Vaccination against hepatitis A and B in persons subject to homelessness in inner Sydney: vaccine acceptance, completion rates and immunogenicity

Abstract

Objectives: To determine acceptance, completion rates and immunogenicity of the standard vaccination schedule for hepatitis A (HAV) and B (HBV) in persons subject to homelessness.

Methods: A convenience sample of clients (n=201) attending a medical clinic for homeless and disadvantaged persons in Sydney was enrolled. Serological screening for HAV and HBV was undertaken. An appropriate vaccination program was instituted. Post-vaccination serology determined serological response.

Results: Although many clients had serological evidence of past infection, at least 138 (69%) clients had the potential to benefit from vaccination. For hepatitis A and B vaccinations, completion rates were 73% (73 of 100 clients) and 75% (69 of 92 clients), respectively; after vaccination, protective antibody was found in 98.2% (56 of 57) and 72% (36 of 50) of clients, respectively.

Conclusion: A successful vaccination program can be mounted with a vulnerable population. We consider a clinic with a well-established history of acceptance and utilisation by the target group; a low staff turnover and regular clientele; inclusion of vaccination as part of routine client care; and counselling (part of pre- and post-serological testing) essential components in achieving good vaccination completion rates.

Key words: Homeless persons, vaccination, Hepatitis, Hepatitis A, Hepatitis B, Hepatitis C.

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There is a growing body of research, both within Australia and internationally, that documents the poor health status and high health risk behaviours of persons subject to homelessness. Identified health conditions and behaviours include high rates of hepatitis C, alcohol dependence and risk factors for other blood-borne viruses. Outbreaks of hepatitis A have also been reported. Vaccination against hepatitis A and B, therefore, has the potential to offer a considerable health benefit to this population group by preventing infection and exacerbation of existing liver disease.

Vaccination against hepatitis A and/or B is widely recommended for patients with chronic liver disease of any etiology and for patients chronically infected with Hepatitis B or C, and for groups whose lifestyles put them at risk of Hepatitis A or B, such as injecting drug users. However, significant obstacles to reaching vulnerable adult populations have been identified and these include: a. Difficulties for healthcare providers in identifying and delivering vaccines to at-risk populations. Specifically, persons subject to homelessness face numerous...
barriers to accessing healthcare, such as the impact of mental illness, a failure to recognise serious symptoms, and a fear of doctors, appointment systems or procedures. Competing priorities, such as worries about immediate daily needs, mean that health and preventive healthcare are often attached a low priority.

b. Limited public health infrastructure to support the vaccination of adults.

c. A lack of awareness among healthcare providers of the practices necessary to achieve high rates of vaccination among adults.

d. Limited reimbursement for adult vaccination.

e. Discrimination against some at-risk populations by healthcare providers.

Not surprisingly then, patient uptake and adherence to approved vaccination schedules has been low in programs targeting vulnerable groups. For example, for the three-dose hepatitis B vaccination schedule, uptake rates of 48% were reported in a sexual health clinic in Australia, with 38% of these clients completing the course; at sexual health clinics in California, uptake rates of 74% were reported, with 30% of clients completing the three-dose schedule, while at other sites serving primarily high-risk clients, uptake and completion rates ranged from 4-66% and 2-40%, respectively; in Alaska, 31% of eligible clients who were injecting drug users completed vaccination after transportation and monetary incentives were implemented.

Research on persons subject to homelessness is limited in Australia. While other research has identified risk factors for hepatitis, and a high self-reported prevalence of hepatitis B and C, we believe no Australian work has looked at serological markers and the opportunities for prevention of hepatitis in this population. Therefore, we undertook this study of people subject to homelessness within the inner city area of Sydney to identify risk factors for hepatitis, determine the serological prevalence of markers for hepatitis A, B and C and to determine the acceptance, completion rates and immunogenicity of the standard vaccination schedule for hepatitis A and B. The results of the risk factor and serological survey are reported elsewhere. This paper reports the results of vaccination acceptance, completion rates and immunogenicity of vaccines against hepatitis A and B.

Enrolled clients completed a short risk assessment form with the assistance of staff as required. This collected basic demographic information, asked about a past history of hepatitis, and about risk factors for blood-borne viruses. Blood was collected for serological screening for hepatitis A, B and C. All clients received pre-test and post-test counseling. Clients with serological markers for hepatitis C or hepatitis B carriage were offered referral to a specialist hepatitis C clinic or a specialist clinician for further assessment.

