



Trinity Fredericks
Kellie Kwan
Donna Mak

Hepatitis A and B vaccination

The rate of uptake and course completion in patients with hepatitis C

Background

Western Australian general practitioners may order Department of Health funded hepatitis A and B vaccines for patients newly notified with hepatitis C to prevent complications associated with co-infections. The aim of this study was to determine vaccination uptake of hepatitis C patients through this program.

Methods

We reviewed hepatitis C notifications and hepatitis A and B vaccine orders received in 2007 and 2008 to determine the rate of vaccine uptake and course completion.

Results

Vaccination orders for initial doses were received for 37% (448/1209) of patients. Vaccination uptake was positively associated with age and non-Aboriginality. Final vaccination doses were ordered for 30% of patients for whom an initial order had been received.

Discussion

Uptake of hepatitis A and B vaccination was higher than that of similar populations. However, vaccination course completion was low. General practitioners need to emphasise to their patients the importance of completing a vaccine course.

Keywords: hepatitis C; immunisation; primary prevention



Hepatitis C virus (HCV) is one of the most commonly reported infectious diseases in Australia and represents a major public health concern. In the 16 year period from 1990 to 2005, over 225 000 people in Australia tested positive for hepatitis C antibodies.¹ There are an estimated 8000–12 000 new HCV infections annually,² 80–90% of which are attributed to injecting drug use.³ Injecting drug users are also at higher risk of exposure to hepatitis B virus (HBV) due to common risk factors and modes of transmission.²

Several systematic literature reviews show that acute or chronic HBV and/or acute hepatitis A (HAV) infection superimposed on chronic HCV is associated with a more severe clinical course, including higher mortality rates.^{4–7} As both these infections are vaccine preventable, the National Health and Medical Research Council, along with numerous international health authorities, recommended vaccinating patients with HCV against these viruses.^{2,8,9}

Previous studies of HAV and HBV vaccination in patients with HCV show that adherence to recommendations is low, ranging from 0–27%.^{8,10–12} Shim et al⁸ found that only 26.8% of susceptible patients infected with chronic HCV had received vaccination for HAV. In this study, three of the unvaccinated patients developed acute HAV infections during follow up, one of whom died due to acute liver failure. In addition to a low vaccination rate, studies have shown that serial vaccination completion among HCV patients ranges from 35–72%.^{8,10,12}

In 2005, the Western Australian Department of Health (DoH) established a program aimed at increasing the accessibility of HAV and HBC vaccines among adults at high risk.¹³ One component of this program allows GPs and primary

health care providers (collectively termed GPs) to order DoH funded vaccines for patients newly notified with HCV on or after 1 September 2005. On receipt of a new HCV notification, DoH sends the notifying GP a personalised vaccine order form for that patient. Notifying doctors who are not GPs are asked to refer the patient to a GP for vaccination.

Four vaccination schedules are available as part of the program:

- standard schedule – combined HAV and HBV vaccine: 0, 1 and 6 months (order initial two doses and final dose after 5–6 months)
- accelerated schedule – combined HAV and HBV vaccine: 0, 7, 21 days and 12 months (order initial three doses and final dose after 11–12 months)
- hepatitis A vaccine – patient known hepatitis B carrier/immune: 0 and 6 months (order initial dose and final dose after 5–6 months)
- hepatitis B vaccine – patient is known hepatitis A immune: 0, 1 and 6 months (order initial two doses and final dose after 5–6 months).

This study aimed to determine the rate of uptake and vaccine order completion of HAV and HBV vaccinations among patients newly notified with HCV in Western Australia by GPs between 1 January 2007 and 31 December 2008.

Methods

The total number of HCV notifications from 1 January 2007 to 31 December 2008 was obtained from the Western Australia Notifiable Infectious Disease Database. The hepatitis A and hepatitis B vaccination order database, established on 1 September 2005, contains the name and demographic details of patients notified with HCV and their notifying doctor, along with the corresponding vaccination order details. From this database, we extracted data for all patients notified with HCV by GPs from 1 January 2007 to 31 December 2008. Data were extracted in August 2009. Multiple vaccination orders for the same patient and patients for whom vaccination

orders forms were not sent due to program ineligibility or incorrect doctor's address, were removed before analysis.

