The effect of administering long-acting oxytetracycline and tilmicosin either by dart gun or by hand on injection site lesions and drug residues in beef cattle

Joyce Van Donkersgoed, Mary VanderKop, Craig Salisbury, Larry Sears, Jaci Holowath

Abstract — Forty yearling cattle were injected intramuscularly with long-acting oxytetracycline and subcutaneously with tilmicosin by dart gun or by hand in a chute 28 days prior to slaughter. The drugs caused injection site lesions and antibiotic residues in the neck and thigh that varied by technique, dose, and site.

Résumé — Conséquences de l’administration par fusil lance-fléchettes ou injection manuelle d’oxytetracycline à libération prolongée et de tilmicosine sur les lésions de site d’injection et sur les résidus médicamenteux chez des bovins de boucherie. Quarante bovins d’un an ont été injectés par voie intramusculaire avec de l’oxytetracycline à libération prolongée et par voie sous cutanée avec de la tilmicosine à l’aide d’un fusil lance-fléchettes ou de façon manuelle dans un corridor de contention 28 jours avant l’abattage. Les médicaments ont causés des lésions de site d’injection et des résidus d’antibiotiques variables selon les techniques, les doses et les sites, dans le cou et la cuisse.


Injection site lesions are found frequently in the top butts, rounds, and blades of beef cattle in Canada, and they reduce beef quality and profits (1–3). Drug residues at the injection site are also a food safety concern (4–7). The probability of lesions and residues increases when large volumes of drugs are administered in one injection site (4,6). Currently, most manufacturers of long-acting oxytetracycline (LAOTC) recommend the use of no more than 10 mL per any one injection site. While this recommendation can be followed when cattle are restrained in a squeeze and injected by hand, it can not be followed when guns and bows and arrows are used to treat cattle with a single therapeutic dose of LAOTC.

There are no published data available on the impact of guns or bows and arrows on the chance of injection site lesions or antibiotic residues. The following study was designed to evaluate the occurrence of injection site lesions and antibiotic residues when LAOTC is administered intramuscularly (IM) at 10 mL or 30 mL per site in the neck or thigh either by dart gun (Medi-Dart, Box 4181, Ponoka, Alberta) or by restraining animals in a chute and treating them by hand. The 10 mL volume was chosen because it is the labeled recommended maximum dose per site; the 30 mL volume was chosen because it is the dose that would be used in one site to treat an animal with a dart gun. Tilmicosin was given subcutaneously (SC) with the dart gun, because the gun can administer animal health products either IM or SC.

Forty beef calves with known treatment history were purchased from a rancher and placed on feed until slaughter. These calves had never received any injections in the left thigh or left neck prior to this time, and the feedlot was instructed to avoid any injections in these experimental sites. Twenty-eight days prior to slaughter (as determined by the feedlot manager), the yearling cattle were allocated to 1 of 4 treatment groups: 1) 30 mL of LAOTC (Liquamycin LA-200, Pfizer Canada, London, Ontario), IM, in the thigh by dart gun and 10 mL of LAOTC, IM, in the neck in the chute by hand, 2) 30 mL of LAOTC, IM, in the thigh in the chute by hand and 10 mL of tilmicosin (Micotil, Provel, Guelph, Ontario), SC, in the neck by dart gun, 3) 10 mL of LAOTC, IM, in the thigh by dart gun and 30 mL of LAOTC, IM, in the neck in the chute by hand, and 4) 10 mL of LAOTC, IM, in the thigh in the chute by hand and 30 mL of LAOTC, IM, in the neck by dart gun (Table 1).

The dart gun was a cross-bow that used a 12-gauge × 1-1/4-inch needle. The same IM or SC needle was used for all animals. The SC needle had holes on the side where the drug was delivered. Cattle were held in small
These cattle were not stressed by the dart gun, with large 1-inch needles, and a new needle was used for each injection. Some of the yearling cattle were too large to fit in the hydraulic squeeze; therefore, they were treated in the chute’s alleyway behind the squeeze. These cattle were not very well restrained during treatment. All treatments by dart gun were given by the same person and all treatments in the chute were given by the same person.

Seven animals treated with 30 mL of LAOTC had visible swellings the day after treatment: one injected in the thigh with the dart gun, 2 injected in the neck with the dart gun, and 4 injected in the neck in the chute by hand. Cattle were sent to slaughter 28 d after treatment, which is the label withdrawal period. Kidneys from half of the animals in each treatment group were tested for antibiotic residues by using the swab test on premises (STOP) (8). Only 50% of the kidneys were tested, because of the limited budget available. All kidneys tested negative for antibiotic residues.

