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THE ANTHELMINTIC EFFECT OF BROTIANIDE* AGAINST FASCIOLA GIGANTICA INFECTIONS IN SHEEP

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Brotianide'in koyunlardaki Fasciola gigantica enfeksiyonlarına etkisi

Özet: Bütün çabalara rağmen *Fasciola gigantica* enfeksiyonları Türkiye'de önemli bir problem olmakta devam etmektedir. Özellikle güney bölgeleri ile Bursa'da Apolyont gölünü çevreleyen köylerde enfeksiyon yerleşmiş durumdadır. Adana mezbahasında kesilen büyük ruminantların ekserisinde bu parazite hemen her gün rastlanmaktadır.

Türkiye'de *Fasciola gigantica*'ya karşı hexachlorophene, oxyclozanide, menichlophan ve belirli bazı bölgelerde ise hexachloroethane taşıyan ilaçlar kullanılmaktadır.

Bu çalışmada yeni bir ilaç olan Brotianide'in suni olarak enfekte edilen koyunlarda muhtelif gelişme safhasındaki *Fasciola gigantica*'ya etkisini denedik. % 4 solusyon halinde kullandığımız bu ilaç 2-4 cc. /10 kg. verildiği hallerde 40 günlük *Fasciola gigantica*'ya etkisi % 68-97 bulunmuştur.

Altmış günlük enfeksiyonlarda 1.2-2.5 cc./10 kg. kullanıldığı zamanlarda bu etki % 90 ve 99 bulunmuş, 90 günlük enfeksiyonlarda 1.2-2 cc./10 kg. verildiğinde ise % 97 ve 100 olmuştur. Yukarıda kullanıldığını bildirdiğimiz doz hudutları (5-15 mg./kg.) içinde ilâcın 32 deney koyununda kötü bir etkisini görmedik.

Yurdumuzda *Fasciola gigantica* ile enfekte bölgelerde mezbahalarda ve mücadelede çalışan meslektaşlarımızın bildirdiğine göre, kesilen hayvanların karaciğerlerinde genç yılan kelebeklerinin karaciğerleri delmeleri izlerine Temmuz ile kış ortası arasında rastlanmakta ve yırtılan hematomlarla hemorajilerden mütevellit ölümlere ise Ekim ile Mart ayları arasında rastlanmaktadır.

Bu gözlemlerin ışığı altında, enfekte bölgelerde Eylülün ortası ile Şubatın sonuna kadar altmışar gün aralarla koyunlara 7.5 mg./kg. Brotianide verilmesi suretiyle *Fasciola gigantica*'dan ötürü ölümlerin önüne geçileceği gibi bu şekil bir sağıtma ile bu kelebeklerin gelişim çemberi kırılacak ve bunların karaciğerlere gelip yerleşmeleri ile olgunlaşıp yumurta meydana getirmelerinin ve dolayısıyla de meraların tekrar enfekte edilmesinin önüne geçilecektir.

* Bay Va 4059. Farbenfabriken Bayer AG, Leverkusen.

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Summary: 4 % solution of Brotianide was found 68-97 % effective when given at 2-4 ml./10 kg. orally to sheep carrying 40 day old *Fasciola gigantica* infections.

It was also found to be 90 and 99 % efficient at the dose level of 1.2-2.5 ml./10 kg. in sixty day old infections and 97 and 100 % when administered 1.2-2 ml./10 kg. in 90 day infections.

No side effect of the drug was seen in any sheep treated within the dose ranges used.

Fasciola gigantica infections still are a severe problem particularly in the southern, and Marmara sea areas of the western parts of Turkey. According to the reports of meat inspectors and field veterinarians of those areas, the spread of the infection has reached critical proportions.

At present, drugs containing hexachlorophene, oxyclozanide, menichlopholan and in restricted areas hexachloroethane are in use in this country against the giant fluke.

The present paper reports the activity of Brotianide (2-acetoxy-3-brom-5-chlor-N-(4'-bromphenyl)-thionobenzamid) against different development stages of *Fasciola gigantica* in sheep.

According to Roseby and Boray (1) the minimum dose rates of Brotianide that gave 90 % or higher efficiency against 6 weeks and 12 weeks old *Fasciola hepatica* infections, were 4.7 mg./kg. and 2.3 mg./kg. respectively and maximum tolerated dose rate was 27 mg./kg. in artificially infected sheep.

Materials and Methods

40, one year old, fat-tailed and male Akkaraman sheep, each weighing 29-36 kilos were used in the experiment. They were fed commercial pellets containing 22 % protein, and grass hay and water (from the city water system) were given ad libitum.

All the animals were naturally infected to a moderate degree with gastro-intestinal and lungworms and 30 % mildly with *Dicrocoelium dendriticum*.

Since *Fasciola hepatica* infections are prevalent in Anatolian sheep, all the animals were dosed with 1 ml. carbon tetrachloride in soft gelatine capsules ten days before they were given encysted *F. gigantica* cercariae.

