Vaccine 27 (2009) 7156–7161

Contents lists available at ScienceDirect

Vaccine

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

Epidemiology of rabies post-exposure prophylaxis—United States of America, 2006–2008☆

Kira A. Christian[a,*], Jesse D. Blanton[b], Michael Auslander[c], Charles E. Rupprecht[b]

[a] Centers for Disease Control and Prevention, Office of Workforce and Career Development, Career Development Division, Epidemic Intelligence Service, 1600 Clifton Rd NE, Mailstop E-92, Atlanta, GA 30333, United States
[b] Centers for Disease Control and Prevention, National Center for Zoonotic, Vector-Borne and Enteric Diseases, Division of Viral and Rickettsial Diseases, Poxvirus and Rabies Branch, 1600 Clifton Rd NE, Mailstop G-33, Atlanta, GA 30333, United States
[c] Kentucky Department for Public Health (Formerly), 8803 Brittany Drive, Louisville, KY 40220, United States

ARTICLE INFO

Article history:
Received 29 August 2009
Accepted 3 September 2009

Keywords:
Rabies
Rabies vaccine
Prophylaxis

ABSTRACT

Background: The United States of America (USA) does not have a national reporting system for rabies post-exposure prophylaxis (PEP). We describe the epidemiology of PEP in the USA so recommendations can be made during a PEP shortage.
Methods: A two-part questionnaire designed to evaluate PEP distribution practices and estimate PEP use was administered to state health department representatives.
Results: Seventy-five percent of participants responded that no public health guidance was needed to make a recommendation for PEP. The annual national average PEP use is 23,415 courses of PEP (range: 10,645–35,845).
Conclusion: PEP is loosely monitored and a precise estimate of PEP use is unknown. Improved national surveillance for PEP is needed.

Published by Elsevier Ltd.

1. Introduction

Rabies remains a significant zoonotic concern because of its substantial case fatality rate and lack of proven treatment after symptoms occur. Human rabies prevention is accomplished by avoiding exposure to rabid animals or through post-exposure prophylaxis (PEP) with modern rabies biologics.

In the United States of America, PEP for unvaccinated persons consists of thorough wound washing, administration of human rabies immune globulin (HRIG; 20 IU/kg body weight infiltrated into the exposure site), and four intramuscular (IM) doses of a cell culture-based rabies vaccine on days 0, 3, 7, and 14 post-exposure [1]. For previously vaccinated persons (pre-exposure vaccination consisting of 3 doses of licensed rabies vaccine on days 0, 7, and 21 or 28, with serologic evidence of a response to prior vaccination, or completion of the full PEP series resulting from a prior exposure), the PEP series can be shortened to 2 doses of vaccine administered on days 0 and 3, and no HRIG [2]. Although administration of PEP is considered relatively safe, compared with other vaccines, rabies biologics (vaccine and HRIG) are expensive and have been associated with adverse reactions [2]. Although rabies biologic supplies have been adequate historically, rabies PEP has been regarded as overused in the USA [3]. Only two commercially produced vaccines are licensed for use and available in the USA, creating a potential for critical supply limitations or shortages of vaccine. In addition, rabies vaccine is required to hyper-vaccinate human plasma donors to produce supplies of HRIG.

The fragile nature of the rabies vaccine supply in the USA was demonstrated during the past five years. In 2004, a voluntary recall of certain lots of the human diploid cell vaccine (HDCV) occurred because of potentially incomplete inactivation, requiring precautionary revaccination of persons starting pre-exposure vaccination with these lots [4]. This situation led to a temporary reduction in available rabies vaccine supply, although no critical supply limitation occurred because of the availability of vaccine from the other producer, and HDCV production continued to replace recalled lots. However, during 2007, the producer of HDCV temporarily halted production of vaccine pending completion and licensing of a new production line. This was followed in January 2008 by a notification from the producer of the purified chick embryo cell vaccine (PCEC), the only other licensed rabies vaccine in the USA, that an impending decrease in production of vaccine was likely as well [5]. This led to a national response in 2008 that closely monitored use of rabies vaccine to prevent a shortage that might lead to vaccine being unavailable to persons with an exposure to a rabid animal.

☆ The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

* Corresponding author. Tel.: +1 404 553 7666; fax: +1 404 553 7619.
E-mail address: dot9@cdc.gov (K.A. Christian).

0264-410X/$ – see front matter Published by Elsevier Ltd.
doi:10.1016/j.vaccine.2009.09.028

At that time, no recent analysis was available regarding how public health jurisdictions across the USA monitor distribution of PEP, particularly with regard to inadequate supplies of biologics.

The USA does not have a national reporting system for rabies PEP. Previous analyses estimated annual PEP use in the USA at 20,000–40,000 full courses. The most recent analysis of PEP that is based on direct surveillance of PEP administration in the USA (data from 21 states) occurred in the early 1980s [6]. This study estimated that approximately 20,000 courses of PEP were administered annually in the USA, and that exposures involving domestic animals accounted for PEP use unproportional to their role in animal rabies circulation. At the time, PEP was estimated to be correctly administered to approximately 88% of the people [6]. More recently, PEP use was reevaluated in the USA in 1992 [3] and it was estimated that approximately 16,000–37,000 courses of PEP were administered annually in the USA. Since that time, information regarding PEP use has been limited to cross-sectional studies within relatively limited study areas and time [7–15]. One of these studies in 1994 surveyed local health departments in Kentucky for a 1-year period and discovered that the majority of PEP was administered in situations where existing recommendations for quarantine or laboratory testing of the animal were not adhered to, thereby potentially resulting in unnecessary use of PEP. The authors of the Kentucky paper also estimated that only 43.5% of PEP was administered through local health departments (and thus captured in their surveillance system) [15]. Despite these findings and the public health impact of rabies exposure and PEP, a national surveillance system for PEP has not been created. As such, national PEP use remains relatively unknown in the USA.

