[Jpn. J. Parasitol., Vol. 34, No. 6, 517-519, December, 1985]

Research Note

Effects of Some Neuropharmacological Agents and Anthelmintics on the Motility of Mature Proglottids of *Diplogonoporus grandis*

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(Received for publication; June 18, 1985)

Key words: motility of *Diplogonoporus grandis*, *in vitro* effects, neuropharmacological agents, anthelmintics

As to the neuropharmacological regulation of the motility of cestode worms, an involvement of acetylcholine (ACh) and 5-hydroxytryptamine (5-HT, serotonin) was suggested only in cyclophyllidean cestodes such as *Taenia taeniaformis*, *Hymenolepis nana* and *Dipylidium caninum* (Artemov and Lure, 1941; Krotov, 1961; Smyth, 1969; Chou *et al.*, 1972; Terada *et al.*, 1982; Mansour, 1984). In our study on *D. caninum*, inhibitory cholinergic and excitatory serotonergic mechanisms were suggested to be in this cestode which were similar to those reported in *Schistosoma mansoni* (Barker *et al.*, 1966; Bueding and Bennett, 1972) and *Fasciola hepatica* (Bueding and Bennett, 1972; Mansour, 1984). In the present study, effects of some drugs including neuropharmacological agents and anthelmintics on the motility of the pseudophyllidean cestode, *Diplogonoporus grandis* were examined by the isotonic transducer method previously described (Terada *et al.*, 1982).

A living strobila having mature proglottids (about 70 cm in length and 7-9 mm in width) was spontaneously expelled on May 11, 1981 from a male veterinary surgeon of 31 years old who was working in a slaughterhouse in Shizuoka prefecture. On the next day, a strobila with a scolex (about 2.9 m in length and 7 mm in the widest width) was expelled from him by treating orally with bithionol (30 mg/kg) and sodium sulfate. A small part (about 1 cm long) of the strobila spontaneously expelled was used as a preparation for this *in vitro* study.

Inhibitory effects on the motility of *D. grandis* were observed by treating the proglottids with eserine (10^{-5} M, an inhibitor of acetylcholinesterase activity) or carbachol (10^{-4}–3×10^{-4} M, an agonist of the cholinergic receptocs) (Fig. 1A, B). Stimulatory effects were seen by 5-HT (10^{-4} M, an agonist of the serotonergic receptors), and the stimulatory effect was antagonized by the addition of eserine (10^{-5} M) (Fig. 1C). On the other hand, γ-aminobutyric acid (GABA, 10^{-5}–10^{-4} M, an agonist of the gabergic receptors), phenylephrine (10^{-6}–10^{-5} M, an α-adrenergic agonist) and isoproterenol (4.7×10^{-6}–2.4×10^{-5} M, a β-adrenergic agonist) had little effect on the motility of this cestcde. These results coincided well with those observed in mature to gravid proglottids of *D. caninum* (Terada *et al.*, 1982).

It was reported that there was a remarkable difference between nemathelminths and plathelminths regarding the sensitivity to anthelmintics (Cox, 1982; Terada *et al.*, 1982). Anti-plathelminth drugs such as bithionol (3×10^{-6}–3×10^{-5} M) and praziquantel (10^{-7}–10^{-6} M) caused stimulatory effects on the motility of *D. grandis*, and spastic paralysis was seen even after washing the preparations with Tyrode's solution (Fig. 2A, B). Similar effects were observed when niclosamide (3×10^{-7}–3×10^{-6} M) was given to the proglottids.

