

Effect of Reserpine on Serum Prolactin, Growth Hormone, and Glucocorticoids in Dairy Cows (39771)

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Prolactin is an important component of the hormonal milieu concerned with initiation and maintenance of lactation (1, 2). Although the mechanisms are not well understood, *in vivo* studies involving removal of various endocrine glands and/or exogenous hormone administration have indicated that hormonal control of lactation may differ among species. For the cow, prolactin initiates milk synthesis by *in vitro* cultures of mammary tissue from pregnant animals (3). However, there is a paucity of information as to the *in vivo* role of prolactin in mammary function for the dairy cow. This is due in part to the large amounts of exogenous prolactin which would be required to increase blood concentrations in the cow. Several compounds, such as prostaglandin F_{2α} and thyrotropin releasing hormone (TRH), cause transient increases in prolactin concentrations in the blood of dairy cattle (4, 5), and TRH administered twice daily will stimulate milk yield in cows (6). However, TRH also releases growth hormone and thyrotropin, hormones which are lactogenic in cattle (1); thus, a specific effect of TRH stimulating lactation via prolactin could not be tested.

Reserpine, an ester alkaloid isolated from certain species of *Rauwolfia*, causes depletion of 5-hydroxytryptamine and catecholamines from the central nervous system (7) and prolactin release from the pituitary of rats (8) and rabbits (9). This increase is presumably the reason that reserpine is mammogenic and lactogenic in estrogen-primed rats and rabbits (10, 11). Reserpine also depletes hypothalamic corticotrophic-releasing factor (12) and pituitary adrenocorticotropin (13) which increases glucocorticoid release from the adrenals of rats (14).

The major objective of our research was to examine whether reserpine increases serum prolactin concentrations in dairy cows. In addition, reserpine effects on serum growth hormone and glucocorticoids also were examined.

Materials and methods. Nonlactating, nonpregnant Holstein cows were fitted with a jugular cannula 24 hr prior to the start of each experiment. Reserpine² and saline were administered by im injection into the hip. Blood was collected via cannula at 30, 20, and 10 min preinjection and at 0.25, 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 10, 12, 24, 36, and 48 hr postinjection. Sera from each experiment were stored at -20° until assayed for prolactin (15), growth hormone (16), and total glucocorticoids (17).

In the initial experiment, cows were given 5 mg of reserpine (2 ml of Sandril; *n* = 10) or saline (2 ml; *n* = 5). Sera were assayed for prolactin, growth hormone, and glucocorticoids and data were analyzed by split plot analysis. Four cows were used in a second study. Reserpine (5 mg) was injected at time zero followed by a second 5-mg injection 48 hr later. In a third study, three cows were used in a mixed-model factorial design to compare 1 mg and 5 mg doses of reserpine.

Results and discussion. The im injection of saline had no effect on serum prolactin, but 5 mg of reserpine resulted in a dramatic increase (Fig. 1). Response to the im injection of reserpine was evident within 30 min, with serum prolactin concentrations being greater than 100 ng/ml between 0.5 and 12 hr postinjection. Peak prolactin concentration (283 ± 37 ng/ml serum; mean ± SE) occurred at 3 hr postinjection. Peak response for the 10 cows receiving reserpine

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² Sandril (2.5 mg of reserpine/ml), Eli Lilly and Co., Indianapolis, Ind. 46200.

ranged from 190 to 511 ng/ml. Prolactin response to the im injection in cows occurred much more rapidly than reported for rats given an ip injection of reserpine (8).

In contrast to previous reports in the rat (12, 14), im injection of 5 mg of reserpine did not alter the serum concentration of either growth hormone or glucocorticoids in dairy cows (Fig. 2). The slightly increased concentration of serum glucocorticoids in reserpine-treated animals at 24 to 48 hr after injection was due to unexplained high concentrations noted in one animal. Moreover, growth hormone and glucocorticoid concentrations in both reserpine- and saline-treated animals were similar to previously reported values for dairy cows (4, 5, 17).

A second study was conducted to determine whether the sustained release of pro-

lactin caused by the reserpine injection would alter the response of the hypothalamic-pituitary axis to a second injection. No alteration was evident in prolactin response curves in the four cows given sequential doses of 5 mg of reserpine (Fig. 3). The area under the curve for the second injection was $100.7 \pm 1.9\%$ (mean \pm SE) of the first injection. Similar responses of prolactin to repeated injections of prostaglandin $F_{2\alpha}$ in cattle have been reported (5). Thus, it may be possible to sustain elevated prolactin concentrations in sera over several days.

A 5-mg injection gave a substantially greater response in serum prolactin than that obtained with the same animals given 1 mg of reserpine (Fig. 4). Cows given the 5-mg dose reached a peak prolactin concentration of 276 ng/ml at 2 hr postinjection

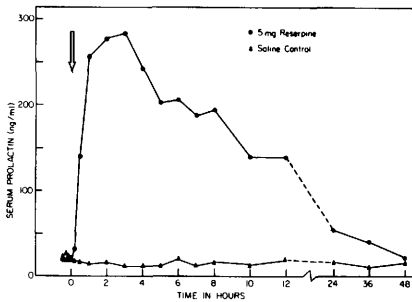


FIG. 1. Serum prolactin concentrations following injection of 5 mg of reserpine ($n = 10$) or saline ($n = 5$) in nonlactating, nonpregnant cows. Arrow indicates time of im injection (2-ml vol). The average standard error for the postinjection samples was 23 and 3 ng/ml for the reserpine and saline groups, respectively.