Data were analysed using SPSS version 17.0 (SPSS Inc., Chicago, IL). Vaccine uptake was estimated by calculating the proportion of patients notified with HCV for whom an initial vaccine order had been received. The median and range of the time interval between the vaccination order form being sent to the notifying doctor and the order being received at DoH, and between initial and final vaccination orders, were also calculated. Chi-square analyses were used to examine differences in ordering patterns based on age, race and gender.

Results

Demographic features

During the 2 year study period, a total of 1209 HCV notifications were received from GPs, representing over 55% of the total number of HCV notifications received in Western Australia. The median age of patients was 39 years (range 0–89 years); 57% were male; 80% were from the metropolitan region; 74% were non-Aboriginal; 6% were identified as Aboriginal, and 20% had an unknown Aboriginal status.

Initial vaccine order

Overall, initial vaccination doses were ordered for 448 patients (37%). Older patients (χ^2 test for trend = 5.38; df=1; $p=0.02$), non-Aboriginal patients and those of unknown Aboriginality were more likely to have had initial vaccine doses ordered (Table 1). The standard schedule of combined HAV and HBV vaccine comprised 70% of vaccine orders (Table 2).

Vaccination order completion

Overall, the completion of vaccination orders was low, with only 30% of patients having had the final vaccination dose ordered (Table 1). A final vaccine dose was more likely to be ordered for patients for whom the standard initial schedules were ordered (32–38%) compared with those for whom an accelerated schedule was ordered (12%) (Table 2).

Discussion

We estimated vaccine uptake by measuring the proportion of patients for whom an initial vaccine order had been received. Some patients may not have received their initial vaccine dose, so

Table 1. Vaccination ordering rates for initial vaccine doses and the final vaccine dose, by patient demographics, 1 January 2007 to 31 December 2008

Demographic features		Initial dose		Final dose	
		Number	%*	Number	%**
Gender	Male (n=686)	255	37.2	73	28.6
	Female (n=523)	193	36.9	61	31.6
Age group (years)	<20 (n=25)	5	20.0	2	40.0
	20–29 (n=232)	76	32.8	15	19.7
	30–39 (n=337)	129	38.3	42	32.6
	40–49 (n=333)	121	36.3	36	29.8
Location	50+ (n=282)	117	41.5	39	33.3
	Metropolitan (n=972)	366	37.7	115	31.4
	Nonmetropolitan (n=237)	82	34.6	19	23.2
Aboriginality	Aboriginal (n=70)	16	22.9	0	0
	Non-Aboriginal (n=898)	355	39.5	110	31.0
	Unknown (n=241)	77	32.0	24	31.2

* Percentage refers to the percentage of patients of a particular demographic feature for whom an initial vaccine order was placed (eg. male = $255/686 \times 100 = 37.2\%$)

** Percentage refers to the percentage of patients of a particular demographic feature for whom an initial vaccine order was placed who also had a final vaccine dose ordered (eg. male = $73/255 \times 100 = 28.6\%$)

Table 2. Distribution of vaccination type among patients for whom initial vaccine doses and the final vaccine dose were ordered, 1 January 2007 to 31 December 2008

Vaccination type	Initial doses		Final dose	
	Number	%	Number	%
Standard hepatitis A and hepatitis B schedule	314	70.1	103	32.8
Hepatitis A vaccine only	53	11.8	17	32.1
Hepatitis B vaccine only	16	3.6	6	37.5
Accelerated hepatitis A and hepatitis B schedule	65	14.5	8	12.3
Total	448	100	134	29.9*

* Note: Percentages don't add up to 100 because they refer to the percentage of patients for whom an initial vaccine order was placed who also had a final dose ordered (eg. standard schedule = $108/314 \times 100 = 32.8\%$)

this method may overestimate vaccine uptake. However, given that GPs were required to complete a personalised order form for that patient, it seems likely that they would take reasonable steps to administer the vaccine to that particular patient. Conversely, we have assumed that patients are not protected against HAV and/or HBV unless we received both initial and final vaccine orders for them. However, if the patient was known to be immune to HAV and/or HBV or had been partially vaccinated, their GP is unlikely to have ordered any vaccines or a complete vaccine course, respectively.

