COST DIFFERENCES BETWEEN COMPLETE AND INCOMPLETE POST-EXPOSURE COURSES OF RABIES VACCINATION

Yuwares Sittichanbuncha[1], Chalermpon Chairat[1], Kittisak Sawanyawisuth[2,3] and Vichai Senthong[2]

[1]Department of Emergency Medicine, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok; [2]Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen; [3]Research Center in Back, Neck Other Joint Pain and Human Performance (BNOJPH), Khon Kaen University, Khon Kaen, Thailand

Abstract. Courses of post-exposure rabies vaccination in clinical practice are often not administered completely. If suspected animals are still alive after 10 days of observation, full post-exposure vaccination will usually be withheld from bite victims. In this study, we compared the cost differences between complete and incomplete courses of post-exposure rabies vaccination. The cost calculations were based on the principle that all patients will have at least one more animal bite in the future. Costs were compared between patients who received post-exposure rabies vaccination and if they completed or did not complete the vaccine regimen. In this study, 46.7% of 372 patients completed the full course of five doses of the rabies vaccine. Based on the study rationale, complete vaccination would save nation budget 224,700 Baht for WHO wound category 2, 801,474 Baht for WHO wound category 3 with equine rabies immunoglobulin treatment, and 2,618,916 Baht for WHO wound category 3 with human rabies immunoglobulin treatment. Physicians should encourage complete courses of post-exposure rabies vaccination to save further costs from animal bites in the future.

Keywords: post-exposure rabies vaccination, cost

INTRODUCTION

Rabies is almost always a fatal disease in unvaccinated people (Wilde *et al*, 2008) but can be prevented by either pre-exposure or post-exposure vaccination (Briggs, 2012). Pre-exposure vaccination is highly effective (Suwansrinon *et al*, 2006) and is recommended for those people who are most at risk such as veterinarians or tourists (Murthy *et al*, 2013). In practice, most people at risk for rabies are in the general population and only attend clinics after being bitten by a possibly infected animal. Post-exposure vaccination is therefore the usual situation in clinical practice (Bailey *et al*, 2013). There are two recommended routes of vaccination for post-exposure vaccination; intramuscular or intradermal (Wilde *et al*, 2012). Intramuscular use is more convenient and more commonly prescribed than the intradermal route (Khawplod *et al*, 2002; Lodmell and Ewalt, 2004).

Correspondence: Vichai Senthong, Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.
Tel: 66 (0) 43 363664, Fax: 66 (0) 43 348399
E-mail: vichaisenthong@gmail.com

In real practice, not all courses of post-exposure vaccination are completed (Moran *et al*, 2000). One reason is that if the suspect animals are still alive after ten days of observation, the likelihood of the animal having rabies is low. In Thailand, physicians, therefore, may not prescribe a complete course of vaccination in this situation (MoPH, 2013). Patient compliance may be another factor in failure to complete the five doses of post-exposure rabies vaccination. Here, we provide a cost-benefit analysis of complete versus incomplete post-exposure rabies vaccination courses taking into account the high possibility of having future animal bites.

MATERIALS AND METHODS

All patients who visited the Emergency Department of Ramathibodi Hospital due to bites from mammalian species, and who received rabies vaccinations, were enrolled. The study period was between January 1 and December 31, 2006. Data were retrieved from medical records. The numbers of patients who completed, or did not complete, courses of rabies vaccination according to WHO guidelines were counted (Sittichanbuncha *et al*, 2014). Baseline characteristics of patients, details of treatment, and outcomes have been described elsewhere (Sittichanbuncha *et al*, 2014).

Cost calculation strategies

The cost calculations were based on the principle that all patients will have at least one more animal bite in the future. Wound categories were defined according to WHO guidelines as 1, 2, and 3 (WHO, 2010). Only those with categories 2 and 3 were used for cost calculation because no vaccination procedures would be required for wound category 1. Cost calculations covered only vaccine-related costs and it was assumed that other costs such as antibiotic treatment, wound care, wound infection, tetanus toxoid, tetanus antitoxin, or transportation costs were similar in all patients. All costs were calculated based on the rabies vaccine available at Ramathibodi Hospital on October 27, 2013 (Table 1). Five doses of rabies vaccine are recommended for WHO wound category 2. For WHO wound category 3, five doses of rabies vaccine plus equine rabies immunoglobulin (ERIG) or human rabies immunoglobulin (HRIG) are recommended. HRIG is recommended if a patient is sensitive to ERIG by skin test.