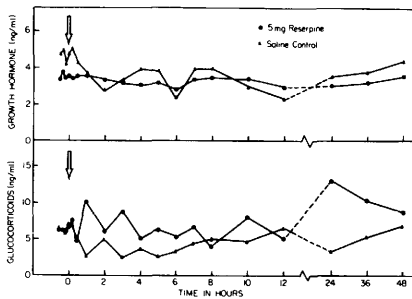


FIG. 2. Serum concentrations of growth hormone and glucocorticoids following injection of 5 mg of reserpine or saline in nonlactating, nonpregnant cows. Arrow indicates time of im injection, and animals are those in Fig. 1. There were no detectable differences between saline and reserpine treatments for either hormone ($P > 0.10$).

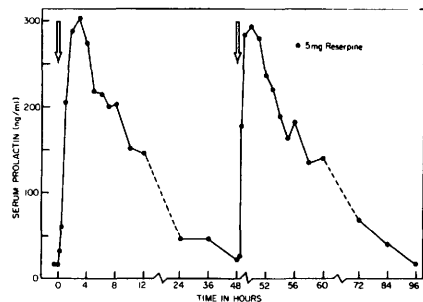


FIG. 3. Serum prolactin concentrations following sequential injections of 5 mg of reserpine in nonlactating, nonpregnant cows. Arrow indicates time of im injection for the four cows. There were no detectable differences between the first and second injections in peak prolactin concentration or area under the curve for prolactin response ($P > 0.10$).

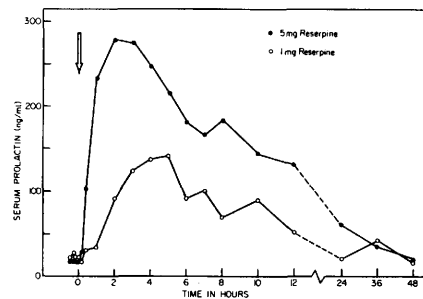


FIG. 4. Serum prolactin concentrations following injection of 1 and 5 mg of reserpine in nonlactating, nonpregnant cows. Arrow indicates time of im injection for the three cows. Peak prolactin concentration and area under the prolactin response curve differed between the 1 and 5 mg doses ($P < 0.01$).

versus a peak level of 140 ng/ml at 5 hr postinjection for cows given the 1-mg reserpine injection. Using preinjection levels of prolactin as a baseline, the area under the prolactin response curve for the 1-mg injection was only 39.5% of the area obtained with the 5-mg dose. This limited comparison indicated that reserpine causes a dose-dependent increase in serum prolactin. A larger dose of reserpine was not examined because the 5-mg injection gave the moderate tranquilizing symptoms characteristic of this compound.

Marked species differences exist in the amount of reserpine required to obtain a prolactin response. The 5-mg injection, which increases serum prolactin more than 10-fold in cows (Figs. 1, 3, and 4), amounts to 7 to 8 μ g of reserpine/kg body weight. In rats, an ip injection of 10 mg of reserpine/kg body weight increases serum prolactin levels from 51 (pretreatment) to 281 ng/ml (4 hr postinjection) (8). This species difference in responsiveness also is apparent in lactogenic response. In estrogen-primed rats and rabbits, the injection of 0.5 to 1.0 mg of reserpine/kg body weight induces lactation as judged by the histological appearance of the mammary tissue (10, 11, 18). Recently we demonstrated that four injections of 5 mg of reserpine (7 to 8 μ g of reserpine/kg body weight) markedly improves lactational performance of nonpregnant cows induced into lactation with an estrogen-progesterone treatment (19).

The present study extends to cattle, the observation that reserpine causes an elevation of serum prolactin for at least 24 hr (Figs. 1, 3, and 4). This prolactin response in dairy cows to a single injection of reserpine lasted much longer than the response obtained with an im injection of either prostaglandin $F_{2\alpha}$ (5) or thyrotropin-releasing hormone (4). Furthermore, reserpine did not alter serum levels of growth hormone or glucocorticoids (Fig. 2). Thus, the lactogenic hormone responses to reserpine may be more specific in cattle than the responses obtained with exogenous TRH or prostaglandin $F_{2\alpha}$ which have been shown to release growth hormone and glucocorticoids (4, 5). In addition, the peak serum prolactin concentration obtained with a 5-mg reser-

pine injection was similar to the peak occurring in dairy cows immediately prior to parturition (1).

Our results indicate that reserpine can potentially be used for *in vivo* studies designed to delineate the role of prolactin in dairy cows. However, reserpine is a tranquilizer drug and possible effects of reserpine on feed intake and animal behavior need to be considered in the design of such studies.

Summary. Nonlactating, nonpregnant Holstein cows were used to examine the effects of an im injection of reserpine. A 5-mg reserpine injection resulted in a rapid (within 0.5 hr) and sustained (at least 24 hr) elevation of serum prolactin. Peak prolactin levels (283 ng/ml) occurred 3 hr postinjection. Serum glucocorticoid and growth hormone concentrations were unaffected by reserpine injection. Two sequential injections of 5 mg of reserpine given at 48-hr intervals gave nearly identical prolactin responses. The prolactin response to reserpine was dose dependent with 1 mg giving approximately 39.5% of the response obtained with 5 mg of reserpine.

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