Each of the animals was infected with 50 one week old metacercariae given in a soft gelatine capsule. These encysted cercariae were obtained from *Lymnaea auricularia* artificially infected under laboratory conditions.

The sheep were divided into four groups. The first and second group each contained 12, and the third group 8 animals. The remaining fourth group of 8 sheep were kept as untreated controls.

The doses were calculated individually according to the body weight of each sheep. A 4 % suspension of Brotianide was given orally without a preliminary fasting to each animal by means of a syringe.

Four sheep of the first group received 2 ml./10 kg., four 2.5 ml./10 kg. and the remaining four sheep 4 ml./10 kg, of the drug, forty days after the infection.

Four sheep of the second group were treated with 1.2 ml./10 kg., four with 2 ml./10 kg., and the remaining 4 with 2.5 ml./10 kg. sixty days after the infection.

Four sheep of the third group were given 1.2 ml./10 kg., and the remaining four 2 ml./10 kg. ninety days after the infection.

Since it is rather difficult to find small flukes in the liver, the treated sheep were slaughtered at least 95 days after the infection. The controlsheep were sacrificed soon after the detection of *F. gigantica* eggs in faecal examinations.

All the livers were examined within two hours of killing. The sliced liver tissue was held in warm 0.85 % NaCl solution to stimulate movement of any undetected flukes to the cut surface. All recovered flukes were put in warm 0.85 % NaCl solution and the number of living *F. gigantica* recovered from each animal was recorded.

Results

The results of the treatment at different periods of the infection and in different dose groups are shown in table I.

In the last four sheep of the first group which received 15 mg./kg. of active ingredient, Brotianide was found to be 97 % effective against 40 day old infections, whereas in the sheep of the same group which received 7.5 and 10 mg./kg. the efficiency of the drug was erratic: 83 and 68 % respectively of the flukes being removed.

In the second group of sheep which were treated sixty days after infection, Brotianide was found 90 % effective when given at 5 mg./kg. and 99 % efficient when used at 7.5 and 10 mg./kg.

In four sheep of the third group which were treated ninety days after infection with 5 mg./kg. of the drug, 97 % of the flukes were removed and in the other 4 which received 7.5 mg./kg. 100 % efficacy was observed.

Within the dose range used (5-15 mg./kg.) the drug did not cause any adverse effect in 32 experimental animals.

Table 1.
The effect of Brotianide against three different development stages of *Fasciola gigantica*

No. of sheep	No. metacercariae given	Days between infection and treatment	Dose rate ml./10 kg. (Suspension 4 %)	Numbers of <i>F. gigantica</i> recovered in livers of sheep at necropsy.	Percent efficiency.
4	200	40	2	0. 4. 4. 5	83.22
4	200	40	2.5	0. 9. 16. 0	67.73
4	200	40	4	1. 1. 0. 0.	97.41
4	200	60	1.2	1. 2. 0. 5	89.67
4	200	60	2	1. 0. 0. 0.	98.70
4	200	60	2.5	0. 0. 1. 0	98.70
4	200	90	1.2	0. 0. 0. 2	97.41
4	200	90	2	0. 0. 0. 0	100
8	400	Untreated controls		13. 14. 15. 21. 22. 22. 23. 25.	

Discussion

Roseby and Boray¹ found the drug to be equally effective whether given by intraruminal injection or orally after stimulating the oesophageal groove. In the experiments reported in this paper, the drug was given orally without stimulating the oesophageal groove since that is a none practical method for use by flock owners and field veterinarians in Turkey. Roseby and Boray¹ found that the minimum dose rates that gave 90 % or higher efficiency in 42 and 84 day old *F. hepatica* infections were 4.7 mg./kg. and 2.3 mg./kg. respectively.

In the present experiments as shown in table I, the minimal dose rate that gave higher efficiency than 90 % against 40 day old giant flukes was 15 mg./kg., whereas in 60 day old infections, the same anthelmintic efficiency was obtained with 7.5-10 mg./kg. and at 90 days with 5-7.5 mg./kg.

No toxic reactions occurred in sheep when the drug was given at a dose range of 5-15 mg./kg. This is less than the maximum tolerated dose rate for sheep of 27 mg./kg. recorded by Roseby and Boray¹.

Meat inspectors and field veterinarians in Turkey usually see puncture wounds in livers made by invading young giant flukes during the period July to mid-winter and deaths from ruptured hematomas and hemorrhage occur between October and March.

Information obtained from these experiments indicates that treatment of sheep with 7.5 mg./kg. of Brotianide at about 60 day intervals from mid-September until late February should give year long protection against deaths from fascioliasis. Such treatment should also break the life cycle by preventing any flukes from reaching maturity and producing eggs.

References

- Roseby, F. B. and Boray, J. C. (1970): *The anthelmintic efficiency against Fasciola hepatica and the toxicity of Bay 4059 in sheep*. Aust. vet. J., 46, 308-310.

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