Two days after slaughter, the left and right front legs were processed and cut into 1-inch (2.2-cm) steaks to visualize injection site lesions. Five tags were lost on the rounds during processing and one blade was trimmed by plant personnel by mistake prior to processing; therefore, 6 subprimals were lost from the data. The same experienced person evaluated all subprimals for lesions. Trim from injection site lesions was weighed, and then samples with observable lesions were sent for microscopic examination and for residue testing.

The microscopic lesions in these tissues were more severe than in previous studies (1–3); therefore, 2 additional categories were created to account for the new types of lesions. The new categories were “granulation tissue” and “abscess.” Granulation tissue consisted of mature fibroblasts that were well aligned and accompanied by extensive neovascularization. These were often associated with hemorrhage and edema, mild to moderate mononuclear cell infiltration, but minimal evidence of neutrophil infiltration. This suggested a relatively mature lesion, but not a typical scar because of the extensive neovascularization. Abscesses consisted of a moderate to wide band of dense fibrous tissue surrounding areas of liquefaction or caseous necrosis. There was edema, neutrophil infiltration, and focally extensive mononuclear cell accumulation with varying degrees of hemorrhage. These lesions showed chronic, active inflammation with little evidence of true healing and were uniformly very severe and extensive.

The injection site samples were received at the Centre for Veterinary Drug Residues (CVDR) in a frozen condition. Subsamples of each site were analyzed for residues of oxytetracycline by using CVDR’s liquid chromatography (LC) method for determination of tetracyclines in tissue (TTC-SP08) (9,10). Residues of tilmicosin were analyzed by using CVDR’s LC method for the determination of tilmicosin in tissue (TIL-SP07) (11).

The proportion of injection site lesions, average weight of trim, median number of steaks with lesions, median residue concentrations, and proportion of animals that exceeded the administrative action levels (AALs) were calculated by treatment (STATISTIX for Windows, Analytical Software, Tallahassee, Florida, USA). The current AALs for veterinary drugs in foods (Food and Drugs Act and Regulations, updated to August 1, 1998, Health Canada) are 0.1 µg/g for oxytetracycline and 0.8 µg/g for tilmicosin. The chi-squared test, analysis of variance (ANOVA), Kruskal-Wallis one-way non-parametric ANOVA, and Spearman's rank correlations were used to assess differences among treatments and lesions, residues, trim, and the number of steaks affected. For an estimate of the economic losses per treatment, calculations were made similarly to previous studies (1,2), by using the International Surveys Limited retail prices for the second quarter of 1998, the average trim weight, and the median number of steaks with lesions.

The results are shown in Table 1. Five (56%) of the animals injected IM with 30 mL of LAOTC in the neck by the dart gun had SC lesions at processing, and 2 (20%) of the animals injected SC with tilmicosin in the neck had SC lesions at processing. The proportion of IM injection site lesions was high for LAOTC, similar to previous findings of 40% to 100% (3,6). There were no significant differences in the occurrence of IM lesions in the blade (P = 0.14) or round (P = 0.15) by treatment. Animals injected by hand in the chute with 30 mL of LAOTC in the neck (P = 0.0002) or in the thigh (P = 0.0002) had significantly more tissue trimmed than in any other treatment. Animals injected by hand in the chute with 30 mL of LAOTC in the neck (P = 0.001) or in the thigh (P = 0.002) had significantly more steaks with lesions than those injected by the dart gun with 30 mL of LAOTC. This was contrary to the expectation that a higher level and severity of lesions would occur when cattle were injected by using the dart gun than by hand in the chute, because the drug is delivered under pressure with the gun. One reason for this result may be that all cattle were not properly restrained in the chute when they were injected by hand, because they were too large to fit into the squeeze. Thus, there may have been more tissue damage than if the cattle had been properly restrained in the squeeze. Unfortunately, those that were treated in the alleyway were not individually recorded from those that were treated in the squeeze to see if this was a factor. In a typical feedlot, cattle within 30 d of slaughter are rarely treated for disease; thus, size is rarely a factor for failure to properly restrain animals in a squeeze.

