Effects of GnRH agonists and antagonists on Danazol-induced precocious puberty rats

Aram Yang, Rimm Huh, Jinsup Kim, Sung Yoon Cho, Dong-Kyu Jin

Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

OBJECTIVES

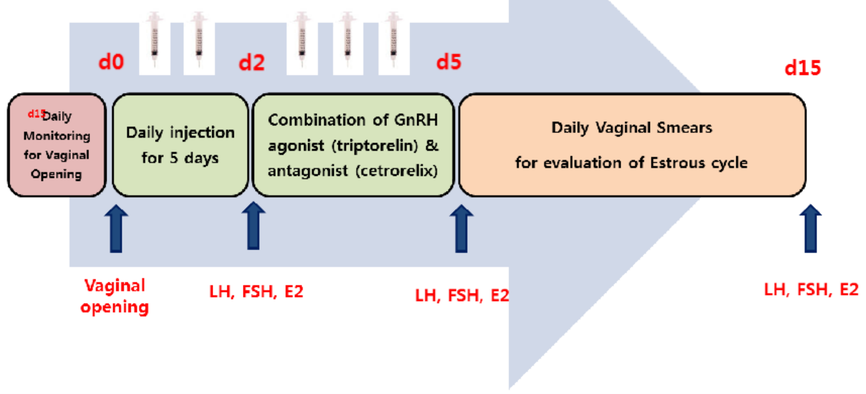
Gonadotropin releasing hormone (GnRH) agonists are a common treatment modality for patients with central precocious puberty.

For investigation of short term & long term effects of GnRH agonists & antagonists on rats with precocious puberty, danazol-induced precocious puberty rats were used as an animal model to compare the effects of GnRH analogues and to assess combinations of treatment with agonistic and antagonistic GnRH analogues.

METHODS

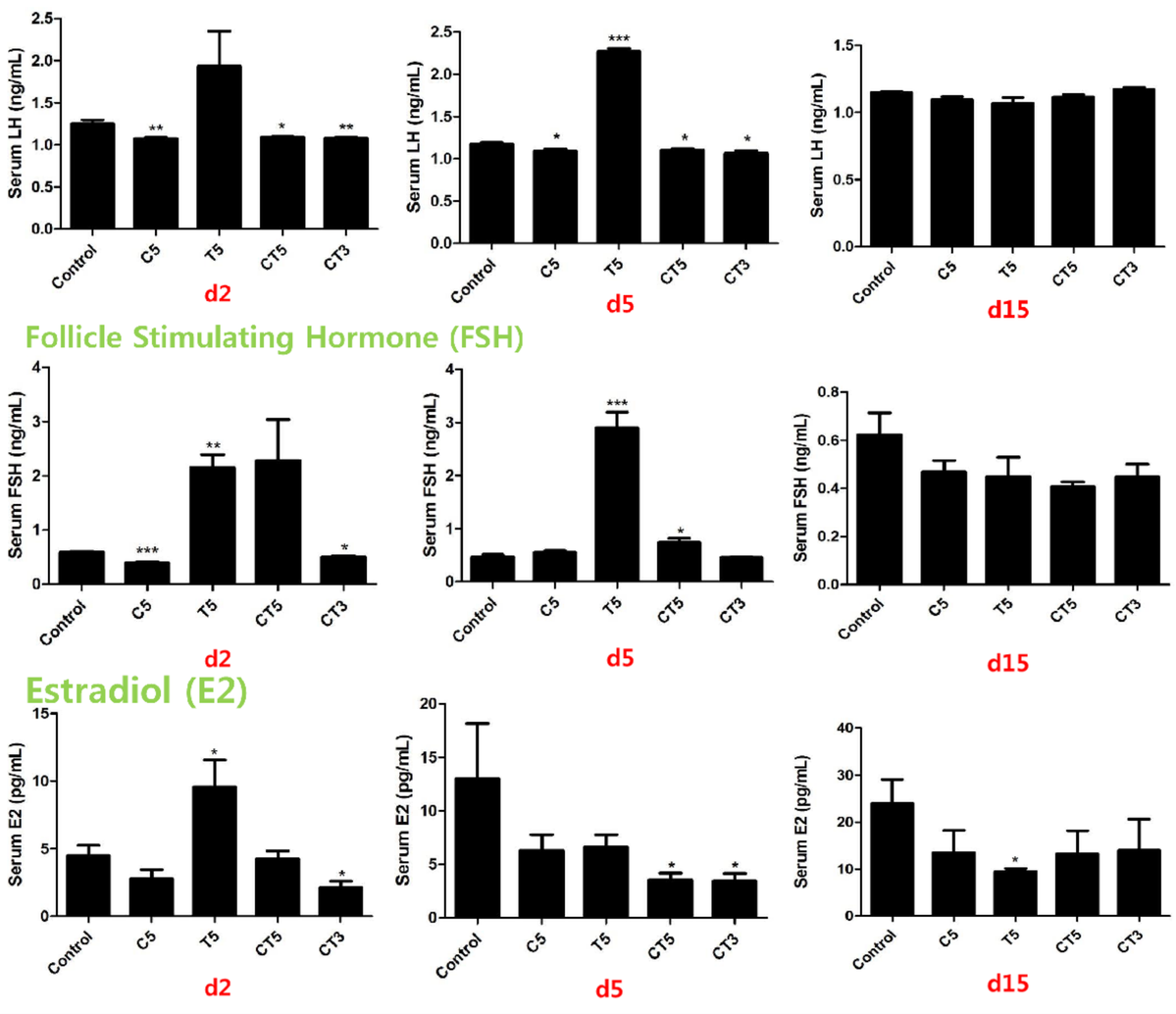
5-d-old female Sprague-Dawley rats were subcutaneously injected with a single dose of 300 ㎍ danazol. After vaginal opening, the rats were injected daily for 5 days with a combination of GnRH agonists (triptorelin) and antagonists (cetrorelix acetate). Serum levels of LH and FSH were obtained on d2, d5 and d15 of treatment.

