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Effect of chronic inhibition of prolactin release on milk production of dairy cows.

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In most mammals, suppression of prolactin (PRL) strongly inhibits lactation. Nevertheless, short term suppression of PRL by bromocriptine has produced inconsistent effects on milk yield in cows and goats. A preliminary experiment was carried out to evaluate the ability of a newer dopamine agonist, quinagolide, to suppress PRL release in cattle. The results indicated that daily injections of this molecule were able to suppress both basal PRL and milking-induced PRL release. An experiment was then carried out to evaluate the effect of long term inhibition of PRL release on milk production of dairy cows. Five Holstein dairy cows in early lactation received daily intramuscular injection of 1 mg of quinagolide during 9 weeks. Four control cows received the vehicle (water). During the 9th weeks, differential milking (1X vx 2X) was applied. Quinagolide reduced the milking-induced prolactin release for the duration of the trial ($P<0.05$). Quinagolide reduced milk production ($P<0.05$). At the end of the period, milk production averaged 36.4±1.4 and 31.8±1.2 kg/d for control and quinagolide treated cows, respectively. Milk composition was not affected by the treatments. Yield of fat ($P<0.01$), protein ($P<0.05$) and lactose ($P<0.05$) were reduced by quinagolide. Feed intake was slightly lower ($P<0.05$) in quinagolide-treated cows but, body weight gain were similar for both groups. Milk production was correlated with prolactin release in quinagolide treated cows ($R=0.61$, $P<0.01$) and control cows ($R=0.64$, $P<0.01$). During differential milking, the inhibitory effect of quinagolide remained in the half gland milked twice a day ($P<0.05$) but disappeared in the half gland milked once a day. In conclusion, chronic administration of an inhibitor of prolactin-release reduces milk production in cattle.

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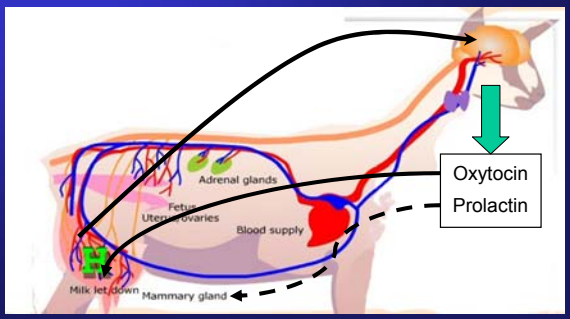
Prolactin

- Essential to lactogenesis in all mammals
- Clearly galactopoietic in most mammals
- Galactopoietic effect of prolactin in cows and goat is still a matter of debate

Evidences against a galactopoietic role of prolactin

- Circulating level of PRL are not correlated with milk production
- Short term inhibition of PRL by bromocriptine gave small or no inhibition of milk production (Karg and Schams, 1974)
- Injection of large doses of PRL did not stimulate milk production (Plaut et al., 1987)

Milking and nursing induce the release of hormones



Evidences for a galactopoietic role of prolactin

- Milking-induced PRL release decreases as lactation advances
- Injection of PRL reproduced the stimulating effect of IMF on milk yield (Wall et al., 2006)
- Short day photoperiod (Bilodeau et al., 1988) and melatonin implants (Auldist et al., 2006) reduce PRL and milk production
- PRL is a survival factor for mammary epithelial cells of rodents (Travers et al., 1996) and cows (Accorsi et al., 2002)

Hypothesis

The milking-induced prolactin release helps to maintain epithelial cell number and activity

Objective

To evaluate the effect on milk production of long term inhibition of prolactin release

Methodology

- Animals:
  - 10 multiparous cows in early lactation
  - 1 control cow removed for mastitis
- Treatments:
  - Daily i.m. injection of 1mg of Quinagolide or 1 ml of water (control) from weeks 1 to 9
  - Differencial milking (1X vs 2X) was applied on week 9

