Blindness in lambs due to inadvertent closantel overdose

A. M. Barlow, J. A. E. Sharpe, E. A. Kincaid

CLOSANTEL is a salicylanilide drug used for the treatment and control of fasciolosis in sheep and cattle. It is also active against Haemonchus contortus and the nasal bot, Oestrus ovis. In combination with benimidazole derivatives, it is a broad-spectrum anthelmintic for the treatment and control of both nematodes and liver fluke infestations in sheep and cattle.

Blindness in sheep has been associated with overdoses of closantel in Brazil (Borges and others 1999) and Australia (Gill and others 1999). Blindness due to a closantel/albendazole mixture was also recorded in Zimbabwe (Obwolo and others 1989). An episode of possible closantel toxicity occurred in the UK in 1998 (J. Wilmington, unpublished observations). This short communication describes the pathological findings of a confirmed incident in the UK. Retinopathy, optic neuritis and myelencephalitis were present in the brain stem, as previously described in association with closantel toxicity in sheep (Gill and others 1999, Obwolo and others 1989, Jubb and壶xtable 1993).

The affected animals were in a group of 80 three- to six-month-old lambs, reared with a further 10 older lambs and 80 ewes. They were grazing permanent pasture which had not received any manure for several years. As some animals had diarrhoea, the owner decided to treat all of them with a combined fluke and worm drench containing 50 mg/ml closantel and 57 mg/ml mebendazole (Mebendox Super: Downland Marketing). Lambs in both groups were supposedly dosed with 5 ml and the ewes with 8 ml of anthelmintic.

Two weeks later, the sheep were moved and eight of the 80 lambs were noticed to be blind. Three affected animals were submitted to the Veterinary Laboratories Agency (VLA) - Langford for ante- and postmortem examination. The animals weighed 12, 17 and 19 kg. The smallest had mild hindlimb incoordination. All three were blind with no menace reflex and had dilated pupils. Euthanasia was carried out using intravenous barbiturate. The eyes, with optic nerves attached, and brain were dissected out in each case, the eyes and brain were fixed in 10% formal saline, processed routinely, sectioned at 5 µm and stained with haematoxylin and eosin. In all three animals, severe bilateral degenerative changes were observed in the retina. These included bullous detachment from the retinal pigment epithelium, a generalised loss of the photoreceptor layer and depletion of both outer and inner nuclear layers (Fig 1). The depletion of the nuclear layers was more severe in the outer nuclear layer, which was reduced to a row of cells and was effaced in places. In the intraorbital optic nerves of two lambs, severe bilateral vascular degeneration, especially towards the periphery of the nerve, with infiltration by gitter cells, was observed (Fig 2). The predominant feature in the intracanalicular portion of the optic nerves was gitter cell accumulation. Perivascular cuffing by mononuclear cells was observed around occasional vessels. In the brainstem of the most severely clinically affected animal, the cerebellar peduncles contained scattered foci of white matter vacuolation, sometimes associated with a gliotic reaction (Fig 3).

In the previous episode in the UK, a group of 20 small hogs were each dosed with 10 ml of an anthelmintic containing 15 mg/ml closantel and 75 mg/ml mebendazole (Supswerm, Lansen Animal Health). A week after treatment, one had died, one had been euthanased and four were blind and exhibited hindlimb incoordination. No eye or optic nerve histology was carried out (J. Wilmington, unpublished observations). The dose rate range for the lambs submitted to VLA - Langford in the present case was 13-3 mg/kg for the 19 kg lamb to 19-8 mg/kg for the 12 kg lamb. The closantel dose rate for sheep is 10 mg/kg. Thus, marginal to double overdosing would have occurred. At these dose rates, 1.34 litres of anthelmintic should have been expended. However, examination of the container indicated that approximately 3.5 litres had, in fact, been used. This would represent an overdose of four to five times the recommended dose rate in the 12 kg lamb, and two to three times in the 19 kg lamb. If overdosing was sporadic rather than consistent for all the sheep, the overdose in individual lambs could have been even greater.

Optic neuritis has been reported with closantel at three times the recommended dose rate (Borges and others 1999).

Thus, it was concluded that inadvertent overdosing with the combined fluke and worm drench was the cause of blindness in these lambs. Prozeszky and Prinaar (1977) indicated that mishandling of the drug rafosanide (a related salicylanilide compound), overestimation of the animal's bodyweight, the use of faulty drenching equipment and failure to read product labelling were the main causes of poisoning. This underlines the necessity for a consistent anthelmintic dosing protocol.