The demographic distribution recorded for patients in this study was similar to that of Australian HCV patients.¹⁴

Vaccine uptake of patients of unknown Aboriginality was similar to those of non-Aboriginal patients. This was probably because patients in Western Australia notified with HCV and of unknown Aboriginality are far more likely to be non-Aboriginal than Aboriginal.¹⁵

The vaccine uptake observed in this study (37%) was higher than any previously reported, including a recent retrospective study of 243 HCV

infected patients where only 8% and 9% of patients diagnosed from 2000 to 2005 received HAV or HBV vaccination respectively.¹² Although we cannot be certain about the cause of this observation, because we did not collect data from patients and doctors about the reasons behind their decision making, it seems reasonable to assume that elimination of some previously identified obstacles to vaccination, including the burden of vaccination cost and practitioner knowledge of the importance of vaccination, was a contributing factor.¹⁶ Low vaccination order rates among Aboriginal (23%) and younger patients (20% in patients aged <20 years) may indicate that the program was less effective at eliminating obstacles to vaccination in these groups and/or be a reflection of their relatively low levels of access to, and use of, GP services.^{17–19}

Although vaccine uptake was higher than that reported elsewhere, vaccine course completion was low. Only 30% of those patients who had an initial dose ordered also had a final dose ordered. This vaccine order completion rate is similar to that found by Macdonald et al² who reported a 21% completion rate among 'at risk' adults treated at primary healthcare centres in Sydney (New South Wales). However, they were considerably lower than the previously mentioned study by Hachem et al¹² who reported that 65–72% of HCV patients completed their vaccine course. Previous studies evaluating the immunogenic response to HBV vaccines in healthy adults reported a seroprotective response of approximately 78% after administration of the second dose of vaccine, which increases to 98% after the final dose.²⁰ The percentage seroconversion reported for HAV vaccine was 99% after the second dose of Twinrix[®] (combined HAV and HBV vaccine) and almost 100% upon serial completion. However, in HCV infected patients, several studies suggest a lower and highly variable immunogenic response rate to HAV and HBV vaccination, which is further diminished in those with advanced or decompensated liver disease.^{10,21} Therefore, vaccine course completion in HCV infected individuals is important to ensure adequate protection against HAV and HBV infections.^{8,12} The literature has suggested that the provision of an accelerated vaccination schedule would improve both patient and physician compliance and improve vaccine course completion.⁸ However, in the current study we found that the provision of an accelerated schedule

of Twinrix[®] resulted in a significantly lower vaccination order completion rate than the standard schedule of Twinrix[®] and HAV and HBV vaccination alone. This may be because the accelerated schedule is recommended for high risk patients in whom compliance may be a problem.¹

Conclusion

The provision of free HAV and HBV vaccines to patients diagnosed with HCV in Western Australia was associated with higher vaccination rates among GPs to those previously reported. However, the low vaccination order completion rate observed in this study was reflective of rates previously reported in similar populations and indicates the need for doctors to emphasise to their patients the importance of completing a vaccine course.

Authors

Trinity Fredericks BSc(Hons) is a program officer, Sexual Health and Blood-borne Virus Program, Communicable Disease Control Directorate, Health Department of Western Australia. trinity.fredericks@health.wa.gov.au

Kellie Kwan BA(Hons), GradCertAppEpi, is Senior Research Officer, Communicable Disease Control Directorate, Health Department of Western Australia

Donna Mak MBBS, MPH, FAFPHM, FACRRM, is a public health physician, Communicable Disease Control Directorate, Health Department of Western Australia, and Head, Population & Preventive Health, University of Notre Dame, Fremantle, Western Australia.

Conflict of interest: none declared.

Acknowledgments

We would like to acknowledge the work done by staff at the Communicable Disease Control Directorate and Western Australian general practices in the implementation of the hepatitis A and B vaccination program.