Because rates of PEP administration in the USA are unknown and supplies of vaccine remain tenuous, estimating the amount of PEP use in the USA is imperative so that more informed recommendations can be made in the event of an actual shortage. Furthermore, discussion relating to development of a national stockpile of rabies biologics will require increased rabies PEP surveillance to best determine when supplies should be released. Monitoring the epidemiology of PEP administration will also provide better understanding of the exposure circumstances in which it is being applied and whether public health recommendations are adhered to. This study evaluates policies and practices of PEP use and obtains an estimate of the rate of PEP administration in the USA. Findings provide information regarding PEP administration in the USA and where additional research is needed.

2. Methods

To describe the epidemiology of PEP use in the USA, a two-part questionnaire was administered to state health department representatives (typically the state public health veterinarian). Only selected questions were analyzed for purposes of this study. Part I of the questionnaire was designed to collect data regarding how jurisdictions monitor PEP distribution. Specifically, responders were asked to address how rabies biologics are tracked and monitored, whether route of exposure is documented, their policies of PEP distribution, and their opinions regarding overuse. Part II of the questionnaire was designed to estimate the number of PEP courses administered in each respondent's state or jurisdiction. Respondents were also asked to estimate proportion of persons receiving PEP according to exposure type and animal.

We distributed the questionnaire in two parts to known health department contacts working in rabies-related assignments in each of the 50 states, Puerto Rico, Washington, DC, and New York City (NYC) (53 total points-of-contact). Persons at these points-of-contact who manage rabies concerns were considered to be the jurisdiction's designated public health veterinarian (e.g., the designated state public health veterinarian as recognized by the National Association of State Public Health Veterinarians, Inc., http://www.nasphv.org), the chief rabies laboratory official, or the local epidemiologist. Questionnaires were distributed through a free, secure, online survey tool, and completion and return of each questionnaire indicated the respondent's approval to participate. Data were stored in a password-protected database and transferred into a statistical software package for analysis.

National PEP estimates were based on survey responses provided in Part II of the survey and used methodology similar to past studies [3,6]. PEP rates were calculated on the basis of estimates provided by respondents and stratified by primary rabies reservoir in each responding state. The primary rabies reservoir for each state was assigned as the terrestrial rabies reservoir affecting the greatest area of a given state. This reservoir was presumed to account for the majority of PEP administration, as reported by a state, in the questionnaire. High and low rates were calculated for each state on the basis of maximum and minimum estimates provided by survey respondents. We considered the mean of these stratified rates to represent the average PEP rate associated with the corresponding predominant rabies reservoir. The estimated population for each county in 2005 was obtained from the U.S. Census Bureau and combined in a geographic information system with reservoir regions estimated from the 2008 annual rabies report to derive the population of each state affected by the major rabies reservoirs [17]. The calculated county-specific PEP rates were then used to estimate the average, low, and high annual courses of PEP used in each state and the District of Columbia. Pre-exposure vaccination data were obtained from records submitted to the Centers for Disease Control and Prevention (CDC) requesting vaccine for pre-exposure vaccination during the vaccine supply limitation during June–October, 2008, and from the estimated number of doses required for pre-exposure vaccination of veterinary students submitted by veterinary schools during the same period.

3. Results

3.1. Questionnaire I

Part I of the questionnaire was completed and returned by 40 respondents (75% response rate). Of the 40 responses to Part I, 32 (80%) responded that private healthcare providers or facilities administer PEP; two (5%) responded that the state or local government provides PEP; and six (15%) responded that a combination of private and public entities supply PEP. Biologics for PEP, which include rabies vaccine and HRIG, were acquired directly by private healthcare providers or facilities in 28 (70%) of the 40 jurisdictions, by state or local governments in three (8%), and by a combination of private and public in nine (23%) jurisdictions. When asked if a state or local health department verifies that a true exposure to rabies virus has occurred for PEP to be recommended, 10 (25%) of the 40 jurisdictions responded *yes*, and 30 (75%) responded that no public health guidance was needed to make a recommendation for PEP.

Considering recent limitations in the rabies vaccine supply, respondents were asked if any changes to their PEP policies or procedures were planned in response to the ongoing supply situation. Twelve (30%) responded *yes*, and 28 (70%) responded that no changes in policy were being made in response to the biologics supply. Twenty-six (65%) respondents indicated that no surveillance system is used for rabies PEP in their jurisdiction. Thirty (75%) of the 40 respondents believed that rabies PEP is overused in their jurisdiction; the remaining 10 believe that it is appropriately used. Responders were asked if they would support creation of a nationally notifiable reporting system for rabies PEP. A total of 23 (58%) responded *yes*, and 16 (40%) responded *no* (one respondent