Methodology

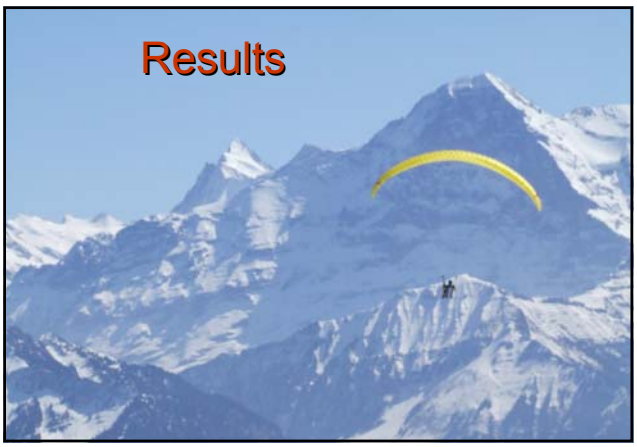
- Blood sampling
  - Weekly samples for metabolite analysis (glucose, NEFA, urea and lactose)
  - Samples were collected before and during the morning milking at weeks -1,1, 4 and 8 for hormone analysis (prolactin, cortisol and IGF-1)

B : Basal

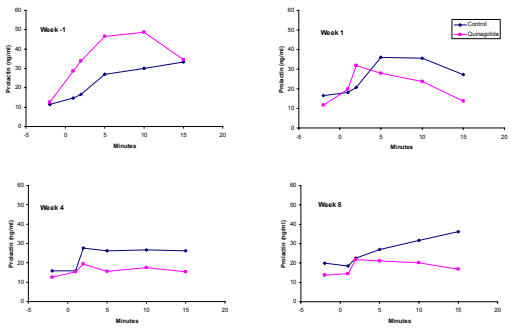
0 : installation of milking unit

Methodology

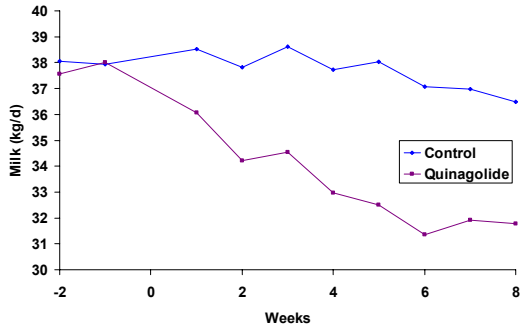
- Milk samples were collected for composition (fat, protein and lactose) and BSA determination
- Mammary biopsies were collected before afternoon milking at weeks -1, 4 and 8 for immunohistology and gene expression analyses



Effect of Quinagolide on milking-induced prolactin release



Effect of Quinagolide on milk production

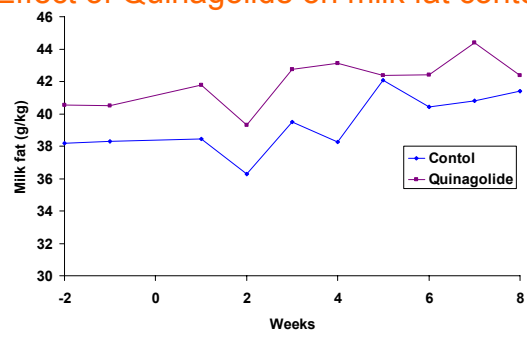


SEM=1,3, P=0,04

Correlation with milk production

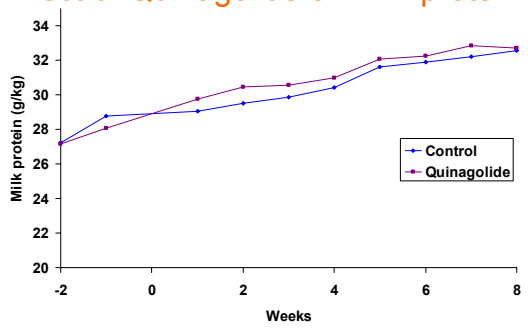
	All animals		Quinagolide		Control	
PRL	R	P<	R	P<	R	P<
AUC	0.57	.001	0.61	.005	0.64	.01
Peak	0.56	.001	0.64	.005	0.61	.02