Clients were offered the choice of either the standard vaccination schedule for hepatitis A and/or B (defined as 0, 6 to 12 months for hepatitis A; 0, 1, 6 months for hepatitis B) or an accelerated vaccination program (defined as 0, 6 to 12 months for hepatitis A; 0, 1, 2, 12 months for hepatitis B). At the time of each vaccination, clients were provided with a written reminder detailing the date of any subsequent vaccination.

Vaccines were administered by intramuscular injection into the deltoid region. The following monovalent vaccines were used: Havrix 1440 manufactured by GlaxoSmithKline (each 1.0 mL dose contains 1440 ELISA units of viral antigens) and Engerix-B manufactured by GlaxoSmithKline (each 1.0 mL dose contains hepatitis B surface antigen protein 20 μg). Clients were given the option of commencing vaccination on the day of study enrolment (an opportunistic vaccination offered as a way of enhancing the initiation of the vaccination course) or after the results of the serological screen were known. Clients who opted to commence vaccination immediately had their vaccination program modified if necessary, once their serological results were known.

Follow-up continued for a period of up to 18 months from the date of commencement of the first vaccination. Post-vaccination serology to determine seroconversion was collected at least three months after the client completed his or her vaccination program. Clients left the study once blood for post-vaccination serology was collected. Clients who failed to seroconvert were referred to the clinic for follow-up care (which usually included booster immunisation). Clients failing to complete the vaccination program within 18 months were considered as lost to follow-up for the purposes of the study.

**Serological testing**

Testing for the following viral hepatitis markers in serum was undertaken using commercial enzyme immunoassay kits, in accordance with the manufacturer’s instructions (Abbott, Wiesbaden, Germany): hepatitis A total antibodies, Axsym HAVAB; antibody to hepatitis B core antigen, Axsym Core; antibody to hepatitis B surface antigen, Axsym AUSAB; hepatitis B surface antigen screen, Axsym HBsAg V2; and hepatitis C antibody screen, Axsym HCV version 3.

Positive screening tests for hepatitis B surface antigen were confirmed using the Serodia-HBs reverse passive haemagglutination test (Fujirebio Inc., Tokyo, Japan). Positive screening tests for hepatitis C antibody were considered confirmed if found to be positive using the Innostest HCV Ab IV enzyme immunoassay (Immugenetics NV, Ghent, Belgium).
The presence in serum of hepatitis A total antibodies (anti-HAV total) was considered a marker of protective immunity. Antibody to hepatitis B core antigen (anti-HBc) indicated previous natural infection and subjects were considered to be immune (or to be carriers if confirmed as positive for HBsAg). An antibody to hepatitis B surface antigen (anti-HBs) level of ≥10 mIU/mL in the absence of anti-HBc indicated protective, vaccine-induced immunity. Samples with anti-HBs concentrations of less than 10 mIU/mL were considered non-reactive.

**Statistical analysis**

Statistical analysis was undertaken using SPSS v.15. Logistic regression was used to explore the relationship between seroconversion to hepatitis B following vaccination and age, gender and presence of hepatitis C antibody.

**Ethics approval**

This study was approved by the South Eastern Sydney Area Health Service Ethics Committee (Eastern Section).

**Results**

Around 450 clients of the clinic were invited to participate in the study by medical and nursing staff. Two hundred and two agreed, 44 clients refused participation and the remainder (approximately 200 clients) failed to reach a decision on participation by the end of the enrolment period. One client revoked consent shortly after enrolment, leaving data for a total of 201 clients.

Clients were aged between 18 and 74 years of age, with a mean age of 42 years (SD=11 years). Eighty-six per cent (n=172) of the participants were male, 14% (n=29) were female.

All participants agreed to pre-vaccination serological testing for hepatitis A, B and C. However, venous access could not be achieved in 11 clients, and poor venous access in others resulted in insufficient specimen, so that not all serological marker results were available for all clients. The results of serological testing are shown in Table 1.

Not all of the clients who participated in the risk factor and serological survey went on to participate in the vaccination program. Of those with the potential to benefit from vaccination, two clients with unknown immunity and 14 clients known to be non-immune to hepatitis A, B or both, either declined vaccination or did not return; and one client became ineligible for the vaccination program before commencing it. These clients have been removed from the analysis of vaccination outcomes.

