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Chronic oxytocin treatment causes reduced milk ejection in dairy cows

Rupert M Bruckmaier*

Institut für Physiologie, Forschungszentrum für Milch und Lebensmittel Weihenstephan, Technische Universität München, Weihenstephaner Berg 3, D-85354 Freising, Germany

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The major milk fraction stored in the bovine udder, the alveolar milk, is not available for milk removal before being actively shifted to the cisternal cavities by the milk ejection reflex (Knight et al. 1994; Pfeilsticker et al. 1996). Tactile teat stimulation, provided by the liner throughout milking, causes continuous release of oxytocin from the neurohypophysis into the blood circulation, which induces myoepithelial contraction and shifting of alveolar milk into the cistern until the end of milking (Bruckmaier et al. 1994; Crowley & Armstrong, 1992; Gorewit et al. 1983; Lefcourt & Akers, 1983). However, milk ejection during machine milking is not complete. A residual milk fraction of 10–30% remains in the udder and is only removed after administration of supraphysiological amounts of oxytocin, usually at least 10 i.u. of oxytocin injected i.v. (Bruckmaier & Blum, 1998). In dairy practice, exogenous oxytocin is often used at high dosages to treat disturbed or incomplete milk ejection. It is reported by farmers and veterinarians that after long-term use of exogenous oxytocin animals become addicted to the treatment and withdrawal of oxytocin causes reduced milk ejection.

The goal of this study was to test the hypothesis that chronic administration of large amounts of oxytocin at each milking causes reduced milk ejection after withdrawal of exogenous oxytocin; and, additionally, to determine whether the milk ejection response to chronically administered exogenous oxytocin changes with time and whether any changes are due to the exogenous oxytocin or due to the injection procedure.

Materials and Methods

Animals and milking

Twenty-one multiparous and clinically healthy Brown Swiss dairy cows with somatic cell counts (SCC) <150 000 in all quarters and normal milk ejection were used. Cows yielded 24–30 kg milk/d and were in different stages of lactation. They were milked twice daily at 5.00 and at 16.00 in a 2 × 2 tandem parlour; the procedure was similar for routine and experimental milking. Each milking included careful machine stripping when milk flow decreased below 0·2 kg/min.

Treatment groups and chronic injections

Cows were randomly assigned to three treatment groups with seven animals in each. Chronic injections were administered i.m. into one musculus semitendinosus 1 min before the start of each morning and evening milking from experimental days 1–22. One group received 50 i.u. of oxytocin diluted in a volume of 5 ml (oxytocin group), one group received 5 ml sodium chloride solution (9 g/l) as a placebo (NaCl group) and one group did not receive any chronic injections (control group).

Treatments at test milkings

To test normal milk ejection, induced by endogenous oxytocin, afternoon milkings on days 0 (=day before the start of chronic treatments), 7, 14, and 21, were performed without pre-milking injections (Experiment 1). After stripping at the end of milking, residual milk was removed after i.v. administration of 10 i.u. of oxytocin into the vena epigastrica caudalis superficialis to animals of all treatment groups.

The response to exogenous oxytocin injected i.m. was tested during the afternoon milkings on days 1, 8, 15, and 22 (Experiment 2). Fifty i.u. of oxytocin was injected i.m. 1 min before the start of milking in all treatment groups. After stripping, residual milk was again removed after i.v. administration of 10 i.u. of oxytocin.

Parameters recorded

Milk fractions were recorded by using a strain gauge system as previously described (Bruckmaier et al. 1994). To test the

*For correspondence; e-mail: bruckmaier@wzw.tum.de

efficacy of milk removal in all treatments we recorded spontaneously removed milk (removed during normal milking including stripping) and residual milk (removed after i.v. injection of 10 i.u. of oxytocin).

Mathematical and statistical analyses

Data are presented as means and SEM. The spontaneously removed milk fraction including stripping (%) and the residual fraction (%) were calculated as a percentage of total milk yield. For statistical analysis, the MIXED procedure of the SAS program package (version 8.01; SAS, 1999) was used. The model included experiment, treatment and experimental day. The individual animal was used as the repeated subject. Differences between means were tested by Bonferroni's *t* test and considered significant if $P<0{\cdot}05$.