The concentration of oxytetracycline in the blade was not significantly (P = 0.10) different among the 3 treatment groups. While there was a significant (P = 0.05) association overall in the oxytetracycline concentrations in the round among treatments, there were no significant 2-way differences between treatments. There were no significant differences in the number of animals that exceeded the AAL in the blade (P = 0.46) or in the round (P = 0.15), by treatment. Failure to find a significant difference among treatment groups may have been due to the small sample size, which was a limitation because of the large costs of this kind of study, or it may have been due to the wide range of values for drug residues within a group of animals that received.
Table 1. The occurrence of injection site lesions and drug residues at the injection site following administration of long-acting oxytetracycline and tilmicosin to beef cattle 28 days prior to slaughter with a dart gun or by hand in a chute

<table>
<thead>
<tr>
<th>Technique</th>
<th>Drug</th>
<th>Dose per site (mL)</th>
<th>Site</th>
<th>Route</th>
<th>Lesions (%)</th>
<th>Trim weight¹ (g (SD))</th>
<th>n steaks with lesions² (range)</th>
<th>Residues (μg/g³) (range)</th>
<th>Exceeded AAL⁴ (%)</th>
<th>Trim loss⁵ ($)</th>
<th>Histology at injection site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medi-dart gun</td>
<td>LAOTC ⁶</td>
<td>10</td>
<td>thigh</td>
<td>IM</td>
<td>44 (4/9)</td>
<td>104 (28)</td>
<td>3 (2–3)</td>
<td>0.05 (0.05–0.06)</td>
<td>0 (0/4)</td>
<td>3.39</td>
<td>100% woody callus</td>
</tr>
<tr>
<td>Hand</td>
<td>LAOTC</td>
<td>10</td>
<td>thigh</td>
<td>IM</td>
<td>88 (7/8)</td>
<td>177 (85)</td>
<td>5 (3–9)</td>
<td>0.50 (0.09–3.41)</td>
<td>57 (4/7)</td>
<td>10.91</td>
<td>43% scar with nodules, 43% woody callus, 14% granulation tissue</td>
</tr>
<tr>
<td>Medi-dart gun</td>
<td>LAOTC</td>
<td>30</td>
<td>thigh</td>
<td>IM</td>
<td>70 (7/10)</td>
<td>117 (75)</td>
<td>2 (1–4)</td>
<td>0.05 (0–5.85)</td>
<td>20 (1/5)</td>
<td>3.92</td>
<td>29% scar with nodules, 71% woody callus</td>
</tr>
<tr>
<td>Hand</td>
<td>LAOTC</td>
<td>30</td>
<td>thigh</td>
<td>IM</td>
<td>88 (7/8)</td>
<td>465 (243)</td>
<td>8 (2–10)</td>
<td>57.7 (0–687.00)</td>
<td>57 (4/7)</td>
<td>17.93</td>
<td>14% woody callus, 43% granulation tissue, 43% abscess</td>
</tr>
<tr>
<td>Medi-dart gun</td>
<td>LAOTC</td>
<td>30</td>
<td>neck</td>
<td>IM</td>
<td>67 (6/9)</td>
<td>101 (42)</td>
<td>2 (1–2)</td>
<td>8.35 (0–27.10)</td>
<td>50 (3/6)</td>
<td>1.61</td>
<td>17% woody callus, 50% granulation tissue, 33% abscess</td>
</tr>
<tr>
<td>Hand</td>
<td>LAOTC</td>
<td>30</td>
<td>neck</td>
<td>IM</td>
<td>100 (10/10)</td>
<td>801 (388)</td>
<td>5 (3–6)</td>
<td>0.17 (0.04–4.27)</td>
<td>50 (5/10)</td>
<td>6.28</td>
<td>30% granulation tissue, 70% abscess</td>
</tr>
<tr>
<td>Hand</td>
<td>LAOTC</td>
<td>10</td>
<td>neck</td>
<td>IM</td>
<td>60 (6/10)</td>
<td>292 (157)</td>
<td>3 (1–5)</td>
<td>0.08 (0–2.74)</td>
<td>17 (1/6)</td>
<td>2.16</td>
<td>20% scar with nodules, 20% woody calluses, 40% granulation tissue, 20% abscess</td>
</tr>
<tr>
<td>Medi-dart gun</td>
<td>tilmicosin⁶</td>
<td>10</td>
<td>neck</td>
<td>SC</td>
<td>60 (6/10)</td>
<td>297 (227)</td>
<td>3 (1–5)</td>
<td>0.87 (0.37–5.13)</td>
<td>60 (3/5)</td>
<td>2.17</td>
<td>50% woody callus, 33% granulation tissue, 17% abscess</td>
</tr>
</tbody>
</table>

