Short Communication

The Safety Evaluation of Permethrin on Dogs When Used in a Prophylactic Dose for Ectoparasite Infection, by Measuring Serum Cholinesterase Activity

Piyarat Chansiripornchai[1*] Pakkawan Satranarakun[2]
Mallavee Kanoksopit[1] Yuthana Nisakulrat[1]

Abstract

The safety of permethrin at a prophylactic dose for ectoparasite infection in dogs was evaluated by the measurement of cholinesterase activity (ChE). On day 0, eight healthy dogs were exposed to spot - on formulation of permethrin. The results of serum ChE activity in all the dogs which measured on day 1 and 4 after exposure to permethrin showed no significant different comparing to those before exposure. There were no clinical signs in all dogs throughout the experiment. The result suggests that using spot-on formulation of permethrin at a prophylactic dose for ectoparasite infection is safe in dogs.

Keywords : cholinesterase, dog, permethrin, toxicity

[1]**Faculty of Veterinary Science, Chulalongkorn University, Henri-Dunant Road, Bangkok 10330**
[2]**Bayer Thai Co., Ltd. North Sathon Road, Bangkok 10500**
[*]**Corresponding author**

บทคัดย่อ

การประเมินความปลอดภัยของเพอร์เมทรินในสุนัขเมื่อใช้ในขนาดป้องกันปรสิตภายนอกโดยการตรวจวัดค่าการทำงานของเอนไซม์โฆลีนเอสเทอเรสในซีรั่ม

ปิยะรัตน์ จันทร์ศิริพรชัย[1*] ภควัน ศาสตรานรากุล[2] มัลลวีร์ กนกโศภิต[1] ยุทธนา นิศกุลรัตน์[1]

ประเมินความปลอดภัยของเพอร์เมทรินในสุนัขเมื่อใช้ในขนาดป้องกันปรสิตภายนอกโดยการตรวจวัดค่าการทำงานของเอนไซม์โฆลีนเอสเทอเรส โดยในวันเริ่มการทดลองให้สุนัขที่มีสุขภาพดี 8 ตัวได้รับยาชนิดหยดหลังที่มีเพอร์เมทรินเป็นองค์ประกอบในขนาดยาที่แนะนำให้ใช้ป้องกันปรสิตภายนอก ผลการตรวจวัดค่าการทำงานของเอนไซม์โฆลีนเอสเทอเรสในวันที่ 1 และ 4 ของการทดลองไม่พบการเปลี่ยนแปลงค่าการทำงานของเอนไซม์ชนิดนี้ และไม่พบอาการผิดปกติทางคลินิกในสุนัขทุกตัวตลอดการศึกษา ผลการทดลองแสดงให้เห็นว่า การใช้ยาชนิดหยดหลังที่มีเพอร์เมทรินเป็นองค์ประกอบในขนาดยาที่แนะนำให้ใช้ในการป้องกันปรสิตภายนอกมีความปลอดภัยเมื่อใช้ในสุนัข

คำสำคัญ : โฆลีนเอสเทอเรส สุนัข เพอร์เมทริน ความเป็นพิษ

[1]คณะสัตวแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ถ. อังรีดูนังต์ กทม. 10330
[2]บริษัทไบเออร์ไทยจำกัด ถ.สาทรเหนือ กทม. 10500
[*]ผู้รับผิดชอบบทความ

Introduction

There are many types of ectoparasiticide used in veterinary medicine. Permethrin is one of the most popular ectoparasiticides usedd in Thailand. Permethrin, a component of Advantix[R], is a pyrethroid insecticide which can kill ticks in dogs. In general, permethrin is safe for use in mammals but there are no reports on any sublethal toxicity studies of this drug.

It is generally accepted that exposure to pyrethroid insecticides such as permethrin can decrease the cholinesterase enzyme (ChE) activity which affects the nervous system function (Balint et al., 1995; Halbrook et al., 1992). The levels of toxicity vary from no clinical signs to nervous system signs such as ataxia, hypoxia, hypersalivation, coma and death (Curtis, 2003). Measurement of ChE activity has appeared to be 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.

