Vaccine 28 (2010) 8105–8111

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Hepatitis A and travel amongst Nova Scotia postsecondary students: Evidence for a targeted vs. universal immunization strategy

Katherine Matheson[a,c], Beth Halperin[b,c,e], Shelly McNeil[c,d,e], Joanne M. Langley[c,e,f], Donna MacKinnon-Cameron[c], Scott A. Halperin[c,e,g,*]

[a] Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada
[b] School of Nursing, Dalhousie University, Halifax, Nova Scotia, Canada
[c] Canadian Center for Vaccinology, Dalhousie University, IWK Health Centre, Capital Health, Halifax, Nova Scotia, Canada
[d] Department of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada
[e] Department of Pediatrics, Dalhousie University, Halifax, Nova Scotia, Canada
[f] Department of Community Health and Epidemiology, Dalhousie University, Halifax, Nova Scotia, Canada
[g] Department of Microbiology & Immunology, Dalhousie University, Halifax, Nova Scotia, Canada

ARTICLE INFO

Article history:
Received 13 May 2010
Accepted 29 September 2010
Available online 16 October 2010

Keywords:
Hepatitis A vaccine
Universal immunization
Travel

ABSTRACT

Background: Canadian guidelines recommend hepatitis A virus (HAV) vaccination for high-risk persons, such as travelers to HAV-endemic areas. The US CDC advocates universal immunization.
Objectives: To explore whether a universal strategy for HAV immunization rather than the Canadian targeted approach for travelers is justified by measuring compliance of postsecondary students with Canadian guidelines.
Methods: A cross-sectional study using an electronic survey method elicited HAV risk factors, immunization history, disease status, and factors affecting immunization status from postsecondary students. Seropositivity was determined by measuring HAV antibodies in saliva from a convenience sample of survey participants within each study group. Statistical analysis used Fisher's exact test and logistic regression.
Results: We received 2279 completed surveys (10.6% response) and 235 saliva samples (58.7% response). A total of 1380 (60.6%) participants had traveled to HAV-endemic regions and 1851 (81.2%) were planning to do so within the next 5 years. Less than half who traveled to HAV-endemic areas reported a history of HAV vaccination (48.0%). HAV seropositivity rates were higher amongst those who traveled to (63.6%) or were planning to travel to (55.0%) HAV-endemic areas than those who had never traveled or had no plans to travel to such areas (17.4%). Only 8.9% of unvaccinated students were seropositive (5.3% of Canadian-born students). Amongst unvaccinated, seropositive students, there was a nonsignificant trend for higher seropositivity in those who had previously traveled to HAV-endemic areas (14.7%) than those who had not traveled abroad (4.4%), suggesting an exposure to HAV during travel. Nearly all (96.5%) unvaccinated students, who were willing to be vaccinated based on current knowledge or if their doctor recommended it, indicated a willingness to receive vaccine if it were provided free of charge.
Conclusions: Current Canadian guidelines for HAV vaccination are not being followed within the postsecondary student population. Given high rates of travel to HAV-endemic areas in this population, a universal approach to HAV vaccination may be warranted.

1. Introduction

Hepatitis A virus (HAV), a member of the *Picornaviridae* family which may be transmitted between humans via the fecal–oral route and in contaminated food and water, causes infection of the liver [1]. Symptoms of HAV infection can include nausea, anorexia, fever, fatigue, and jaundice [2]. The disease is usually self-limiting, but complications such as fulminant hepatitis, cholestasis, prolonged relapsing disease, and active autoimmune hepatitis occur rarely [1,3,4]. HAV infection is associated with significant morbidity; most symptomatic individuals are unable to work for two to four weeks and 20% require hospitalization [5].

Studies in the United States and Canada have identified an increased incidence of HAV infection amongst members of certain

* Corresponding author at: Canadian Center for Vaccinology, Dalhousie University, IWK Health Centre, 5850/5980 University Avenue, Halifax, NS, Canada B3K 6R8. Tel.: +1 902 470 8141; fax: +1 902 470 7232.
E-mail address: scott.halperin@dal.ca (S.A. Halperin).

0264-410X/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.vaccine.2010.09.107

groups [6,7] including travelers to countries where HAV infection is endemic [8–10], men who have sex with men [11,12], intravenous drug users [13,14], and others [15]. A safe and effective HAV vaccine has been available since 1994 [16]. Current Canadian guidelines recommend HAV vaccination for designated high-risk groups including intravenous drug users, men who have sex with men, people with hemophilia A or B receiving plasma-derived clotting factors, residents in communities with high rates of infection or recurrent outbreaks, and travelers abroad [17]. With these guidelines, many Canadians continue to be infected with HAV; indeed, seven years after the introduction of HAV vaccine, over 1000 infections were still reported annually in Canada. Although the rate of infection has decreased from 8.7 to 1.47 cases per 100,000 between 1996 and 2004 in all Canadians, rates in young adults 20–24 years of age remain at over 2 per 100,000 [18]. The actual incidence of such infection is likely to be much greater than the reported incidence due to nonrecognition of symptoms, asymptomatic infection, and underreporting [19].