As separate vaccines were used, the results on compliance, timing and serological response are reported by vaccination type. Therefore, some clients are common to both groups.

**Vaccination against hepatitis A**

**Compliance**

One hundred and eight clients commenced vaccination with Havrix 1440. As per protocol, some clients commenced vaccination before serological results were known. Hence, five clients were withdrawn from the vaccination program once pre-vaccination serology indicating immunity became available. Other withdrawals included: one client who developed a medical condition that excluded him from the vaccination program; one client who died of causes unrelated to the study; and one client who was withdrawn as a precautionary measure following an event post-vaccination. Therefore, 100 clients required a second vaccination to complete the schedule and 73% (n=73) of these completed the schedule within 18 months of their first vaccination (Figure 1).

**Timing**

The median number of days between the first and second vaccination was 193 days with an interquartile range of 182 to 238 days (n=73, 27 clients did not receive a second vaccination within an 18-month period).

**Serological response in previously non-immune clients**

Fifty-six of 57 (98.2%) previously non-immune clients who returned for follow-up had detectable antibodies on post-vaccination serology.

**Vaccination against hepatitis B**

**Compliance**

One hundred and two clients commenced vaccination with Engerix-B. As per protocol, some clients commenced vaccination before serological results were known. Seven clients were withdrawn from the vaccination program once pre-vaccination

<table>
<thead>
<tr>
<th>Hepatitis</th>
<th>Serological results</th>
<th>Count (n=201)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Positive anti-HAV</td>
<td>89 (44.2%)</td>
</tr>
<tr>
<td></td>
<td>Negative anti-HAV</td>
<td>100 (49.8%)</td>
</tr>
<tr>
<td></td>
<td>Unknown serology</td>
<td>12 (6.0%)</td>
</tr>
<tr>
<td>B</td>
<td>Positive anti-HBc</td>
<td>60 (29.9%)</td>
</tr>
<tr>
<td></td>
<td>Positive anti-HBs (≥10 mIU/mL) in the absence of positive anti-HBc</td>
<td>39 (19.4%)</td>
</tr>
<tr>
<td></td>
<td>Non-immune (Negative anti-HBc and anti-HBs &lt;10 mIU/mL)</td>
<td>90 (44.8%)</td>
</tr>
<tr>
<td></td>
<td>Unknown serology</td>
<td>12 (6.0%)</td>
</tr>
<tr>
<td>C</td>
<td>Positive anti-HCV</td>
<td>85 (42.3%)</td>
</tr>
<tr>
<td></td>
<td>Negative anti-HCV</td>
<td>103 (51.2%)</td>
</tr>
<tr>
<td></td>
<td>Unknown or indeterminate serology</td>
<td>13 (6.5%)</td>
</tr>
</tbody>
</table>

Note: a) Three clients also had positive serology for HBsAg indicating chronic carriage
serology indicating immunity became available. In addition, one client was withdrawn when he developed a medical condition that excluded him from the study; one client died of causes unrelated to the study; and one client was withdrawn as a precautionary measure following an event post-vaccination. Therefore, 92 clients required further vaccinations to complete the schedule. Ninety-one of these clients completed the schedule within 18 months of their first vaccination (Figure 2).

Timing
For clients receiving the standard schedule, the median number of days between the first and second vaccination was 32 days with an interquartile range of 28–42 days (n=84, seven clients did not receive the second dose). The median number of days between the second and third vaccination was 156 days with an interquartile range of 139 days to 178 days (n=69, 22 clients did not receive the third dose within an 18-month period). There were 28 days between both the first and second vaccination, and the second and third vaccination for the one client receiving the accelerated schedule; the fourth dose was not received within an 18-month period.

Sero logical response in previously non-immune clients
Thirty-six out of 50 previously non-immune clients who returned for follow-up showed seroconversion on post-vaccination serology (i.e. went from an anti-HBs level of <10 mIU/mL to ≥10 mIU/mL), giving a seroconversion rate of 72%. Fourteen clients failed to seroconvert.

Logistic regression models were utilised to predict seroconversion for hepatitis B from client age (years), gender, and presence of hepatitis C antibody. None of these variables were statistically significantly associated with seroconversion, in either univariate or multivariable analysis.