FIG 1: Depletion of the outer (arrow) and inner (arrowhead) nuclear layers of the retina (R) in a lamb, ×120. C Choroid, S Sclera

FIG 2: Anterior optic chiasma showing gitter cell infiltration (G) with vacuolation of white matter (V), ×120.
FIG 3: Section of the brain of the most severely clinically affected lamb showing the cerebellar peduncle and vacuolated white matter. x 120. The arrow indicates a neuron.

It was considered that this incident posed no risk to the human food chain because the animals were already prohibited from sale for human consumption by the long with drawal period of this anthelmintic. In addition, the worst-affected lambs had been culled for postmortem examination. However, a routine report was completed under the Suspected Adverse Reaction Surveillance Scheme for the Veterinary Medicines Directorate.

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References


The Veterinary Formulary

THE fifth edition of The Veterinary Formulary, published by the Pharmaceutical Press in association with the British Veterinary Association, has been extensively revised and is now available. The formulary is available, price £69.95; overseas £75.00, U.K. members £59.95, overseas members £68.00. Available from Cairns Online Books, 6 Bourne Enterprise Centre, Worthing Road, Shoreham-by-Sea, West Sussex BN43 5BD, telephone 01903 880422, fax 01903 883866, e-mail cairns@cran.ton.co.uk (Visa/Mastercard/Eurocard accepted.)

The role of gastrin in the aetiology of abomasal displacement in dairy cows

I. Sen, M. Ök, K. Turgut, F. M. Birdane, H. Güzeldereks

ABOMASAL displacement occurs most frequently in high-yielding cows during early lactation (Helin and Nelson 1995, Turgut and Ök 1997). Its specific aetiology is currently unknown. However, it has been suggested that the frequent occurrence of abomasal displacement in dairy cows during early lactation might be due to increased exposure to factors that induce abomasal atony, and the presence of an abdominal wall immediately after parturition which allows the abomasum more room to move (Constable 1991, Geishausser 1995, Shaver 1997).

Gastrin is synthesised and secreted by enterochromaffin-like cells, from the antrum and small intestinal mucosa. In dogs, increased gastrin secretion elevates gastric sphincter pressure, delays gastric emptying, and promotes pyloric muscular hypertrophy (Hall and others 1989); it has therefore been stated by some researchers that increased gastrin secretion might predispose dogs to gastric dilatation-volvulus (Leib and others 1984). However, Vlaminck and others (1986) found no significant differences between serum gastrin levels of normal cows and cows with abomasal dilatation. Because of the multiple effects of gastrin, abnormalities in plasma gastrin levels might play a role in the aetiology of abomasal displacement in cattle. The aim of the present study was to investigate the potential relationship between plasma gastrin levels and abomasal displacement.

Ten cows with right-sided abomasal displacement (RASD), nine cows with left-sided abomasal displacement (LASD) and eight healthy cows were used. All of the cows were Holstein. The age of the animals varied from three to eight years with a mean (sd) age of 5 (1.5) years. All were in early lactation (seven to 12 days) and had been fed a high-concentrate diet. On admission, the animals had been ill for an average of three days.

All of the cows received routine clinical examinations, including abdominal auscultation, palpation of the abdomen for splashing sounds, liver percussion, rectal examination and abdominal ultrasonography. The diagnosis of abomasal displacement was verified by laparotomy.

Heparinised venous blood samples were taken from the jugular vein from all the cows. Plasma gastrin levels were measured by the radioimmunoassay method (Double Antibody Gastrin, MPA Diagnostic Products). Blood gas analysis and sodium, potassium and inorganic calcium measurements were performed by Gomtiar instruments (Refer to Veterinary Record 1988, 128, 2-7).

For data evaluation, a comparison by one-way analysis of variance and Duncan's test was applied to determine the differences between all groups (P<0.05 for Windows, SPSS). The cows with abomasal displacement had moderate appetite, little defecation, and decreased rumen motility and milk production. Auscultation of the left (in the case of RASD) and right (in the case of LASD) abdomen revealed tympanic resonance (a 'ping' sound) over the last three ribs (10th to 13th). Splashing sounds were also heard on the abdominal wall where 'ping' sounds were present. Liver percussion was negative in the cows with RASD. In three cows with RASD, the displaced abomasum was palpated by rectal examination.