Antibodies to HAV develop following an acute infection and provide a reliable marker of past infection. National surveillance and seroprevalence studies done in the United States have demonstrated a remarkable decline in disease since the introduction of hepatitis A vaccine in 17 states with rates above the national average, and led to childhood immunization programs for HAV [20–25]. However, under Canadian guidelines HAV vaccination remains targeted at high-risk groups and is not universally recommended [17].

The rates of reported HAV infection in Canada are highest in young to middle-aged adults [26]. Overseas travel is common amongst postsecondary students, either as part of their educational programs or upon completion of their studies before entering the workforce. We undertook a survey of four groups of postsecondary students in Nova Scotia to examine their knowledge of HAV infection and HAV vaccine, their travel behaviors and intentions, and their rates of HAV vaccination and infection in an effort to explore whether a universal immunization strategy for HAV rather than the current targeted approach is justified.

2. Methods

2.1. Phase I participant recruitment

The study protocol was approved by the Research Ethics Boards at the IWK Health Centre and the Nova Scotia Community College (NSCC). In phase I of the study, a cross-sectional study of four groups of postsecondary students was conducted: undergraduate, graduate and medical students at Dalhousie University, and students attending the NSCC campuses in Halifax Regional Municipality. These students were surveyed regarding their knowledge, attitudes, and beliefs about HAV, HAV vaccine, and indications for use of the vaccine. Subjects were recruited through mass e-mails and reminder e-mails sent from administrative offices of the participating educational institutions. The survey was made available electronically and students received a link to it from the initial e-mail. An information letter about phase I of the study was included with the questionnaire. Consent to participate in the survey was implied by the act of completing the questionnaire electronically. To encourage participation, students who completed the survey were able to choose to enter a lottery for a chance to win a $350 gift certificate at a local shopping center.

2.2. Survey design and validation

The survey had 53 items and was self-administered, web-based, and anonymous unless participants agreed to participate in the second phase of the study. The methods outlined by Dillman were followed during survey design [27]. The survey was based on similar surveys of knowledge and attitudes regarding immunization and travel [28]. It included questions to determine the participants' level of education, travel history, immunization history, and history of HAV infection. Other questions were designed to elicit knowledge, attitudes and beliefs regarding immunization and HAV. The questionnaire was piloted amongst health research professionals and postsecondary students to assess content validity, readability, test–retest reliability, and time to complete. The web-based survey was developed using Remark Web Survey® software (Gravic, Inc., Malvern, PA). Data management and analysis were performed with SAS® software (version 7.0; SAS Institute, Inc., Carey, NC).

2.3. Phase II subject recruitment

Phase II participants were recruited from amongst the participants in phase I. Those who completed phase I of the study were contacted by e-mail in order to briefly explain phase II and were asked to provide their names and addresses if they were interested in taking part in the study. Interested individuals were then mailed a consent form with detailed information about the study purpose, what was involved, and the potential benefits and harms. To encourage participation, participants had the opportunity to enter their names into a second draw for a $400 shopping gift certificate.

2.4. Specimen collection and analysis

Antibody collection kits were sent to approximately 100 randomly selected students from each group who had indicated willingness to participate in phase II of the study. Saliva specimens were collected using the Omni-SAL (Saliva Diagnostic Systems, Medford, NY) device consisting of a fluid-absorbing pad and handle with a saturation color indicator. The absorbing pad is held under the tongue until saturated with saliva and subsequently transferred to a vial containing preserving buffer. This allows for nonrefrigerated specimen storage for several days without compromising suitability for antibody analysis [29,30]. Detailed, easy-to-follow instructions for saliva collection were provided. Study participants returned samples to a designated location at their respective campus. Sample collection tubes were labeled with the participant's study number and date of collection. Samples were stored at the laboratories of the Canadian Center for Vaccinology prior to batch shipping to the laboratories of the Vaccine Evaluation Center in Vancouver for assaying for HAV IgG using an ultrasensitive capture enzyme immunoassay-based method [31]. Participants with no history of HAV vaccination with positive titers were classified as previously infected.

2.5. Sample size and statistical analysis

Data were analyzed using SAS® software (SAS Institute, Inc., Cary, NC). Analysis of proportions was performed by constructing binomial point estimates and exact binomial confidence intervals for each group. Relationships of demographic characteristics, immunization history, and knowledge, attitudes, and beliefs were assessed using Fisher's exact test. Analysis for continuous variables consisted of point estimates and confidence intervals for means. Logistic regression was used to examine the association of knowledge, attitudes, beliefs, and immunization history with willingness to receive the HAV vaccine. Independent predictors of HAV seropositivity in phase II were determined by multivariate analysis.

A sample size of 385 participants for phase I and 246 participants for phase II was needed to ensure that the half-width of the 95% confidence intervals of the point estimates was a maximum of ±5%.