Effect of Quinagolide on milk fat content



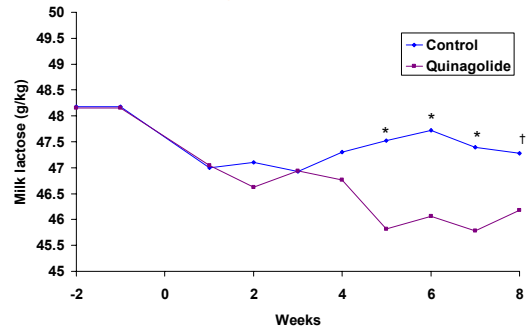
SEM=1.5, NS

Effect of Quinagolide on milk protein



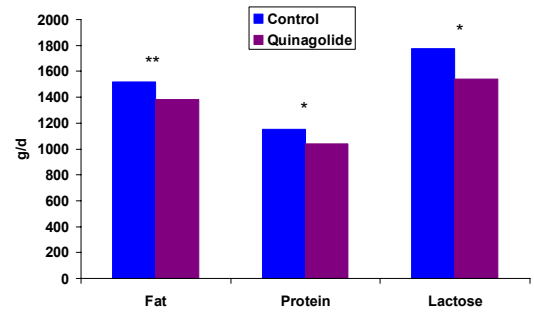
SEM=0,7; NS

Effect of Quinagolide on milk lactose

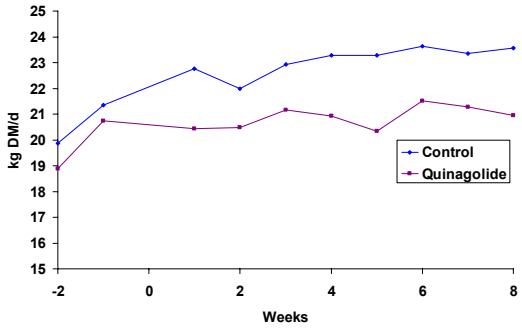


SEM=0,6; P=0,14

Effect of Quinagolide on components yield

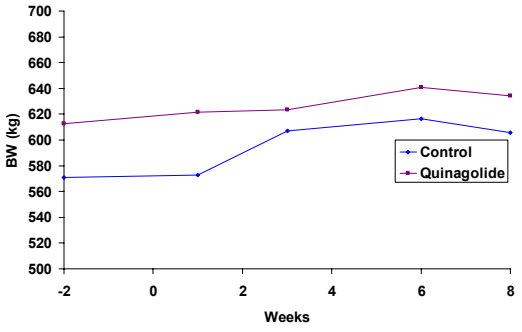


Effect of Quinagolide on feed intake



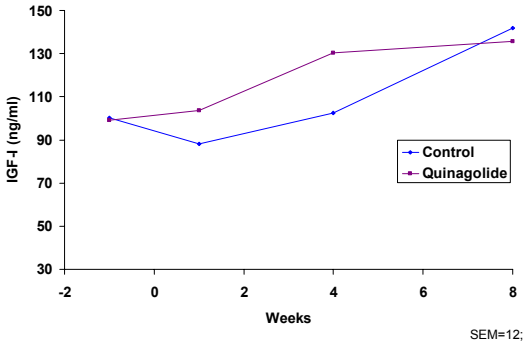
SEM=0,6; P=0,04

Effect of Quinagolide on body weight



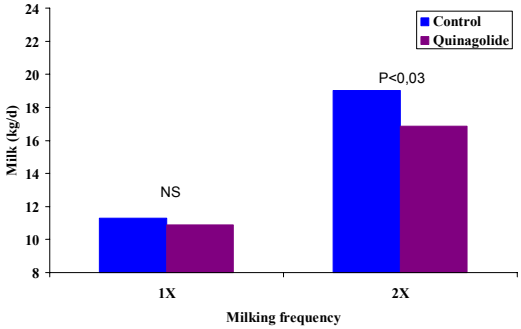
SEM=12; NS

Effect of Quinagolide on IGF-1



SEM=12; NS

Effect of Quinagolide and differential milking on milk production



Other variables

- No effect of Quinagolide on blood lactose and milk BSA
- No effect of Quinagolide on blood metabolites (NEFA, urea, glucose)
- No effect of Quinagolide on health

Conclusions

- Quinagolide treatment inhibits prolactin-release in cattle
- Quinagolide treatment decreases milk production
- This effect is not due to an opening of the tight junctions
- Milking frequency affects the responsiveness to the treatment