Short Communication

Effects of Permethrin at a Prophylactic Dose for Ectoparasite Infection on Cholinesterase Activity in Dogs

Piyarat Chansiripornchai* Niwat Chansiripornchai

Abstract

Effects of permethrin at a prophylactic dose for ectoparasite infection on cholinesterase (ChE) activity was evaluated. Eight healthy dogs were exposed to a spot-on formulation of permethrin on day 0. The results of serum ChE activity in all of the dogs which was measured at 24 h after exposure to permethrin significantly decreased when compared to those before exposure. However, the serum ChE activity in all the dogs which was measured at 36 and 96 h after exposure to permethrin showed no significant difference as compared to those before exposure. There were no clinical signs in all dogs throughout the experiment. The results suggest that using spot-on formulation of permethrin at a prophylactic dose for ectoparasite infection is safe in dogs.

Keywords : cholinesterase, dog, permethrin, toxicity

Faculty of Veterinary Science, Chulalongkorn University, Henri-Dunant Road, Pathumwan, Bangkok 10330. Thailand

***Corresponding author E-mail: spiyarat@hotmail.com**

Thai J. Vet. Med., 2009. 39(4): 343-347

บทคัดย่อ

ผลของเพอร์เมทรินในขนาดที่ใช้ป้องกันปรสิตภายนอกต่อค่าการทำงานของเอนไซม์โฆลีนเอสเทอเรสในสุนัข

ปิยะรัตน์ จันทร์ศิริพรชัย* นิวัตร จันทร์ศิริพรชัย

ศึกษาผลของเพอร์เมทรินในขนาดที่ใช้ป้องกันปรสิตภายนอกต่อค่าการทำงานของเอนไซม์โฆลีนเอสเทอเรส โดยให้สุนัขสุขภาพดีจำนวน 8 ตัวได้รับเพอร์เมทรินชนิดหยดบนผิวหนัง ทำการตรวจวัดค่าการทำงานของเอนไซม์โฆลีนเอสเทอเรสใน 24 ชั่วโมงหลังการหยดยา พบว่ามีค่าลดลงอย่างมีนัยสำคัญเมื่อเปรียบเทียบกับค่าก่อนได้รับยา อย่างไรก็ตามพบว่าค่าการทำงานของเอนไซม์ชนิดนี้ไม่แตกต่างจากค่าก่อนการได้รับยาเมื่อตรวจวัดที่ 36 และ 96 ชั่วโมงหลังการหยดยา และไม่พบอาการผิดปกติทางคลินิกในสุนัขทุกตัวตลอดการทดลอง ผลการศึกษาแสดงให้เห็นว่าการใช้เพอร์เมทรินในรูปยาหยดบนผิวหนังในขนาดที่ใช้ป้องกันปรสิตภายนอกมีความปลอดภัยเมื่อใช้ในสุนัข

คำสำคัญ : โฆลีนเอสเทอเรส สุนัข เพอร์เมทริน ความเป็นพิษ

คณะสัตวแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ถนนอังรีดูนังต์ ปทุมวัน กรุงเทพฯ 10330
***ผู้รับผิดชอบบทความ E-mail: spiyarat@hotmail.com**

Introduction

Permethrin is a pyrethroid insecticide used in both agricultural and domestic products (Sutton et al., 2007). Permethrin is a type I pyrethroid which has a low toxicity compared with type II pyrethroid such as cypermethrin (Rao and Rao, 1995). Permethrin acts on voltage-dependent sodium channels by extending the channel opening causing an increased sodium current; consequently, depolarization is prolonged leading to a repetitive firing of the nerve (Ray, 1991; Sutton et al., 2007). Moreover, permethrin inhibits ChE by interaction at the hydrophobic aromatic surface region of the enzyme, thus reducing in ChE activity (Rao and Rao, 1995).

Permethrin is used in numerous formulations for the control of insect on pets such as ticks on animals and in environment. In Thailand, spot-on formulation of permethrin for dogs is available at a concentration of 65% (w/v). Since cats are sensitive to permethrin either by direct contact or secondary exposure through contact with other pets treated with permethrin (Merola and Dunayer, 2006) the product is contraindicated in this species.