Results

Total milk yield and cows' entering of the parlour for milking

Total milk yield including residual milk did not change significantly throughout the experiment in any experimental group. Total milk yields on days 0, 1, 7, 8, 14, 15, 21 and 22, respectively were 14·9±0·9, 14·8±0·9, 14·7±0·8, 16·4±1·4, 15·2±1·0, 16·2±1·4, 14·9±0·9 and 14·9±0·9 kg in the control group, 13·6±0·9, 13·2±0·8, 12·8±0·8, 13·2±1·0, 13·2±1·0, 13·5±1·3, 13·7±0·8 and 13·7±0·8 kg in the NaCl group, and 12·4±0·9, 12·4±1·2, 12·0±0·8, 11·9±1·0, 11·6±0·7, 12·4±1·3, 11·9±0·8 kg and 11·8±0·8 kg in the oxytocin group. Thus carry-over effects of previous treatment days on total milk production were not obvious. Stripping yield was 0·0–0·3 kg in all animals throughout the experiment and did not change with any of the treatments.

Chronically injected animals of both the NaCl and oxytocin groups increasingly refused to enter the milking parlour voluntarily and had to be fetched by the milker, whereas the voluntary entering of the parlour was not affected in the control group. During the milking procedure, no behavioural changes were observed in any of the treatment groups during the entire experiment. Relations between milk ejection and behavioural changes of individual animals were not obvious.

Experiment 1

As shown in Fig. 1, the spontaneously removed milk fraction did not significantly change on days 0, 7, 14, and 21 in control and NaCl groups. In contrast, the spontaneously removed milk fraction had significantly ($P<0{\cdot}05$) declined on day 7 as compared with day 0 in the oxytocin group and remained at this reduced level until day 21. However, the individual reaction of the oxytocin group animals was very

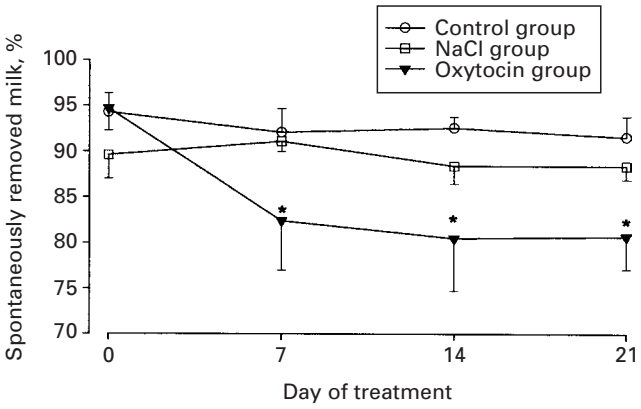

Fig. 1. Spontaneously removed milk fraction (normal milking+stripping without any pre-milking injection at this particular milking; 100%=total milk yield including residual milk) on the day before (day 0) and on days 7, 14 and 21 of chronic injection before each milking. Circles, control group, no chronic injection; squares, NaCl group, i.m. injections of 5 ml NaCl solution (9 g/l); triangles, oxytocin group, i.m. injections of 50 i.u. of oxytocin. Values are means with SE for 7 animals on each treatment. (*) Group mean is significantly different from respective mean on day 0 ($P<0{\cdot}05$).

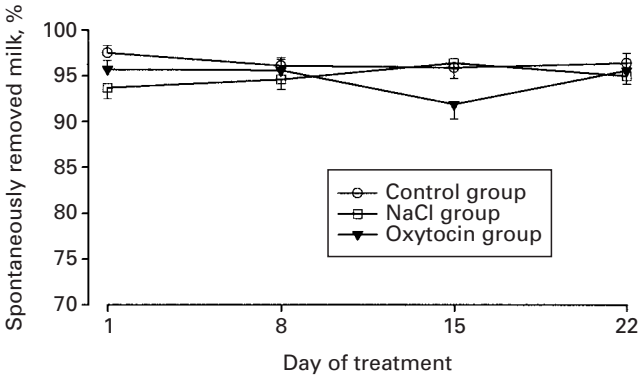

Fig. 2. Removed milk fraction (normal milking+stripping; 100%=total milk yield including residual milk) after pre-milking i.m. injection of 50 i.u. of oxytocin in all groups. Control group (circles) and NaCl group (squares) receiving oxytocin injection only before one milking on days 1, 8, 15 and 22. Oxytocin group (triangles) receiving oxytocin before each milking days 1–22. Values are means with SE for 7 animals on each treatment.

variable, as indicated by the large SEM-bars on days 7, 14 and 21 (Fig. 1). The spontaneously removed milk fraction in the oxytocin group ranged 91–98% on day 0, but 54–96%, 54–95% and 61–87% on days 7, 14 and 21, respectively.

