THE EFFICACY OF A KILLED VACCINE AGAINST PARATUBERCULOSIS (SILIRUM®) IN CATTLE. A FIELD STUDY

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INTRODUCTION

Vaccination has been considered to be one of the most efficient methods for the control of paratuberculosis. The use of either killed or live vaccines has been shown to reduce, in all susceptible species, the number of clinical cases and shedding of *Mycobacterium avium* subsp. *paratuberculosis* (Map) in faeces more rapidly and with lower economic costs than other procedures such as culling of faecal culture positive individuals (Jorgensen, 1983; Argente, 1992; Van Schaik et al., 1996; Groenendaal, H. and Galligan, D.T., 2003). Pathological methods have been used for the assessment of the efficacy of vaccines (Nisbet et al., 1962; Juste et al., 1988). A classification of lesions that associates pathological features with the different stages of Map infection has been proposed (Pérez et al., 1996; González et al., 2005). In sheep, it has been shown that vaccination does not prevent the infection, but modifies the inflammatory response towards focal lesions restricted exclusively to the intestinal lymphoid tissue, whereas in unvaccinated animals, lesions spread to different mucosal areas (Juste et al., 1994; García Marín et al., 1995). In this field study, the efficacy of a killed vaccine against paratuberculosis in adult cattle has been assessed using a histopathological method for the evaluation of paratuberculosis associated lesions in culled animals.

MATERIALS AND METHODS

The study has been carried out in a Friesian dairy herd, showing approximately a 12% of annual clinical cases of the disease, and formed by 468 adult cows. A 75% of the total, regardless the age or clinical status, was vaccinated with a single dose of SILIRUM® (CZ Veterinaria) and the remaining 25% kept as unvaccinated controls. For a period of 30 months post-vaccination (mpv), all the culled animals, for any reason, have been recorded and pathological studies carried out in 79 of them. Cellular and humoral peripheral immune responses have been also assessed by IFN-γ production and ELISA tests respectively.

RESULTS AND DISCUSSION

Vaccination against paratuberculosis induced a strong humoral immune response in the majority of vaccinated animals. The number of cows positive to ELISA test reached its highest point at 5 mpv (85% approx.) and began to decrease until 21 and 25 mpv showing no differences with controls (Figure 1). As it can be seen in Figure 2, a strong cellular immune response was also induced by vaccination. The percentage of vaccinated...
animals positive to IFN-γ test was 100% at 1 mpv, decreasing slowly to approximately 80% at the end of the study.

Figure 1.- Percentages of cows positive to ELISA test according to their vaccination status and date post-vaccination.

Thirty months after vaccination, 191 animals have been culled from the herd for any reason (48.1% of the unvaccinated group and 39% of the vaccinated). Percentage of culled animals, in all periods in which the study was divided, was higher in unvaccinated animals than in vaccinated cows, except in 12-18 mpv period (9.4% and 8.75%) and 24-30 mpv (10.5% and 8.5% in vaccinated and control respectively), where no significant differences were found.

Figure 3.- Percentages of culled animals according to their vaccination status and period of culling

Pathological studies were carried out in samples of intestine and associated lymph nodes from 79 of the culled animals. Lesions were classified (González et al., 2005) as focal/multifocal, formed by well-defined small granulomas located in the Peyer’s patches or lymph nodes, thought to be subclinical forms related to initial or latent phases of the disease respectively, with low mycobacterial load (Figures 4 and 5), and diffuse or severe, showing a widespread granulomatous enteritis associated with clinical signs and high levels of Map in the tissues (Figures 6 and 7).

Figure 4.- FOCAL LESION. Small well-defined granulomas in ileal lymph node cortex and paracortex (H-E 40x).

Figures 5a and 5b.- MULTIFOCAL LESION. Small well-defined granulomas located in ileocecal valve Peyer’s patch and related mucosa with low Map load (H-E 40x; Z-N 100x).

