BRIEF REPORT

BROMOCRIPTINE SUPPRESSES POSTPARTUM EXACERBATION OF COLLAGEN-INDUCED ARTHRITIS

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We administered bromocriptine (Parlodel) to arthritic mice immediately postpartum, and found that the drug suppressed the clinical exacerbation of joint involvement that was seen in untreated animals. Approximately 50% reduction in severity of disease was achieved with bromocriptine ($P < 0.001$). The effect may be due to suppression of the prolactin release that normally occurs postpartum.

Immunization of susceptible strains of mice with heterologous type II collagen leads to a disease which causes pathologic changes in the joints that are similar to those that occur in humans with rheumatoid arthritis (1). We have shown that in DBA/1 mice, there is a remission of this disease during gestation and an exacerbation after parturition (2). Parturition is associated with many hormonal changes, one of the more significant of which is a decrease in the circulating levels of progesterone. The resulting increase in prolactin levels may be involved in the postpartum exacerbation of symptoms of collagen-induced arthritis.

Bromocriptine, a dopaminergic-receptor stimulant, is prescribed for the control of hyperprolactinemia in cases of hypogonadism and/or galactorrhea, and for the suppression of puerperal lactation. We tested its effect in mice with collagen-induced arthritis after they had given birth.

MATERIALS AND METHODS

Nine-week-old female DBA/1 mice (Olac, Bicester, UK) were injected intradermally with 100 μg of bovine type II collagen in Freund's complete adjuvant. An intraperitoneal injection of 100 μg of type II collagen in 0.1*M* acetic acid was administered 3 weeks later (2). Syngeneic matings resulted in pregnancies 4–8 weeks after the primary immunizations.

At parturition, the mice were randomly assigned to either the treatment group or the control group (12 animals per group). The treatment group was given daily subcutaneous injections of 0.1 mg (approximately 5 mg/kg of body weight) of bromocriptine (Parlodel; Sandoz, Middlesex, England) dissolved in ethanol:water (100 μl), 1:1 volume/volume, over 5 days, commencing on the day the mice gave birth. Mice in the control group received 100 μl of the ethanol:water vehicle only.

The severity of arthritis was assessed in individual mice by use of a clinical scoring system (0–4 per limb; maximum score 16) (2).

RESULTS

The mean clinical scores in both groups of mice with collagen-induced arthritis are presented in Figure 1. There was an increase in the mean clinical scores in both groups of mice after parturition. However, in the mice given bromocriptine injections, the increased

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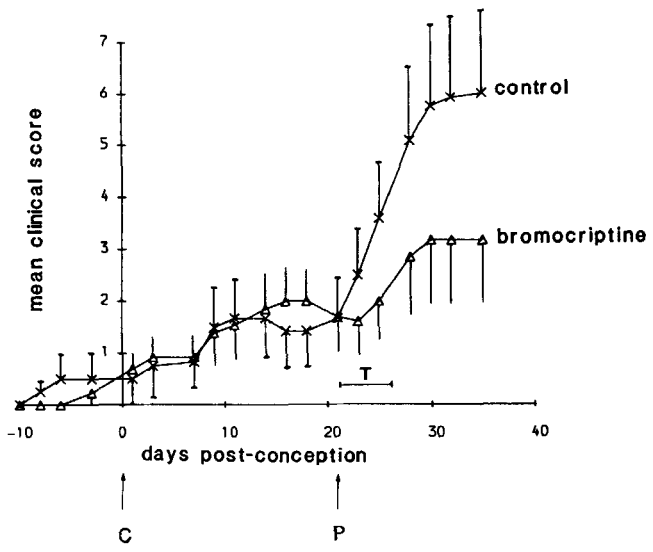

Figure 1. Progression of collagen-induced arthritis in bromocriptine-treated and control mice (n = 12 in each group) before, during, and after pregnancy. Primary immunization with type II collagen in Freund's complete adjuvant was done 4–8 weeks before conception (C). Mice were given bromocriptine or 50% ethanol daily for 5 days following parturition (P). Results are expressed as the mean and SEM clinical score, by number of days postconception. T = treatment period.

clinical involvement was less marked after the treatment period. The final severity index in the treated animals was approximately 50% of that in the control animals. This difference was statistically significant ($P < 0.001$ by Student's t-test).

DISCUSSION

T lymphocytes are known to be involved in the pathogenesis of collagen-induced arthritis (3). It is possible that the ability of T lymphocytes to respond to antigenic stimulation may be modified by prolactin (4). In addition, it has been shown that bromocriptine suppresses inflammation in animals with adjuvant-induced arthritis and that the administration of prolactin reverses this effect (5). Recently, bromocriptine has been used successfully to treat 35 patients with psoriatic arthritis (6).

We do not know if sustained use of bromocriptine would maintain remission of collagen-induced arthritis, but therapy with bromocriptine has been used for months, and even years, in patients with galactorrhea, infertility, and pituitary adenomas (7). We postulate that the diurnal pattern of prolactin release, with the highest levels occurring during nocturnal sleep, may contribute to the symptoms of morning stiffness in patients with arthritis.

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