In general, permethrin is considered to be of low toxicity to dogs when used as directed by the manufacturer (Richardson, 1999). However, there have been many reports on the toxicity of pyrethroid insecticides in dogs (Bates, 2000; Martin and Campbell, 2000). The lethal toxicity of pyrethroid in animals has been published but the sublethal toxicity of the agent has not been studied, especially, the effect of permethrin at the prophylactic dose that is used in small animal practices. It is accepted that exposure to pyrethroid insecticides such as permethrin can decrease cholinesterase enzyme (ChE) activity which affects the nervous system function (Balint et al., 1995; Hakbrook et al., 1992; Rao and Rao, 1995). Measurement of ChE activity appears to have been useful in monitoring the sublethal toxicity of insecticides and also in the safety evaluation of the drug's use prior to clinical signs are being detected (Chansiripornchai et al., 2008).

This study was performed to evaluate the effect of permethrin spot-on formulation at a prophylactic dose for ectoparasite infection on ChE activity in dogs.

Materials and Method

Eight healthy dogs with normal hematological and biochemical profiles from a private animal hospital were used as experimental animals. On day 0, blood samples were taken from all the dogs for the measurement of alanine aminotransferase (ALT) and the creatinine for liver and kidney function test, respectively. ChE activity was also measured. After taking the blood, a spot-on formulation of permethrin (Protical®, Schering Plough, Germany) at the recommended dose of 65% (w/v) was administered to the back of all the dogs and they were kept in a conventional area. At 24, 36 and 96 h after exposure to permethrin, blood samples were taken from all dogs for measurement of ChE, ALT and creatinine. The ALT and creatinine levels were analyzed using an automatic analyzer (FujiDri-Chem 3500i, Fuji, Japan). The ChE activity was measured as described by Ellman et al. (1961) using colorimetric determination by spectrophotometer (UV-160a), Shimadzu, Japan). Data was analyzed using the repeated measure ANOVA ($p<0.05$).