Discussion
The Haymarket Foundation Clinic is a federally funded clinic that meets the acute medical needs of its clients, offers regular care for ongoing medical problems and assists clients in accessing relevant social and medical specialist services. The clinic targets homeless and disadvantaged persons, and all medical services are provided at no cost to the individual. Other services, such as a needle and syringe exchange program, mail collection, showers, toilets and haircuts are also offered. The clinic has a regular clientele (around 80% of whom are male), and with a low staff turnover, clients and staff are usually well known to each other. This study reports the results of a convenience sample of clients (those attending the clinic during the study period, and who were considered to be able to give informed consent), so care must be exercised in generalising our results to all clinic patients, or to homeless persons in the wider community.
Around 49% of eligible clients invited by clinic staff to participate in the risk assessment survey and the vaccination program actually did so within the study period. This uptake rate is similar to that reported elsewhere, but lower than we anticipated. This may have been due to the fact that vaccination was associated with research and required the signing of a consent form, which clinic staff observed caused suspicion and concern for some clients. A survey of barriers to free vaccination against hepatitis B in other settings of at-risk clients identified factors such as client concerns about the possibility of side effects, a mistrust of the vaccine or the government, a fear that the vaccine contains small amounts of disease or virus, and a fear of needles as impediments to vaccination programs.

However, once clients commenced vaccination, completion rates for the standard vaccination schedule for both hepatitis A and B were high relative to other studies in vulnerable populations. Actual completion rates are likely to be even higher than reported, as staff continued to vaccinate clients when they presented to the clinic beyond the 18-month period of their enrolment in the study. All clients received pre- and post-serological test counselling, which provided staff with an opportunity to counsel clients on risk factors and explain the purposes and requirements of vaccination; and at each vaccination a written reminder detailing the date of the next vaccination was provided. The vaccination program, while part of a specific research project, was incorporated into the routine medical care of clients, so that clients were also reminded about their vaccination schedule at other clinic visits or, if timely, vaccinated when presenting for other reasons. We considered the combination of these strategies essential for promoting compliance in this population group, as has been recommended in a review of strategies to improve vaccination in high-risk adults. Convenience has been identified in other situations as important to client care. Finally, we also consider client counselling, which in our case occurred as part of pre- and post-serological testing, to be an essential component in achieving high completion rates.

Universal vaccination of infants and pre-adolescents against hepatitis B has been recommended since 1996 by Australia's National Health and Medical Research Council. A government-funded vaccination program for these groups has been in place since around 2000. This program will eventually reduce the population at risk of contracting hepatitis B; however, this will take several decades. In the meantime, a significant proportion of the adult population remains susceptible. This is of particular concern in those adults engaging in activities putting them at risk of blood borne viruses. Universal vaccination against hepatitis A, on the other hand, is not undertaken in Australia, so the presence of a susceptible population will continue for the foreseeable future.

Risk-taking behaviour among our population of persons subject to homelessness was high, yet around 69% of the clients remained vulnerable to hepatitis A, B or both, and had the potential to benefit from vaccination. The prevalence of hepatitis B carriage was higher than the general Australian population, as was the proportion of clients with antibodies to hepatitis C. Both of these serological markers may be associated with chronic liver disease, putting this population further at risk if exposed to additional hepatic infection. For example, the clinical and pathological severity of liver disease has been shown to be increased in patients co-infected with hepatitis B and C, and the risk of acute liver failure was increased in patients with chronic liver disease when super-infected with hepatitis A. Indeed, a study of homeless persons in Bristol, found a significantly higher incidence of hospital admission for hepatitis A infection in those suffering hepatitis C co-infection. Therefore, vaccination against hepatitis A and B in this vulnerable population has the potential to offer considerable health benefits, given their risk behaviors, and underlying diseases.

This study suggests that a successful vaccination program can be mounted with a vulnerable population. Completion rates were reasonable, and it is likely that had vaccination been standard care, as opposed to part of a research project, uptake rates would have been higher among the clinic population. We consider that there are a number of features of the Haymarket Foundation Clinic that made it an ideal and successful setting for this vaccination program. First, it had a well-established history of acceptance and utilisation by the target group; second, there was a low staff turnover and many clients were regulars at the clinic, and third, the clinic had the ability to include vaccination as part of routine client care. Finally, we also consider client counselling, which in our case occurred as part of pre- and post-serological testing, to be an essential component in achieving high completion rates.
Acknowledgements

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References