Effect of tamoxifen on linear growth of precocious female SD rats

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INTRODUCTION

Tamoxifen is a selective estrogen receptor modulator , which is administrated in girls with peripheral precocious puberty such as McCune-Albright syndrome.

AIM

To explore the effect of tamoxifen on the linear growth of precocious pubertal female rats.

METHOD

At 16-22 day of age, 16 precocious pubertal female rats(induced by 300 μg danazol s.c. at 5-day old), were randomized blocks (brood) to 2 groups(n=8). Group TAM received once weekly 20mg/kg tamoxifen s.c for 5 times, while Group Ctrl received solvent injections. Rats were killed 5 weeks later. Measurements of body weight and length(=nose-anus length) were taken every 3-4 days. Vaginal opening was observed from 4-week age. On the day of sacriface, body weight, body length and left tibial length were measured, plasma were taken for determining E2 level, IGF-1 (IRMA) and IGFBP-3 (IRMA) concentrations; liver samples were taken for detecting GHRmRNA、IGF-1mRNA and IGFBP-3mRNA by real-time RT-PCR; right tibia were fixed, demineralized and processed for paraffin-embedding. Paraffin sections were HE stained for growth plate measurements. IGF-1 and IGF-1R level on growth plate were immunohistochemical localized and image analysed.

RESULTS

1. Skeletal growth: Tamoxifen decreases both of the body weight and body length without influencing the tibial length.
2. Growth plate HE measurement: Tamoxifen increases the width of PZ[(185.0±12.7μm)VS (172.5±61.0μm), P<0.05], decrease the width of HZ[(167.5±37.0μm) VS (188.3±33.7μm), P<0.05] and cell number[(7.2±1.0) VS (8.9±0.6),P<0.05] in HZ without changing total EGP width[358.1±45.0 VS (373.3±35.7μm),P<0.05].
3. Plasma concentration determination: Tamoxifen does not alter plasma E2 level, decreases plasma IGFBP-3 level （443.8±65.5 ng/ml versus 537.7±94.1 ng/ml, P<0.05）. Tamoxifen does not alter hepatic GHRmRNA, IGF-1mRNA or IGFBP-3mRNA, and does not alter local IGF-1and IGF-1R level on growth plate.

CONCLUSIONS

Tamoxifen inhibited growth, especially weight gain and fat accumulation. Besides, tamoxifen has dual effects of anti-estrogen and estrogen-like on the growth plate. So tamoxifen is inapplicable for central precocious puberty treatment. The safety of tamoxifen for peripheral precocious puberty needs to be reevaluated.

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