¹Average weight of tissue trimmed per subprimal because of injection site lesions (SD = standard deviation)
²Median number of steaks per subprimal with an injection site lesion (range)
³Median concentration of antibiotic residues per subprimal (range)
⁴Administrative action limit (oxytetracycline > 0.1 μg/g, tilmicosin > 0.8 μg/g)
⁵Average economic loss from trim and devaluation of the subprimal
⁶Long-acting oxytetracycline (Liquamycin LA-200, Pfizer Canada, London, Ontario)
⁷Tilmicosin (Micotil, Provet, Guelph, Ontario)
identical treatment. There were quite a few animals that exceeded the AAL with the 30 mL dose of LAOTC when the 28-day withdrawal period was followed, indicating that drug residues at the injection site are of concern when large volumes of drug are administered in one site. Even with the 10 mL dose for LAOTC and tilmicosin, there were animals that exceeded the AAL at the injection site after the withdrawal period. Failure of the STOP to predict the presence of oxytetracycline residues in injection sites has been reported previously (12). However, the STOP test is not used nor was it designed to detect the presence of antibiotic residues at an injection site.

The amount of tissue trim was not correlated with the level of oxytetracycline residues in the blade \( r = -0.14, P = 0.54 \), but it was correlated with the level of oxytetracycline residues in the round \( r = 0.42, P = 0.05 \). Nouws (4) reported a correlation \( r = 0.60, P < 0.08 \) between tissue irritation and oxytetracycline recovery in the neck of calves. The high level of residues at the injection site may be due, in part, to tissue irritability that may affect the absorption of the drug (4,6). Other research (4,7) has similarly found antibiotic residues of oxytetracycline at the site of injection after the withdrawal period. With tilmicosin, there was considerable reaction in the underlying muscle, suggesting that the dart gun’s needle may have gone into the muscle. This may have resulted in a higher chance of antibiotic residues than would be expected under normal situations where the product is injected SC only. Properly administered SC injections of tilmicosin did not result in injection site lesions (2) or residues in previous research (Freedom of Information Summary, New Animal Drug Application, 140-929; Micotil 300 (tilmicosin phosphate); March 3, 1992). Unfortunately, in this study, there was no comparison group with the tilmicosin treatment by hand in the chute to see if the IM reaction was due to the technique.

Cattle injected with 30 mL of LAOTC appeared to have more lesions categorized as “granulation tissue” and “abscess” than did those injected with 10 mL LAOTC, where “woody calluses” and “scars with nodules” were more common. The exception to this trend (2,4,5) was cattle treated with 30 mL of LAOTC in the thigh by the dart gun. The occurrence of lesions, amount of trim, number of steaks affected, residue concentrations, percentage of animals that exceeded the AAL, and the microscopic lesions were similar in animals injected with 30 mL or 10 mL of LAOTC in the thigh by the dart gun. Yet the trend (5,6) was for more tissue trim, more abscesses, more steaks affected, and a higher level of residues in cattle that were injected with 30 mL by hand in the chute in either the neck or the round than in those injected with 10 mL. This contradictory finding with the dart gun in the round may suggest that either the animals did not receive the full dose of 30 mL (if some leaked out of the injection site) or this technique is not as irritating to tissue as is injecting by hand in the chute. This work should be repeated in larger groups of animals to reliably determine the difference in tissue reactivity between injections given by dart gun and by hand in the chute, and to determine the blood drug levels to see if animals receive the total dose of the antibiotic administered.

The economic losses from the injection site lesions ranged from $1.61 to $17.93. Based on economic losses and the chance of drug residues at the injection site, we recommend that 30 mL of LAOTC, IM, should never be administered to cattle in one injection site in the neck or in the rump by any technique. Injections should not be given in the top butt or thigh, because of the difficulty of finding injection site lesions and trimming tissue that may contain antibiotic residues (5), and the high economic losses when sirloin and round meat cuts are damaged by injection site lesions (1,2). In this study, even 10 mL of LAOTC, IM, by hand, or 10 mL of tilmicosin, SC, by the dart gun in the neck caused tissue trim, economic losses, and residues that were of concern from a quality and food safety perspective.

Results of this study show that a 28-day withdrawal period is not sufficient for meat safety at the injection site for some long-acting antimicrobials administered to cattle in the chute by hand or by dart gun. To protect the consumer against chemical hazards, withdrawal periods may have to be based on the measurement of the antibiotic residues at the injection site, while taking into account the drug formulation, the volume injected in a site, the site of injection, the species, the disease status, the route, and the technique (6).

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References


