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MARKED HISTOLOGICAL CHANGES IN THYMUS OF DAIRY COWS TREATED WITH rbST; RESULTS OF 3 ANIMAL EXPERIMENTS

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Introduction

Growth hormone or somatotropin (ST) is a naturally occurring hormone secreted by the pituitary gland in mammals. Since the late 1980s recombinant human, bovine and porcine ST have been used clinically (human) or for increased milk production (bovine) or performance (pigs). The recombinant bovine ST (rbST) is produced using recombinant technology and its structure is almost similar to the endogenous form. At present two major forms of rbST are commercially available. Posilac was developed by Monsanto and is sold by Eli Lilly – Elanco Animal Health division. Boostin (Hilac) is produced by LG Life Sciences. Effects of rbST in dairy cattle are an increased milk production with 11-15 %. But side effects are an increased incidence of health disorders which was the reason for Canada and the European Union to ban its use.
Growth hormone levels decrease with age as thymic involution progresses. Regrowth of the thymus has been found to occur in rbST treated rats, mice and dogs. We have conducted three experiments with rbST where we sampled thymus of cows for histological evaluation.

Materials and methods

Animal experiments:
In the first experiment 3 control cows and 4 treated cows were used. All cows were between 4 and 6 years of age, of the Holstein Friesian breed (HF), in their 4th or 5th lactation and had calved 5 months before the start of the experiment. The 3 control cows were treated with placebo and the 4 other cows were treated 6 times with two-weekly injections of Posilac (500 mg/ sometribove zinc suspension injection, Monsanto). The animals were slaughtered one month after the last treatment.
In the second experiment 8 cows were treated for 4 times with two-weekly injections of Posilac. All cows were lactating HFs, not pregnant and varied in age and stage of lactation. All animals were slaughtered 4 weeks after the last injection.
In the third experiment 2 cows were treated with Posilac and 2 cows were treated with Boostin S (Hylac, 500 mg, LG Live Sciences, Korea) 3 times with two-weekly injections. The animals were not pregnant, and were giving about 20 litres / day. The animals were slaughtered 3 weeks after the last injection.

Histology
Samples of the cervical part of the thymus were sampled and fixed in 4 % buffered formalin and routinely processed to paraffin sections. Sections (5 µm thick) were stained with haematoxylin-eosin (HE) according to Mayer and assessed microscopically.

Results

Histology:
The results of the histology and thymus weights are listed in table 1. In general control adult cows from experiment 1 showed severe fatty infiltration in the thymus with cortical and medullary atrophy leaving only fat and remnants of cortex and medulla around the vessels (figure 1). The bST treated cows showed regeneration of the thymus with varying degrees of lymphocytic hyperplasia (figure 2) until the features of a normal calf thymus (figure 3), with only a little fatty infiltration.

Table 1. Treatment, weights of thymus and histology

Animal number	Treatment	Weight thymus (gram)	Histology
9497	Vehicle	27.9	Severe fatty infiltration, cortical atrophy
7513	Vehicle	59.2	Severe cortical atrophy, mainly fatty tissue left
8248	Vehicle	131.4	Cortical atrophy, fatty infiltration
4005	Posilac	198.9	Intact thymus, hyperplasia
5319	Posilac	108.9	Hyperplasia, small amount of fat
2982	Posilac	129.6	Relative intact thymus, hyperplasia, small amount of fat
1966	Posilac	296.2	Much thymus tissue left, hyperplasia
6957*	Posilac	n.d.	Only fat sampled
7894	Posilac	168	Much thymus tissue left, hyperplasia
6348	Posilac	150	Much thymus tissue left, hyperplasia
6973	Posilac	142	Hyperplasia, some fatty tissue
7597	Posilac	192	Hyperplasia, some fatty tissue
7554	Posilac	316	Hyperplasia, some fatty tissue
6328	Posilac	132	Hyperplasia, some fatty tissue
7749	Posilac	508	Hyperplasia, necrosis Hassall body
6137	Boostin	n.d.	Hyperplasia, some fat, small haemorrhage
8910	Posilac	n.d.	Intact thymus like a calf
1102	Boostin	n.d.	Intact thymus like a calf
8930	Posilac	n.d.	Intact thymus, like a calf, small haemorrhage

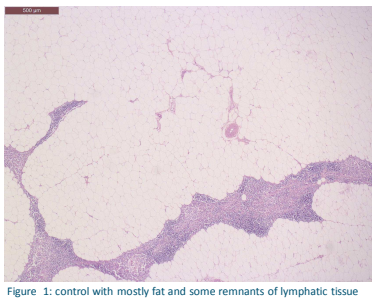
Figure 1: control with mostly fat and some remnants of lymphatic tissue

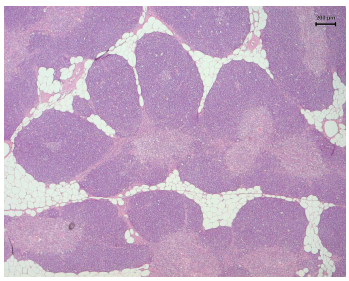
Figure 2, treated animals showing regeneration of thymus tissue

Conclusions

rbST treated cows after a withdrawal time of 3-4 weeks showed marked histological regeneration of the thymus which showed a huge difference with the thymus of control dairy cows.
Histological screening of thymus tissue of dairy cows can be a promising method to control illegal use of rbST.

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