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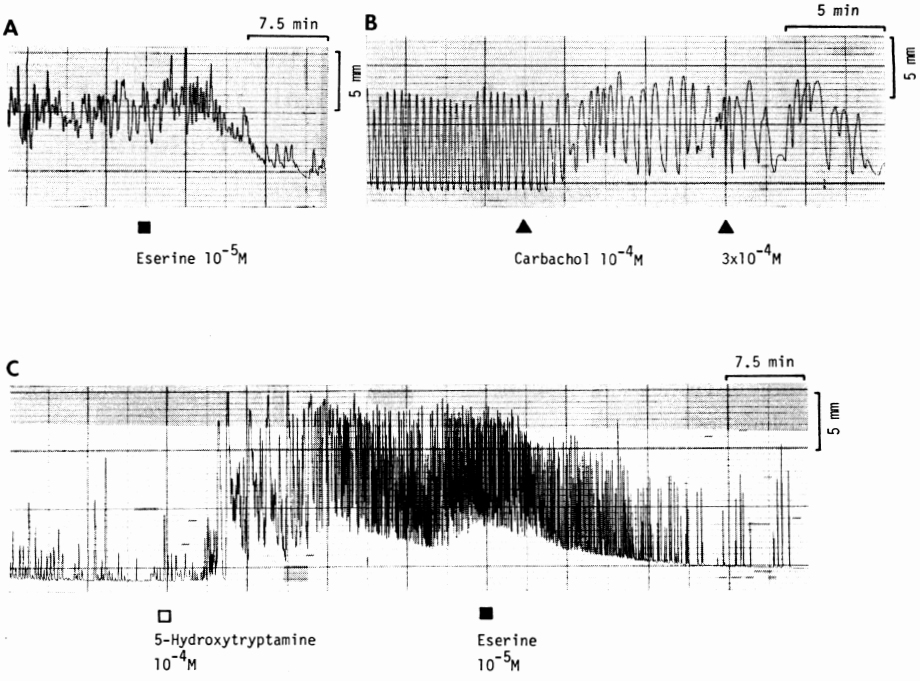

Fig. 1 Effects of some neuropharmacological agents on the motility of mature proglottids of *Diplogonoporus grandis*. The proglottids-preparation (about 1 cm long) was suspended in Tyrode's solution with a tension of 0.5 g.

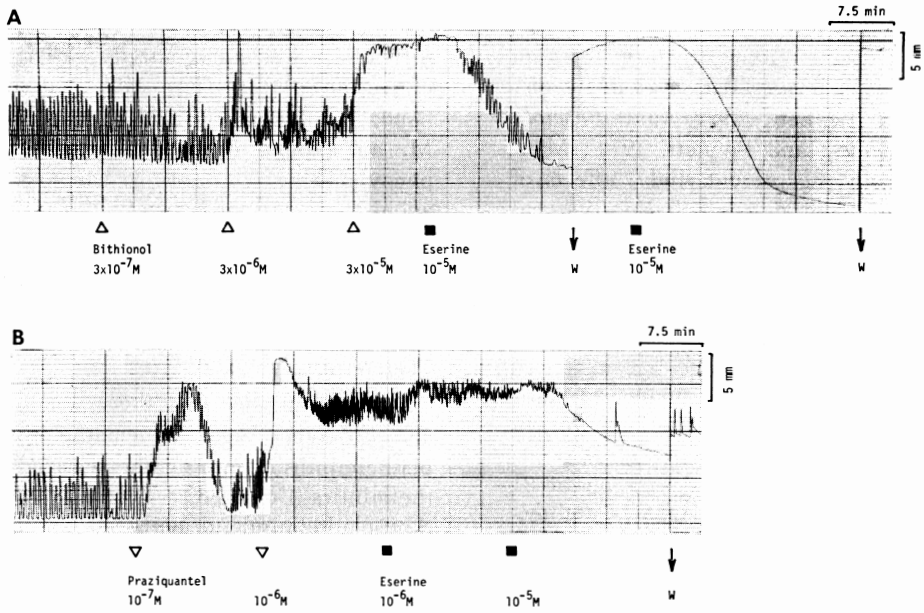

Fig. 2 Effects of bithionol (A) and praziquantel (B) on the motility of mature proglottids of *D. grandis*. Antagonistic effect of eserine on the stimulatory action of these anthelmintics was also examined. At times shown by point W, the preparations were washed for about 30 min with Tyrode's solution.

Additionally, the stimulatory effects of these anti-plathelminth drugs were all antagonized by the treatment with eserine (10^{-5} M) (Fig. 2 A, B). Little effect was, however, caused by anti-nemathelminth drugs such as avermectin B_{1a} (3.6×10^{-6} M) and pyrantel (10^{-5} M). Thus, similar sensitivity to drugs including neuropharmacological agents and anthelmintics was observed between mature proglottids of *D. grandis* and mature to gravid ones of *D. caninum*.