RESULTS

During the study period, 372 patients met the study criteria. Of those, 174 patients (46.7%) completed all five doses of rabies vaccine (Verorab: Purified Vero Cell Rabies Vaccine; PVRV). The other 198 patients (53.3%) did not complete the vaccine schedule.

If all 174 fully vaccinated patients were bitten once again by mammals, the total costs for rabies vaccine would be 121,800 Baht regardless of the wound category (Table 2).

For those who had not completed the vaccinations, the vaccine costs would depend on wound type, ERIG allergy, and the risk of being bitten. Wound category 2 would require only rabies vaccination, while wound category 3 would require rabies vaccination plus either ERIG or HRIG. In addition, if the animals were still alive after ten days, the patients may only have received three doses of rabies vaccination and therefore would need revaccination with future exposure. The total costs were lowest with wound category 2 (and caused by animals that were known to have remained alive) at 207,900

Table 1
Details of rabies vaccines at Ramathibodi Hospital (Accessed October 27, 2013).

Vaccines	Dose/vial	Price/vial	Recommended doses	Total cost
Verorab (Sanofi Pasteur)	0.5 ml	350 Baht	5 doses	1,750 Baht
ERIG (Favirab)	1,000 IU/5 ml	971 Baht	40 IU/kg	2,913 Baht (weight 60 kg)
HRIG (Berirab P, Sanofi Pasteur)	300 IU/2 ml	3,023 Baht	20 IU/kg	12,092 Baht (weight 60 kg)

Verorab, Purified Vero Cell Rabies Vaccine, PVRV; ERIG, equine rabies immunoglobulin; HRIG, human rabies immunoglobulin.

Table 2
Costs of post-exposure rabies vaccination if complete or incomplete vaccination had been received after a previous exposure.

Wound category (percentage)[a]	Previous complete vaccination *N* = 174	Previous incomplete vaccination (animal has remained alive) *N* = 198	Previous incomplete vaccination (rabies infected or unknown animals) *N* = 198
2 (3.80%)	2 doses of Verorab 2 x 350 x 174 = 121,800	3 doses of Verorab 3 x 350 x 198 = 207,900	5 doses of Verorab 5 x 350 x 198 = 346,500
3 with ERIG (95.40%)	2 doses of Verorab 2 x 350 x 174 = 121,800	3 doses of Verorab 3 x 350 x 198 = 207,900 3 vials of ERIG 3 x 971 x 198 = 576,774 = 784,674	5 doses of Verorab 5 x 350 x 198 = 346,500 3 vials of ERIG 3 x 971 x 198 = 576,774 = 923,274
3 with HRIG (95.40%)	2 doses of Verorab 2 x 350 x 174 = 121,800	3 doses of Verorab 3 x 350 x 198 = 207,900 4 vials of HRIG 4 x 3023 x 198 = 2,394,216 = 2,602,116	5 doses of Verorab 5 x 350 x 198 = 346,500 4 vials of HRIG 4 x 3023 x 198 = 2,394,216 = 2,740,716

Verorab, Purified Vero Cell Rabies Vaccine, PVRV; ERIG, equine rabies immunoglobulin; HRIG, human rabies immunoglobulin. [a]Indicated percentage of wound category based on clinical study; costs shown in Thai Baht (USD 1 ≃ THB 30).

Table 3
Cost savings if received complete course of rabies vaccinations by wound categories compared with previous incomplete vaccinations.

Wound category	Previous complete vaccination $N = 174$	Previous incomplete vaccination (animal has remained alive) $N = 198$	Previous incomplete vaccination (rabies infected or unknown animals) $N = 198$
2	0	86,100	224,700
3 with ERIG	0	662,874	801,474
3 with HRIG	0	2,480,316	2,618,916

ERIG, equine rabies immunoglobulin; HRIG, human rabies immune globulin; costs shown in Thai Baht (USD 1 ≃ THB 30).

Baht and highest with wound category 3 (and bites caused by animals of unknown infection status) and received HRIG at 2,740,716 Baht. Cost savings were calculated in each situation as shown in Table 3 and compared with those who completed post-exposure rabies vaccination.

DISCUSSION

In one example of real practice, the course of post-exposure rabies vaccination was completed in only 46.7% of patients. Even though physicians may discontinue post-exposure rabies vaccination if suspect animals are alive after ten days of observation, we recommend that the vaccination course be completed. This is based on the theory that people are likely to be bitten by animals more than once in their lifetimes. The maximum cost saving of 2,618,916 Baht may be applied (Table 3).