As it can be seen in Table 1, a significant reduction in the number of cows with paratuberculosis associated lesions have been observed in vaccinated (56.6%) with respect to control animals (92.3%). A clear reduction in percentage of diffuse or severe lesions present has been also seen (15.1% of vaccinated vs 34.6% of controls).

Table 1.- Distribution of cows according the lesional type and vaccination status of culled animals.

<table>
<thead>
<tr>
<th>Type of lesion</th>
<th>Control (%)</th>
<th>Vaccinated (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without lesion</td>
<td>2 (7.7)</td>
<td>23 (43.4)</td>
</tr>
<tr>
<td>Focal/Multifocal</td>
<td>15 (57.7)</td>
<td>22 (41.5)</td>
</tr>
<tr>
<td>Diffuse</td>
<td>9 (34.6)</td>
<td>8 (15.1)</td>
</tr>
<tr>
<td>Total lesion</td>
<td>24 (92.3)</td>
<td>30 (56.6)</td>
</tr>
</tbody>
</table>
When considering the different dates post-vaccination, similar results were observed (Table 2) with a progressive reduction in the number of animals showing lesions from 24 mpv in vaccinated cows and an increase in animals showing diffuse or severe lesions in control cows.

### Table 2.- Percentages of lesional types of paratuberculosis according to vaccination status of the animals and period of culling.

<table>
<thead>
<tr>
<th>GROUP</th>
<th>Type of lesion</th>
<th>0-12 mpv (n=6)</th>
<th>12-24 mpv (n=12)</th>
<th>24-36 mpv (n=8)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N° animals</td>
<td>%</td>
<td>N° animals</td>
<td>%</td>
<td>N° animals</td>
</tr>
<tr>
<td>CONTROL (n=26)</td>
<td>Without lesion</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>8.3</td>
</tr>
<tr>
<td></td>
<td>Focal/Multifocal</td>
<td>5</td>
<td>83.3</td>
<td>6</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Diffuse</td>
<td>1</td>
<td>16.7</td>
<td>5</td>
<td>41.6</td>
</tr>
<tr>
<td>VACCINATED (n=50)</td>
<td>Without lesion</td>
<td>3</td>
<td>30</td>
<td>10</td>
<td>47.6</td>
</tr>
<tr>
<td></td>
<td>Focal/Multifocal</td>
<td>6</td>
<td>60</td>
<td>7</td>
<td>33.3</td>
</tr>
<tr>
<td></td>
<td>Diffuse</td>
<td>1</td>
<td>10</td>
<td>4</td>
<td>19</td>
</tr>
</tbody>
</table>

Vaccination of adult cows has been shown to be an efficient method for reducing the number of clinical cases, as seen by the reduction of cows showing diffuse lesions, that are probably high shedders (Pérez et al., 1996; González et al., 2005). In experimental studies (Nisbet et al., 1962; Juste et al., 1994) it has been shown that vaccination does not prevent infection of animals, but modifies the inflammatory response towards a limitation of the progression of granulomatous lesions. The results obtained in this study support this hypothesis, since an increase of cows with no lesions and showing focal forms was observed in vaccinated animals in contrast to controls. It has to be taken into account that animals with severe lesions have been encountered at 36 mpv, suggesting that protection conferred by the vaccine is not absolute. This could be due to individual factors, that predispose to poor immune responses (Doyle, 1964), or the advanced stage of Map infection at the time of vaccination that has not enabled the vaccine to induce any modification in the inflammatory response.

This is a preliminary part of a field study in which the effect of vaccination on fecal shedding and milk production is being also assessed.

### CONCLUSIONS

Vaccination of adult cows against paratuberculosis with a single dose of SILIRUM® has shown to be a valuable method for reducing the number of culled animals and those showing severe lesions associated with clinical signs.

The effect of the administration of SILIRUM® to adult animals, presumably already infected, would be the modification of the inflammatory response towards focal or latent lesions, subclinical or even the total disappearance of pathological changes.

Strong cellular and humoral immune responses mounted after vaccination persist in the animals for at least two years post-vaccination.

### REFERENCES


