FENBENDAZOLE IN CYSTICERCOSIS CELLULOSAE

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Cysticercosis cellulosae, caused by the larval stage of *Taenia solium*, is one of the most important public health problems for both human and hogs in endemic areas; Africa, India, Parkistan, China, Korea, and continental Latin American countries. As yet there is no effective therapeutic measures which can destroy the larvae in tissues and organs of the body except surgical excision (Faust, Russel and Jung, 1976). Recently, Fenbendazole, methyl-[5-(phenyl-thio)-benzimidazole-2-carbamate (Hoechst Farbwerke AG), has been reported to be highly effective at low dosage levels against trichinosis (Sujata et al, 1976), larval echinococcosis (Hinz, 1978; Eckjert et al, 1978), as well as intestinal helminthic infections (Brugh and Haas, 1976; Colglazier et al, 1977; Marti et al, 1978; Craig and Bell, 1978). These informations prompted us to use this drug against cysticercosis cellulosae in pigs.

The study was carried out in Cheju Island, where has been reported as one of the heavy endemic foci of taeniasis in Korea (Cho et al, 1967). By the survey on the infection of *Cysticercus cellulosae*, 18 naturally infected native pigs, weighing 38 to 113 kg, were purchased and moved to Cheju Animal Health Laboratory for the purpose. The pigs were divided into 8 groups and non-treated control. Panacur(; 1 g granules contained 222 mg active ingredient of Fenbendazole) was administered orally in each group according to the Fenbendazole base. The drug regimen were 45 and 20 mg/kg body weight/day for 14 consec. days in 2 groups, and 25, 15 and 5 mg/kg body weight/day for 14 and 7 consec. days in 6 groups, respectively.

To assess the effectiveness, treated pigs, together with non-treated controls, were sacrificed and autopsied 20-39 days after the completion of medication. *Cysticerci cellulosae* were derived from muscles, heart, tongue, eyes and brain, and examined for the changes after treatment, and then, all meat was cut into thin slices to examine for the cysts. Light microscopes, and scanning and transmission electron microscopes were employed for the examination.
For scanning electron microscopy (SEM), cyst bladder of *Cysticercus cellulosae* (*C. cellulosae*) was carefully incised to exposure the head portion of larvae. Motile scoleces were immobilized by light anesthesia using 1% MS 222. Specimens were fixed in 4% glutaraldehyde in 0.1M cacodylate buffer (pH 7.2) for 2 hr, washed several times with distilled water, immersed in 1% tannic acid for 30 min, and rinsed again. Dehydration was done in graded series of ethanol. The specimens were dipped in isoamyl acetate, and transferred into a Hitachi HCP-1 critical-point dryer. The dried specimens were mounted on metal stubs, sputtered with gold, and examined with a Hitachi S-450 scanning electron microscope.
For transmission electron microscopy (TEM), the exposed larvae were fixed as before. The specimens were dissected and divided into 3 portions; scolex, pseudoproglottids and bladder, and fixed again for 1 hr. After rinsing in cold buffer, the specimens were postfixed in 1% osmium acid for 2 hr, dehydrated in ascending series of aceton, and embedded in a mixture of Epon 812 and 815. Ultra-thin sections were cut with a LKB ultramicrotome and stained with saturated uranyl acetate and Reynold's lead citrate. The specimens were studied in a Hitachi HU-12 electron microscope, operating at 100 kv.

In the results of autopsies after treatment, Fenbendazole was proved to be highly effective against *C. cellulosae* at every dosage group of pigs. The cysts in muscles were deflated and shrunk, and looked like small rice grains or millet seeds in size and shape. Muscle fibers of treated pigs became vivid and fresh. The cysts in tongue showed as a small whitish granular mass. Degenerated cyst in conjunctiva was seen as a pinpoint pearly dot. However, the cysts in brain were diverse in size, and appeared to be in process of disintegration. Some scoleces showed even active movement. Therefore, electron microscopic examinations were focalized on the changes of *C. cellulosae* in brain.
In the SEM of treated *C. cellulosae* in brain, rostellar part was completely destroyed, and hooklets were entirely exposed. Contraction of scolex, neck and pseudoproglottids were conspicuous compared to the untreated larvae. Tegumental surface of suckers were remarkably degenerated, and showed crater-like appearance. Microtriches were disintegrated and disappeared, and membrane blebs were found on the tip of degenerated surface. Neck and pseudoproglottids regions were also severely affected and showed spongeform appearance.
In the TEM of pseudoproglottids of treated *C. cellulosae* in brain, microtriches were sparse and disappeared. Knob-like elevation was observed on the tegumental surface. Increase of small vacuoles, granules and lipid droplets were prominent in the syncytial tegument. Thin sections of neck and bladder showed partial or complete disappearance of tegument from the necrotized cytoplasm. In the subtegumental region, basal lamina, fibrous zone, circular and longitudinal muscles, cytoplasmic extensions, mitochondria, Golgi apparatus, flame cells, nucleus, and other microorgans and inclusions were disorganized and had lack of normal structural details. Among them, thin sections of flame cell revealed marked atrophy and disintegration of nucleus, rootlet and basal body. Flagella retained barely the 2 and 9 arrangement of cilia, but were disrupted and partly disappeared in the periphery of the lumen.
C. cellulosae in muscles after treatment showed marked surface changes and contraction of scolex, neck, and bladder by SEM. Thin sections revealed intensive degeneration, necrosis and disruption of tegument and subtegumental regions.
Body weight of the treated pigs showed remarkable increase after the administration of Fenbendazole compared to the non-treated infected controls. Some pigs showed decrease of appetite during the treatment, but none was interfered the completion of medication by the side effect.

Conclusions:

Cysticercosis cellulosae was successfully treated by the oral administration of Fenbendazole at a daily dose of 5 mg/kg body weight for 7 consecutive days. The effectiveness was assessed by the scanning and transmission electron microscopic observations of the larvae in pigs after treatment.

Selected references: Faust, E.C., Russel, P.F. and Jung, R.C.: Clinical Parasitology, 1968, Lea & Febiger(Philadelphia), 8th ed.:529 ; Sujatha, S., Fernando, E. and Denham, D.A.: J. Parasitol. 1976, 62(6): 824 ; Hinz, E.: Zbl. Bak. Parasit. Inf. Hyg. 1978, 241:388 ; Eckjert, J., Barandun, G. and Pohlenz, J.: Sw. Med. Wochenschrift, 1978, 108(29):1104 ; Brugh, K. and Haas, J.: Ann. Trop. Med. Parasitol. 1976, 70(2):205 ; Colglazier, M.L., Enzie, F.D. and Kates, K.C.: J. Parasitol. 1977, 63(4)724 ; Marti, O.G., Stewart, T.B. and Hale, O.M.: J. Parasitol. 1978, 64(6):1028 ; Craig, T.M. and Bell, R.R.: Am. J. Vet. Res. 1978, 39(6):1037 ; Cho, Kee-Mok, Hong, S.O., Kim, C. H. and Soh, C.T.: J. Korean Med. Med. 1967, 7(4):455.