According to a previous study, most patients had WHO wound category 3 (355/372 or 95.4%) (Sittichanbuncha *et al*, 2014). Only 3 (0.8%) had wound category 1 and 14 (3.8%) had category 2 wounds. These data suggest that anyone bitten again by animals will suffer wound category 3 and hence require immunoglobulin therapy if the previous vaccinations were not completed (WHO, 2010). It is likely that most bites will be inflicted by animals other than those owned by the patient. For example, in Bangkok, only 8.5% of bites were inflicted by animals on their owners (Bhanganada *et al*, 1993). So, in most cases, animals inflicting bites are likely to be feral strays and not available for subsequent monitoring. In such cases, the patients should receive five doses of rabies vaccine and/or immunoglobulin. The costs for post-exposure rabies vaccination, in fact, are high from rabies immunoglobulin, but not from the rabies vaccine (Table 3).

This study provides preliminary data comparing costs of future rabies vaccination based on real clinical practice and the assumption that all patients will need rabies vaccination again at least once in the future. Prospective data and actual cost analysis in terms of cost effectiveness are needed. From the present data, it may be worthwhile for bite victims to be given complete courses of post-exposure

rabies vaccination to save costs of future vaccination and in particular, immunoglobulin use and risk of immunoglobulin allergy. This study was based on a total study population of only 372 patients (Sittichanbuncha *et al*, 2014, in press). When the current total population of Thailand of 67,108,507 people, however, is taken into account the suggested protocol may make a significant saving in the national budget. In conclusion, incomplete courses of post-exposure rabies vaccination may have higher costs than complete vaccination if future vaccination is needed.

ACKNOWLEDGEMENTS

This study was supported by TRF grants from Senior Research Scholar Grant, Thailand Research Fund grant number RTA5580004 and the Higher Education Research Promotion and National Research University Project of Thailand, Office of the Higher Education Commission, Thailand through the Health Cluster (SHeP-GMS), Khon Kaen University. We would like to acknowledge Prof James A Will for editing the manuscript via the Faculty of Medicine Publication Clinic, Khon Kaen University, Thailand.

REFERENCES

Bailey AM, Holder MC, Baker SN, Weant KA. Rabies prophylaxis in the emergency department. *Adv Emerg Nurs J* 2013; 35: 110-9; quiz 120-1.

Bhanganada K, Wilde H, Sakolsataydorn P, Oonsombat P. Dog-bite injuries at a Bangkok teaching hospital. *Acta Trop* 1993; 55: 249-55.

Briggs DJ. The role of vaccination in rabies prevention. *Curr Opin Virol* 2012; 2: 309-14.

Khawplod P, Tantawichien T, Wilde H, *et al*. Use of rabies vaccine after reconstitution and storage. *Clin Infect Dis* 2002; 34: 404-6.

Lodmell DL, Ewalt LC. Rabies cell culture vaccine reconstituted and stored at 4 degrees centigrade for 1 year prior to use protects mice against rabies virus. *Vaccine* 2004; 22: 3237-9.

Ministry of Public Health (MoPH), Department of Disease Control. Thai guideline for rabies management. Nonthaburi: MoPH, 2013. [Cited 2013 Dec 24]. Available from: URL: http://thaigcd.ddc.moph.go.th/uploads/pdf/pat_3/Rabies/Rabies_CPG56_QA_Low.pdf

Moran GL, Talan DA, Mower W, *et al*. Appropriateness of rabies postexposure prophylaxis treatment for animal exposures. Emergency ID Net Study Group. *JAMA* 2000; 284: 1001-7.

Murthy S, Keystone J, Kissoon N. Infections of the developing world. *Crit Care Clin* 2013; 29: 485-507.

Suwansrinon K, Wilde H, Benjavongkulchai M, *et al*. Survival of neutralizing antibody in previously rabies vaccinated subjects: a prospective study showing long lasting immunity. *Vaccine* 2006; 24: 3878-80.

World Health Orgainzation (WHO). Rabies vaccines: WHO position paper--recommendations. *Vaccine* 2010; 28: 7140-2.

Wilde H, Hemachudha T, Jackson AC. Viewpoint: Management of human rabies. *Trans R Soc Trop Med Hyg* 2008; 102: 979-82.

Wilde H, Wacharapluesadee S, Hemachudha T. Currently approved post-exposure rabies prophylaxis regimens. *Travel Med Infect Dis* 2012; 10: 162-3.