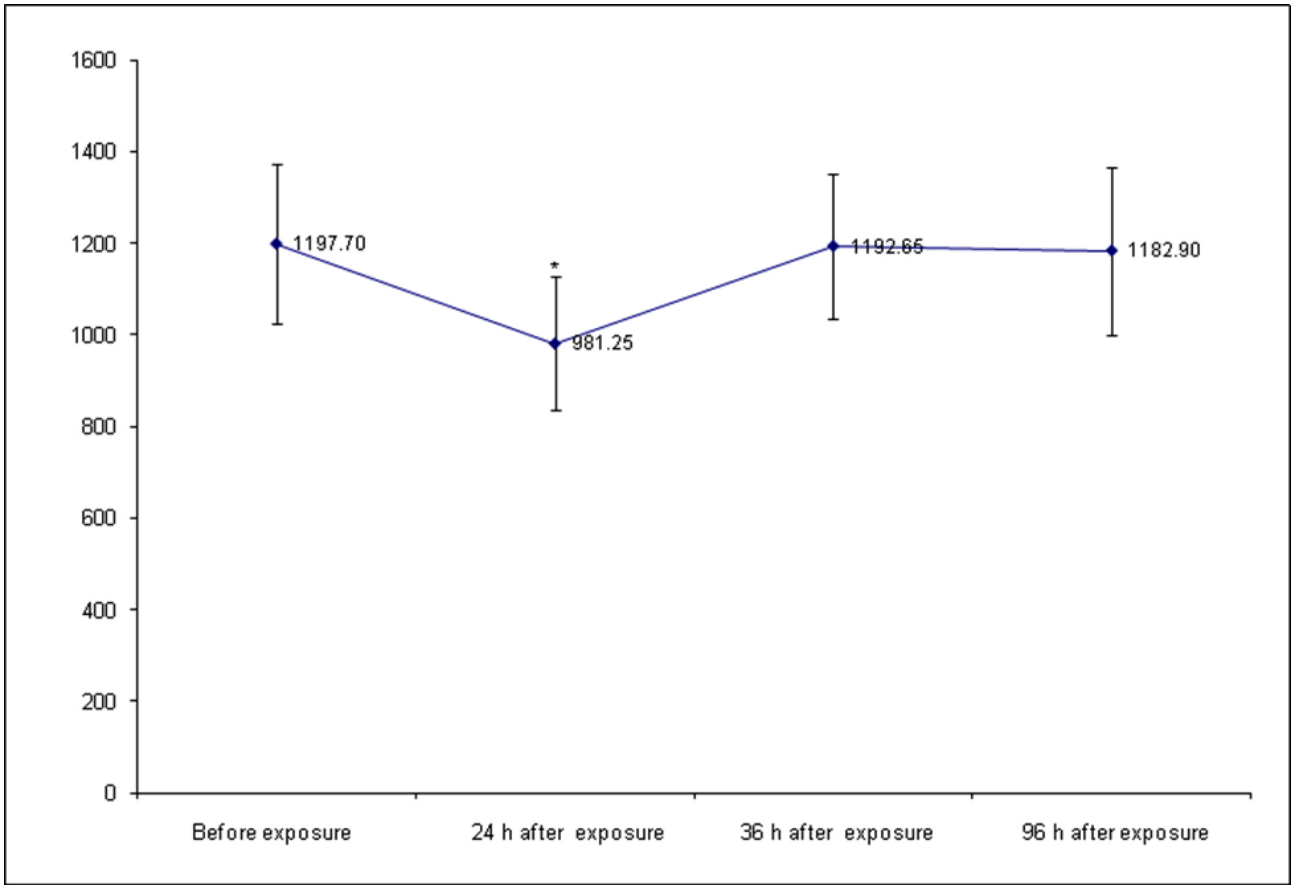
Results and Discussion

Pyrethroids are recognized as the fourth major class of insecticides and they interfere with the function of the nervous system like other major classes of insecticides such as organochlorines, organophosphates and carbamates (Elliot, 1997). The widespread use of pyrethrins and pyrethroids has increased in animals and humans and has led to an interest in their toxicoses. Dermal exposure of permethrin by application to the skin and hair coat is the most frequent route that leads to intoxication, particularly in cats (Anadon et al., 2009). Although pyrethrins and pyrethroids are generally regarded as safe in dogs, their sublethal toxicity should be evaluated for toxicological data. The determination of serum ChE activity is used for the evaluation of intoxication by organophosphate, carbamate and pyrethroid insecticides which are ChE inhibitors (Balint et. al., 1995; Halbrook et. al., 1992; Rao and Rao, 1995). The colorimetric method for the measurement of ChE activity as described by Ellman et al. (1961) using thiocholine ester as a substrate and 5, 5'- dithiobis-(2- nitrobenzoic acid) as a coloring agent offers good accuracy and is widely used (Okabe et al., 1997).

In the present study, the effect of 65% (w/v) permethrin spot-on formulation at a prophylactic dose for ectoparasite infection in dogs was evaluated by the measurement of ChE activity. As a result, serum ChE activity in all the dogs significantly decreased within 24 h after exposure to permethrin (Figure 1). This result may concur with the study determined by Ansari et al. (1990) which found that using cypermethrin, a pyrethroid insecticide, at a prophylactic dose for ectoparasite infection in cattle can decrease ChE activity on day 1 after exposure and can increase to the normal level within 7 days after exposure. However, the serum ChE activity in the dogs at 36 hr after exposure increased and showed no significant difference when compared with that before exposure. Moreover, there were no clinical signs in any dogs throughout the experiment and the ALT and creatinine levels were also within normal range (Table 1).

On the other hand, a previous report of using a combination spot-on formulation of permethrin and imidacloprid (Advantix®, Bayer, Germany) at a prophylactic dose for ectoparasite infection in dogs indicates that the 60% (w/v) of permethrin in this product did not have any effect on serum ChE activity (Chansiripornchai et al., 2008) but using 65% (w/v) of permethrin in our present study decreased the ChE activity within 24 h after exposure. This result suggests that using a higher concentration of permethrin may effect ChE activity and may cause clinical signs in the animal. Since 65% (w/v) permethrin spot-on formulation is the highest concentration of this product in Thailand, therefore it is safe to use the product for dogs.