Experiment 2

As shown in Fig. 2, the spontaneously removed milk fraction after oxytocin administration pre-milking did not significantly change on days 1, 8, 15 and 22 in control, NaCl and oxytocin groups. Means of spontaneously removed

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milk fraction were numerically slightly higher in all treatment groups on days 1, 8, 15, and 22 as compared with days 0, 7, 14, and 21 respectively (Experiment 1; Fig. 1). However, this difference was only significant ($P<0{\cdot}05$) in the oxytocin group on days 8, 15 and 22 as compared with days 7, 14 and 21; in the NaCl group on days 15 and 22 as compared with days 14 and 21; and in the control group on day 22 as compared with day 21, respectively.

Discussion

Amounts of milk secreted, i.e. total milk yield including residual milk, was not altered throughout the study, although chronic oxytocin treatment is reported to increase milk yield in several studies (Ballou et al. 1993; Knight, 1994). The slightly improved udder evacuation due to pre-milking oxytocin injection (Experiment 2 as compared with Experiment 1), albeit expected to occur at each milking in the oxytocin group, did not cause any measurable increment of milk secretion. It has to be mentioned that the animals used in this study are routinely intensively stripped by the milker and the numerical improvement of udder evacuation by pre-milking oxytocin administration was not even significant at the start of the experiment. Pre-milking oxytocin administration may be much more effective on udder evacuation and hence may stimulate milk secretion in less intensive milking routines.

Chronic pre-milking oxytocin treatment reduced the spontaneously removed milk fraction within one week, if oxytocin administration was omitted. The suspected addiction to exogenous oxytocin was obvious. However, spontaneous milk ejection in some individuals was almost not reduced until the end of experiment whereas, in other cows, only half of the stored milk could be removed without oxytocin administration. Two possible reasons for the reduced spontaneous milk ejection are apparent: reduced release of oxytocin from the pituitary or reduced sensitivity to oxytocin in the udder, possibly due to down-regulation of an oxytocin receptor. Additional work focusing on oxytocin release and mammary gland sensitivity to oxytocin is therefore in progress.

Chronic injection of NaCl as a placebo did not reduce spontaneous milk ejection. Behavioural changes prior to milking were not only observed in the oxytocin group but also in the NaCl group. On the other hand, this had no negative effect on spontaneous milk ejection during the course of subsequent milking. An inhibition of milk ejection as a consequence of the injection procedure at each milking with only a placebo injected was therefore excluded.

Pre-milking oxytocin administration increased the spontaneous milk fraction numerically, in part even significantly in all groups. The response to pre-milking oxytocin remained unchanged in all groups during the entire experimental period. Chronic oxytocin injection before milking obviously did not cause a desensitization to this treatment. In contrast, a 5-d continuous infusion of oxytocin caused reduced milk yields during the treatment and post-treatment periods (Graf et al. 1973), possibly owing to a desensitization of oxytocin receptors. Owing to the short half-life of oxytocin of only few minutes (Bruckmaier et al. 1994), plasma concentrations of oxytocin in this study probably hovered around baseline level during most of the day, with elevated values only within an hour of injection.

Even after pre-milking oxytocin administration, however, there was still residual milk left which was removed after i.v. injection of 10 i.u. oxytocin. Injection of 50 i.u. oxytocin i.m. was shown to cause variable plasma concentrations of oxytocin in the upper physiological range during milking (J Macuhova, V Tancin, RM Bruckmaier, unpublished observation). Despite a threshold level of oxytocin to be surmounted during milking for maximum milk ejection (Schams et al. 1984; Bruckmaier et al. 1994), continuously very high oxytocin levels can obviously slightly improve the efficacy of milk ejection and the percentage of spontaneously removed milk during the further course of milking. However, even after i.m. oxytocin administration before milking (Experiment 2) the residual fraction was only slightly diminished. Therefore, a significant carry-over effect of partially removing residual milk by i.m. oxytocin injection in the morning on the residual fraction at evening test milkings was not very likely.

Recovery of milk removal, i.e. spontaneously removed milk fraction, from chronic oxytocin treatment occurred unexpectedly fast and was already complete 2 d after the end of treatment (data not shown). Despite this, the voluntary entering of the parlour remained disturbed for up to one week after the end of injections.

In conclusion, administration of oxytocin for milking caused reduced milk ejection within one week of chronic treatment if oxytocin was withdrawn. Therefore, regular administration of oxytocin should be carefully planned and only be performed if udder health is endangered by large amounts of milk remaining in the udder.

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