Long acting iodine injections in sheep – what happens?

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Introduction

Clinical and subclinical iodine deficiencies are common trace element problems in sheep in Otago, Southland and Wairarapa. In the case of clinical deficiency and goitre, diagnosis is generally obvious with the observation of significantly enlarged thyroid glands in new born lambs; however, subclinical deficiency is less obvious and relies on the measurement of thyroid/bodyweight ratios in dead new born lambs. Generally the diagnosis of subclinical deficiency is confirmed if 20 lambs are sampled and a ratio in excess of 0.8g/kg is detected. Cases of marginal deficiency are defined as ratios of 0.4–0.8g/kg but these are considered ambiguous (Knowles and Grace 2007).

In 2007 Gribbles Veterinary introduced the serum inorganic iodine test to the veterinary market for use in practice. This seemed a much easier option for detection of subclinical deficiency as the recommendation of bleeding five sheep involved significantly less work and was much simpler than relying on farmers to supply 20 dead new born lambs for a retrospective field observation.

Coupled with this, Hicks et al. 2007 demonstrated the total iodine profile from a field observation conducted in Southland. This paper described the total iodine profile in blood following Flexidine (iodised peanut oil containing 26% organically bound iodine manufactured by Bayer Animal Health) supplementation, but unfortunately there were only four data points for the serum iodine data and the ‘long tail’ of total iodine decay was assumed, based on the decay of the urinary iodine profile. Urinary iodine measurements are now considered as unreliable (Hill and Gill 2013).

In 2012, Bruère undertook a field observation as part of a Farm IQ project observing serum inorganic iodine measurements over time in a flock of two-tooth ewes prior to and subsequent to Flexidine administration. The average measurement prior to mating was 19.95ug/L and the average measurement at three months following supplementation was 29.3ug/L for ewes treated with Flexidine and 22ug/L for untreated ewes. This was well below the level defined as marginal in both instances. This created uncertainty about the decay curve following supplementation, particularly as he was trying to compare scientific data where total iodine was the test used and in this case serum inorganic iodine was how the laboratory results were reported. There were no data available to demonstrate the correlation between total iodine and serum inorganic iodine. Hill and Gill 2013 demonstrated a strong correlation between serum total iodine and serum inorganic iodine where the R squared value was 0.92535. As a guide for the total iodine range of 35–95ug/L was matched by the serum inorganic iodine range of 15–55ug/L or put another way, about half.

To our knowledge there has never been a trial to demonstrate the dynamics of serum inorganic iodine profile following Flexidine administration. The manufacturer’s recommendations for Flexidine use in New Zealand are that 1.5ml of Flexidine should be administered by intramuscular injection to ewes one month before mating or not less than two months before lambing. The dose volume is not altered between pre-mating and pre-lambing. The logical assumption here is that the pre-mating injection
will provide sufficient iodine for the benefits of improved conception rates, preventative goitre effects and improved lamb survival and that the pre-lambing injection will provide sufficient iodine for the benefits of preventative goitre effects and improved lamb survival.

In practice supplementation is generally carried out in the early autumn prior to mating, adding to an already full animal health schedule on most sheep farms. On properties where ewe conception rates are usually adequate, there appears to be an opportunity to move the administration of Flexidine to ewe scanning time about two months prior to lambing. As the period of required efficacy is shortened in such a scenario, it seemed logical that a smaller dose volume may be sufficient to prevent goitre and also protect lamb survival.

Objective of the trial

To demonstrate the serum inorganic iodine profile in sheep following a range of different dose volumes of Flexidine over time. The trial was conducted at two sites – in the North Island on a property in the Wairarapa and in the South Island on a property in South Otago. This was not a production response trial.

Trial design

One hundred two-tooth ewes were identified at each site and double tagged. These were randomly allocated into five groups of 20 ewes. The treatment regimens were as follows on each property. The first group was given 2.5ml Flexidine one month prior to mating, the second group was given 1.5ml Flexidine one month prior to mating, the third group was given 0.75ml Flexidine one month prior to mating and a second 0.75ml at pregnancy scanning time about two months prior to lambing and the fourth group was given 0.75ml at pregnancy scanning time about two months prior to lambing. A fifth group remained untreated as a control group.

On both properties all groups were run together in one mob along with the rest of the non-trial two-tooth ewes and fed as per normal practice for each farm. On the Wairarapa property this constituted typical hill country feeding with a ryegrass/white clover mix. On the property in South Otago this was ryegrass/white clover mix apart from a period of just over one months feeding with swedes from 10 July – 13 August. For the first 10 days swede feeding baleage was also fed.

All 100 sheep were blood sampled at monthly intervals from just prior to the first Flexidine injection until 253 days later on the Wairarapa property and 230 days later on the South Otago property. Over the lambing period the testing interval was extended to approximately two months as we didn’t wish to disturb new born lambs as both trial properties were commercially run operations.

