Effect of Estrogen Antibodies on Pregnancy in the Rat

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Key words

Estradiol
Estriol
Antibodies
Pregnancy

Abstract

Treatment of pregnant rats with small amounts of non-specific estrogen antibodies did not inhibit pregnancy but increased the percent males in the litter. Administration of specific antibodies to estradiol immediately following mating prevented pregnancy in all animals, while administration at mid-pregnancy caused only some reduction in the number of pregnant animals. Administration of specific estriol antibody had no effect following mating but caused nearly total resorption of fetuses at mid gestation.

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Antibodies to estriol and estradiol were produced in two different ways. Estradiol chlorocarbonate was linked to bovine serum albumin and injected into a group of rabbits over a period of several months. The antibodies isolated were found to be relatively nonspecific, having a cross-reaction with estrone and estriol varying from 30 to 100%. Specific antibodies were produced by linking 6-ketoestriol and 6-ketoestradiol via the oxime at C β to bovine serum albumin, and injecting a series of rabbits. Following isolation of the antibodies, and using the indirect method of assay described by Abraham, cross-reaction with related estrogens varied from < 1 % to 3%.

The different antibodies were then used to study their effects on implantation, on the sex distribution of the offspring, and on the progress of pregnancy in the rat.

Nonspecific estradiol antibodies (cross-reactivity of 30% with estriol), when injected in doses up to 10 mg for four days after mating, had little significant effect on the rate of pregnancy, or the size of the litter. It did, however, have a marked effect on the sex distribution of the offspring in that there were 65% males produced. Mating of the offspring from this experiment reestablished a sex ratio of 1:1.

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In another series of experiments, specific antibodies to estradiol and to estriol, produced through the 6-keto oxime derivative, were administered for four days post coitum in one series of animals. Another group of rats were treated similarly on days 11–14 of pregnancy. Estriol-specific antibody, when given four days post coitum, resulted in a pregnancy rate of 82%, not significantly different from normal. The average number of implants per horn varied from 4.5 to 6 which is also essentially normal. However, administration of specific antibody to estradiol

abolished all pregnancies, probably by preventing implantation which requires the effects of the estradiol surge.

In the second group of animals, specific antibody to estradiol, when given at mid-pregnancy, showed some decrease in the number of animals pregnant (50%) and most of those animals had a normal litter, all of which were born alive. Administration of the estriol-specific antibody in the same dosage, on days 11–14, virtually eliminated all existing pregnancies. Only one animal of eight bore a single live young and another animal had two stillborn.

Thus, it appears that antiestradiol, when given early in pregnancy, is capable of preventing reproduction completely, while such treatment in mid-pregnancy had markedly less effect. On the other hand, treatment with estriol-specific antibody early in pregnancy has no significant effect, but at mid-pregnancy nearly completely abolishes all pregnancies. It would appear from this information that estradiol and estriol have distinct and different roles in the early processes of reproduction and the maintenance of pregnancy, further suggesting that estriol plays a role in mammalian reproduction considerably different from that usually ascribed to it as a weak estrogen.