References

1. Razali K, Thein HH, Bell J, et al. Modelling the hepatitis C virus epidemic in Australia. *Drug Alcohol Depend* 2007;91:228–35.
2. Macdonald V, Dore GJ, Amin J, van Beek I. Predictors of completion of hepatitis B vaccination in attendees at a primary health care centre. *Sex Health* 2007;4:27–30.
3. Dore GJ, Law M, Macdonald M, et al. Epidemiology of hepatitis C virus infection in Australia. *J Clin Virol* 2003;26:171–84.
4. Keeffe EB. Is hepatitis A more severe in patients with chronic hepatitis B and other chronic liver disease? *Am J Gastroenterol* 1995;90:201–5.
5. Vento S, Garofano T, Renzini C, et al. Fulminant hepatitis associated with hepatitis A virus superinfection in patients with hepatitis C. *N Engl J Med*

- 1998;338:286–90.
6. Koff RS. Risks associated with hepatitis A and hepatitis B in patients with hepatitis C. *J Clin Gastroenterol* 2001;33:20–6.
7. Reiss G, Keeffe EB. Hepatitis vaccination in patient with chronic liver disease. *Aliment Pharmacol Ther* 2004;19:715–27.
8. Shim M, Khaykis I, Park J, Bini EJ. Susceptibility to hepatitis A in patients with chronic liver disease due to hepatitis C virus infection: missed opportunities for vaccination. *Hepatology* 2005;42:688–95.
9. Commonwealth of Australia. Australian Immunisation Handbook, 9th edn. 2008. Available at <http://immunise.health.gov.au/internet/immunise/publishing.nsf/Content/handbook-home> [Accessed 15 February 2010].
10. Arguedas MR, McGuire BM, Fallon MB. Implementation of vaccination in patients with cirrhosis. *Digest Dis Sci* 2002;47:384–7.
11. Wong V, Wreghitt TG, Alexander GJM. Prospective study of hepatitis B vaccination in patients with hepatitis C. *BMJ* 1996;312:1336–7.
12. Hachem CY, Kramer JR, Kanwals F, El-Serag HB. Hepatitis vaccination in patients with hepatitis C: practice and validation of codes at a large veteran's administration medical centre. *Aliment Pharmacol Ther* 2008;28:1078–87.
13. Western Australian Department of Health. Guidelines for the provision of hepatitis A and B vaccine to adults in Western Australia at risk of acquiring these infections by sexual transmission and injecting drug use 2008. Available at www.health.wa.gov.au/circularsnew/circular.cfm?Circ_ID=12421 [Accessed 15 February 2010].
14. Western Australian Department of Health. The epidemiology of notifiable sexually transmitted infections and blood-borne viruses in Western Australia 2005–2007. Available at www.public.health.wa.gov.au/cproot/826/2/2005%20Epi%20of%20Notifiable%20STIs%20and%20BBVs%20in%20WA.pdf [Accessed 4 February 2010].
15. Mak DB, Watkins RE. Improving the accuracy of Aboriginal and non-Aboriginal disease notification rates using data linkage. *BMC Health Serv Res* 2008;8:118.
16. Keeffe EB. Hepatitis A and B superimposed on chronic liver disease: vaccine-preventable diseases. *Trans Am Clin Climatol Assoc* 2006;117:227–38.
17. Australian Institute of Health and Welfare. Indigenous Australian access to health care 2006. Available at www.aihw.gov.au/indigenous/health/access.cfm [Accessed 12 March 2010].
18. Britt H, Miller GC, Charles J, et al. General practice activity in Australia, 2008–09. *General Practice Series no. 25*. Available at www.aihw.gov.au/publications/gep/gep-25-11013/gep-25-11013.pdf [Accessed 12 March 2010].
19. Fahrudin S, Britt H. Indigenous patients. In: Britt H, Miller GC, editors. *General practice in Australia, health priorities and policies 1998 to 2008*. *General Practice Series no. 24*. Available at www.aihw.gov.au/publications/gep/gep-24-10721/gep-24-10721-c06.pdf [Accessed 12 March 2010].
20. GlaxoSmithKline. Twinrix (hepatitis A inactivated & hepatitis B (Recombinant) vaccine) prescribing information 2009. Available at http://us.gsk.com/products/assets/us_twinrix.pdf [Accessed 12 March 2010].
21. Leroy V, Bourliere M, Durand M, et al. The antibody response to hepatitis B virus vaccination is negatively influenced by the hepatitis C virus viral load in patients with chronic hepatitis C: a case-control study. *Eur J Gastroen Hepat* 2002;14:485–9.

correspondence afp@racgp.org.au