Conclusively, it seems reasonable from the *in vitro* studies as well that anthelmintics like bithionol are clinically sellected to both the cyclophyllidean and pseudophyllidean cestode infections.

References

1) Artemov, N. M. and Lure, R. N. (1941): Über den Gehalt von Acetylcholin und Cholinesterase in den Geweben der Bandwürmer. Bull. Acad. Sci. U.R.S.S., Ser. Biol., 2, 278-282.
2) Barker, L. R., Bueding, E. and Timms, A. R. (1966): The possible role of acetylcholine in *Schistosoma mansoni*. Brit. J. Pharmacol., 26, 656-665.
3) Bueding, E. and Bennett, J. (1972): Neurotransmitters in trematodes. In Comparative Biochemistry of Parasites, ed. by van den Bossche, H., Academic Press, New York and London, 95-99.
4) Chou, T.-C. T., Bennett, J. and Bueding, E. (1972): Occurrence and concentrations of biogenic amines in trematodes. J. Parasitol., 58, 1098-1102.
5) Cox, F. E. G. (1982): Modern Parasitology, Blackwell Scientific Publications, Oxford, London, Edinburgh, Boston and Melbourne, 346 p.
6) Krotov, A. I. (1961): Materialy po izucheniyu mekhanizma deistvii ditrazina i preparatov iz semyan tykvy na askarid i tsestod. Med. Parazitol. i Parazitar. Boleznei, 30, 666-674.
7) Mansour, T. E. (1984): Serotonin receptors in parasitic worms. Ad. Parasitol., 23, 1-36.
8) Smyth, J. D. (1969): The Physiology of Cestodes. W. H. Freeman Co. Publishers, San Francisco, 340 p.
9) Terada, M., Ishii, A. I., Kino, H. and Sano, M. (1982): Studies on chemotherapy of parasitic helminths (VI). Effects of various neuropharmacological agents on the motility of *Dipylidium caninum*. Jpn. J. Pharmacol., 32, 479-488.

短　報

大複殖門条虫成熟体節の自動運動に対する数種の神経薬理学的薬物および駆虫薬の作用について

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条虫類虫体の自動運動の神経薬理学的調節に関しては，幾つかの円葉類虫種において，acetylcholine および 5-hydroxytryptamine (5-HT, serotonin) の関与が示唆されているのみである．今回，擬葉類虫種，大複殖門条虫の自然排出直後の虫体を入手する機会を得たので，その成熟体節の薬物感受性について検討を加えた．得られた結果は以下の如くである．1) 大複殖門条虫の自動運動は，eserine (10^{-5}M) ないし carbachol (10^{-4}～3×10^{-4}M) で抑制された．5-HT (10^{-4}M) は興奮作用を示し，その作用は eserine (10^{-5}M) により拮抗された．一方，γ-aminobutyric acid (10^{-5}～10^{-4}M)，phenylephrine (10^{-6}～10^{-5}M) ないし isoproterenol (4.7×10^{-6}～2.4×10^{-5}M) はほとんど影響を及ぼさなかった．2) 大複殖門条虫の自動運動に対し，bithionol (3×10^{-6}～3×10^{-5}M)，praziquantel (10^{-7}～10^{-6}M) ないし niclosamide (3×10^{-7}～3×10^{-6}M) は興奮作用をひき起こした．これらの作用は，虫体を Tyrode 液で洗浄後も持続しており，また，eserine (10^{-5}M) により拮抗された．一方，avermectin B_{1a} (3.6×10^{-6}M) ないし pyrantel (10^{-5}M) はほとんど影響を及ぼさなかった．これらの結果は，円葉類虫種，瓜実条虫についての *in vitro* での結果とよく一致していた．従来，条虫症の治療には，円葉類および擬葉類のいずれの虫種に対しても，bithionol などの同一駆虫薬が用いられてきたが，今回の知見は，*in vitro* 実験の面から，その妥当性を傍証したものと言えよう．