The blood samples were all submitted to Gribbles Veterinary for analysis. Samples from ten sheep from each group were tested for serum inorganic iodine and the remaining samples had the serum separated and stored. Advice received indicated that as long as we were comparing the four treatment groups to the control group, testing 10 animals in the first instance would be sufficient for statistical analysis. The statistical analysis was carried out by Professor Cord Heuer and the Epicentre at Massey University.
The trial was parented under the oversight of AgResearch, Palmerston North and complied with animal ethics guidelines.

**Trial results – Wairarapa**

The data demonstrated a logical dose effect over time i.e. the higher the initial dose, the higher the initial level of serum inorganic iodine. As time progressed the decay of the levels also followed a logical curve. This is demonstrated in Figure 1 where it can be observed that the ewes receiving the 2.5ml dose one month prior to mating have an average peak serum inorganic level of 265ng/ml (same as 265ug/L) in comparison to the group receiving the 1.5ml dose where the average one month peak was 160ng/ml (same as 160ug/L). As time progressed the decay curve of the 2.5ml group was steeper approximately four months after supplementation.

The 2.5ml and 1.5ml curve intersected at approximately 225 days following supplementation which suggests any benefit of effect of using the higher dose is not likely to last beyond this period of 225 days.

The 0.75ml dose one month prior to mating and again at scanning also followed logical expectations and peaked about one month following supplementation on both occasions.

The 0.75ml dose at scanning only peaked at about one month following supplementation and then decayed as expected.

![Figure 1. Graph of Wairarapa data demonstrating the serum inorganic profiles over time](image-url)

**Statistical Interpretation – Wairarapa**

The method used to determine statistical significance was based on comparison of confidence intervals. In all treatment groups there was a ‘gap’ between the confidence intervals and the control over most of the curve. In some instances there was minor overlapping of the confidence intervals. Where there is a ‘gap’ the observation is highly significant, where there is overlapping the observation is moderately significant.
Trial results – South Otago

The South Otago graph looked a little different from the Wairarapa graph. For instance after one month the serum inorganic iodine dipped and then recovered at three months for the 2.5ml, 1.5ml and 0.75ml groups treated one month prior to tupping. Following the scanning treatment of the 0.75ml/0.75ml group and the 0/0.75ml group the serum inorganic iodine levels increased in all the treatment groups and interestingly, while the 0/0.75ml group started from a lower level, it increased the most.

The control group’s serum inorganic iodine levels actually showed a slight increase during the period of brassica grazing although they were still in the ‘marginal range’. The thiocyanate goitrogens released when the brassicas are grazed, block the actual uptake of inorganic iodine by the thyroid gland, hence they do not have any depressant effect on the measured serum inorganic iodine levels.

The two-tooth ewes on the South Otago property (including the trial animals) experienced an outbreak of Salmonella hindmarsh in July and three of the trial animals died between 17–20 July.

Statistical analysis – South Otago

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Discussion

Within a fortnight of administration pre-tup, the serum inorganic iodine levels on both properties increased well above those of the control group, suggesting that the administration of Flexidine can be as close as two weeks prior to mating. The only proviso here though is that iodine sufficiency is not required earlier than this for normal physiological processes.

The raw data suggest that on both properties there was no advantage in using a 2.5ml dose over a 1.5ml dose one month prior to mating.

The decay curve of the 0.75ml/0.75ml group would suggest it is unlikely that a single 0.75ml dose prior to mating would last sufficiently long to provide adequate SII levels over the pre-lamb and lambing period.

The raw data from both trials show that a smaller dose of Flexidine (0.75ml) at scanning may be sufficient to protect lambs from the effects of goitre and poor lamb survival. The statistical analysis from the Wairarapa and South Otago show this is significant. It is interesting to observe that the decay rate of the 0.75ml/0.75ml and the 0/0.75ml groups is similar to the 2.5ml and 1.5ml groups after scanning.

There have been 'rumblings' that the standard 1.5ml dose administered one month prior to mating may not provide sufficient protective effect over the critical pre-lamb and lambing period. The raw data would not support this contention and it seemed there was no advantage seen by increasing the pre-tup dose from 1.5ml to 2.5ml.

What of the statistics?

The graphs look convincing. The statistics endorse the significance of the results. The sample size for testing showed sufficient power to demonstrate moderate to high significance at most points of the data.

Field trials conducted at veterinary clinics

Veterinary practitioners are often encouraged to look at conducting field trials to test their thoughts and ideas. Very easy to say, significantly more difficult to do. In most cases, as it stands in New Zealand now, you would be parented through the local AgResearch organisation for animal ethics approval. Be prepared to spend time working your way through a web based application process and requiring assistance from AgResearch clerical staff.

Funding applications are challenging. Most organisations will tell you that your application falls outside the parameters for application in the first instance so you do need to be very persistent. Be prepared to have to tell your story and convince others that your idea is worth investigating over and over again.

Our advice, yes continue to do trials but be aware of the likely stumbles along the way.
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