Figure 1. Serum cholinesterase activity (micromole of substrate hydrolyzed/min/ml) in the dogs after exposure to permethrin (n = 8)



*significant difference (p<0.05)

Table 1. The ALT and creatinine levels in dogs on day 0, 1 and 4 after exposure to permethrin

	ALT*			Creatinine**		
Dog No.	D0	D1	D4	D0	D1	D4
1	31	30	29	1.1	0.9	0.9
2	25	23	26	0.7	0.7	0.9
3	31	31	28	0.8	0.9	0.8
4	38	41	37	0.8	0.9	0.9
5	45	49	53	1.0	0.8	0.8
6	20	20	21	0.5	0.6	0.6
7	32	30	31	0.4	0.4	0.5
8	28	29	26	1.1	1.2	1.2

*Normal level 8.2-57.3 (IU/1) (Fraser et al., 1991), **Normal level 0.5-1.6 (mg/dl) (Fraser et al., 1991)

Acknowledgments

We wish to thank Mr. Wiritpol Chanwaowam, Miss Sukolapa Chiarasumran and Miss Boonyarat Temeecharoentaworn for laboratory assistance.

References

Anadon, A., Martinez-Larranaga, M.R. and Martinez, M.A. 2009. Use and abuse of pyrethrins and synthetic pyrethroids in veterinary medicine. Vet. J. 182(1): 7-20.

Ansari, M.Z., Kumar, A., Prasad, R.L., Basu, A., Sahai, B.N. and Sinha, A.P. 1990. Clinicobiochemical use of serum cholinesterase following treatment with synthetic pyrethroid, cypermethrin and fenvalerate, in cattle and buffalo experimentally infested with *Boophilus microplus*. Indian J. Exp. Biol. 28(3): 241-244.

Balint, T., Szegletes, T., Szeglets, Z., Halask, K. and Nemcsok, J. 1995. Biochemical and subcellular changes in carp exposed to the organophosphorus methidathion and the pyrethroids deltamethrin. Aquatic Toxicol. 3(3): 279-295.

Bates, N. 2000. Pyrethrins and pyrethroids. In: Handbook of Poisoning in Dogs and Cats. 1st ed. Oxford: Blackwell Sciences, UK. 228-230.

Chansiripornchai, P., Satranarakun, P., Kanoksopit, M. and Nisakulrat, Y. 2008. The safety evaluation of permethrin on dogs when used in a prophylactic dose for ectoparasite infection, by measuring serum cholinesterase activity. Thai J. Vet. Med. 38(1): 39-42.

Elliot, M. 1977. Synthetic pyrethroids. In: Synthetic Pyrethroids. American Chemical Society, Washington D.C., USA. 1-28.

Ellman, G.L., Courtney, K.D., Andres, V. and Featherstone, R.M. 1961. A new and rapid colorimetric determination of acetylcholinesterase activity. Biochem. Pharmacol. 7: 88-95.

Fraser, C.M., Bergeron, J.A., Mays, A. and Aiello, S.E. 1991. Clinical values and procedures. In: The Merck Veterinary Mannual. 7th ed. 969.

Halbrook, R.S., Shagart, L.R., Watson, A.P., Munro, N.B. and Linnabary, R.D. 1992. Characterizing biological variability in livestock blood cholinesterase activity for biomonitoring organophosphate nerve agent exposure. J. Am. Vet. Med. Assoc. 201(5): 714-725.

Martin, A. and Campbell, A. 2000. Permethrin toxicity in cats. Vet. Rec. 25: 639.

Merola, V. and Dunayer, E. 2006. The 10 most common toxicoses in cats. Vet. Med. 101(6): 339-342.

Okabe, H., Sagesaka, K., Nakajima, N. and Noma, A. 1977. New enzymatic assay of cholinesterase activity. Clin. Chemica Acta. 80: 87-94.

Rao, G.V. and Rao, K.S.J. 1995. Modulation in acetylcholinesterase of rat brain by pyrethroids *in vivo* and *in vitro* kinetic study. J. Neurochem. 65(5): 2259-2266.

Ray, D.E. 1991. Pesticides derived from plants and other organisms. In: Handbook of Pesticide Toxicity. Academic Press, USA. 585-636.

Richardson, J.A. 1999. Permethrin spot-on toxicosis in cats. J. Vet. Emerg. Crit. Care. 10: 103-106.

Sutton, N.M., Bates, N. and Campbell, A. 2007. Clinical effects and outcome of feline permethrin spot-on poisonings reported to the Veterinary Poisons Information Service (VPIS), London. J. Feline Med. Surg. 9: 335-339.