This study was performed to confirm the safety and to evaluate the sublethal toxicity of permethrin when used as an ectoparasiticide at recommended doses in dogs by measuring ChE activity.

Materials and Method

Eight healthy dogs with normal hematological and biochemical profiles from private animal hospital were used as experimental animals. On day 0, blood samples were taken from all dogs for the measurement of alanine aminotransferase (ALT) and creatinine for liver and kidney function tests, respectively. ChE activity was also measured. After taking the blood, spot-on formulation of permethrin (Advantix[R], Bayer, Germany) at the recommended dose of 50% (w/v) was administered to the back of all dogs and then they were kept in a conventional area.

On days 1 and 4 after exposure to permethrin, blood samples were taken from all the dogs for measurement of SGPT and creatinine. ChE activity was also measured.

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

Table 1. Serum cholinesterase activity in the dogs after exposure to permethrin (n = 8)

D	ChE activity* (mean ± sd)
D_0	1587.32 ± 171.78
D_1	1572.83 ± 194.48
D_4	1587.26 ± 236.95

*micromole of substrate hydrolyzed/min/ml

Table 2. The ALT and creatinine levels in dogs on days 0, 1 and 4 after exposure to permethrin

Dog no.	ALT*			Creatinine**		
	D_0	D_1	D_4	D_0	D_1	D_4
1	34	36	35	1.2	1.1	1.2
2	30	27	27	1.0	1.1	0.9
3	24	23	22	1.0	0.9	1.0
4	35	32	30	0.9	0.9	1.0
5	27	25	21	1.0	0.9	0.9
6	31	30	29	0.9	0.9	1.0
7	16	16	18	0.9	0.9	0.9
8	25	22	25	1.1	1.0	0.9

*normal level 8.2-57.3 (IU/l) (Fraser et al., 1991)

**normal level 0.5-1.6 (mg/dl) (Fraser et al., 1991)

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

The determination of serum ChE activity is used clinically for the evaluation of intoxication by organophosphate, carbamate and pyrethroid insecticides, which are potent ChE inhibitors (Balint et al., 1995; Srichairat, 1996). Intoxication from such insecticides results in a marked reduction of ChE activity. The colorimetric method as described by Ellman (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 side effects of permethrin at a prophylactic dose of 50% (w/v) for ectoparasite infection in dogs was evaluated by the measurement of ChE activity. Serum samples were used for the determination of ChE activity since previous study had recommended that serum, rather than plasma should be used to diminish the interference from the action of the added substance such as anticoagulants (Panichkriangkrai and Subhachalat, 1996). The serum ChE activity in all the dogs measured on D_1 and D_4 after exposure to permethrin

showed no significant difference when compared with that before exposure (D_0) (Table 1). The ALT and creatinine levels in 8 dogs were within normal range throughout the experimental period (Table 2). Furthermore, there were no clinical signs in any of the dogs throughout the experiment. These results may not concur with the study determined by Ansari (1990) which found that using cypermethrin, a pyrethroid insecticide, at a prophylactic dose for ectoparasite infection in cattle can decrease ChE activity. In general, pyrethroids are classified into type I and type II compounds based on structure and toxicological differences. Since permerthrin, a component of Advantix^R, is a type I pyrethroid which has lower toxicity compared with cypermethrin, a type II pyrethroid (Rao and Rao, 1995), permethrin is a safe pyrethroid insecticide.

In conclusion, using spot-on formulation of pyrethrin in a prophylactic dose for ectoparasite infection is safe in dogs.

References

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.

Curtis D.W. 2003. Neurotoxicological syndromes. A practical guide to canine and feline neurology. 18: 572-573.

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 prodedures. In: The Merck Veterinary Manual. 7th ed. P. 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.

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

Panichkriangkrai, W. and Subhachalat, P. 1996. Concurrent studies of plasma and serum cholinesterase activity in six species of domestic animals. Thai J. Vet. Med. 26(2): 157-163.

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.

Srichairat, S. 1996. A rapid screening test for serum cholinesterase activity. Thai J. Vet. Med. 26(2): 113-120.