments for immunisation against hepatitis B. Lack of compliance for the second and third dose is due more to unawareness of the consequences. This may be due to a language problem.

4. Serological testing after third dose

Although this was not the primary objective of our audit, we realised that very few of the infants were serologically monitored after completion of the vaccination schedule. This is especially important for preterm infants as their immune response may be reduced and therefore a fourth dose indicated [1, 5]. On enquiry some colleagues argued that they would prefer a fourth booster to blood testing, since it would be cheaper and avoid painful blood sampling.

5. Improved general vaccination in newborns and adolescents

The most effective way of reducing the burden of

hepatitis B is general vaccination of both newborns and adolescents in addition to selective vaccination on the first day of life based on antenatal screening. The success of such a policy has been demonstrated in Italy, where it was introduced in 1991. In 1994/95 hepatitis B immunisation was achieved in more than 90% of the target population and the incidence of acute hepatitis B in 15 to 24-year-olds was reduced by 50% [12]. Even more successful was the inclusion of hepatitis B immunisation in the routine vaccination schedule for infants. In 1998, 94.5% of all infants in Italy were vaccinated at the age of 24 months, and in northern Italy up to 98% [13]. In Switzerland by contrast, in the years 1999–2003 only 52% of adolescents had received at least one active immunisation against hepatitis B, with wide variation between cantons (from 7% in Appenzell to 88% in Nidwalden) [14].

Conclusions

The success of the immunisation strategy following maternal screening and selective immunisation of newborns at risk for HBV infection is limited for many reasons (lack of screening results at birth, problems with correct documentation and inadequate communication). To overcome these drawbacks, selective vaccination strategy should be improved and general vaccination strategy, including infants, should be reconsidered.

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