Female Sprague-Dawley rats (5 days of age)
→ SC injected with a **single dose of 300 ㎍ danazol**

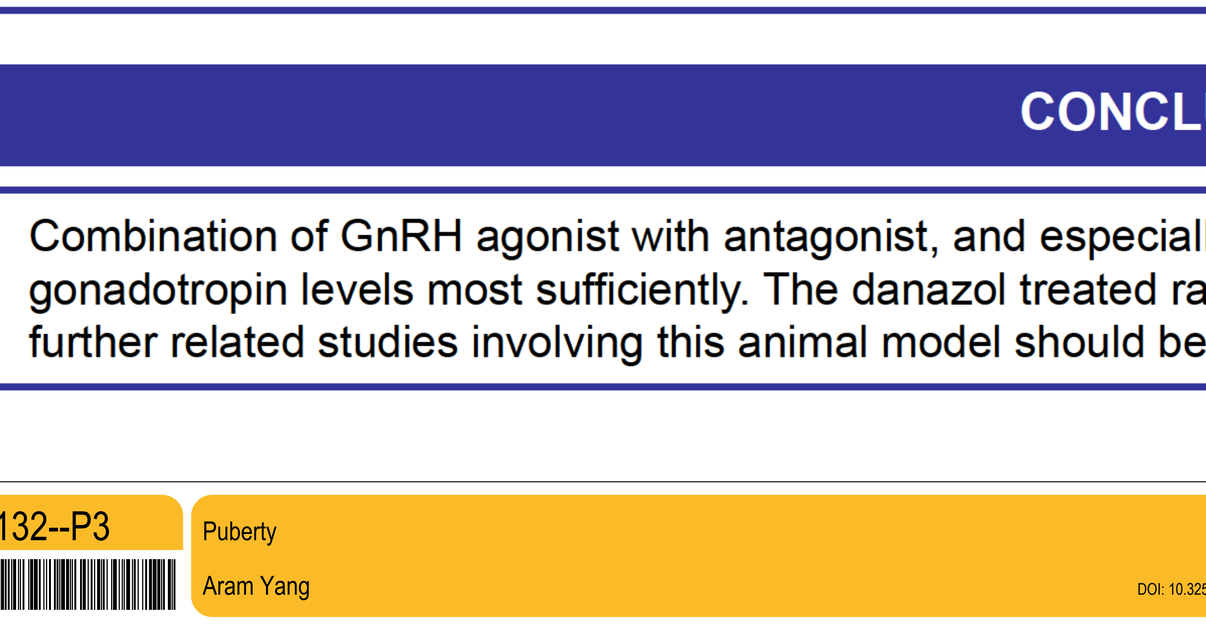


Group	Treatment	Dose
Control	Vehicle	-
C5	Cetrorelix acetate	30㎍/d, 5d
T5	Triptorelin	30㎍/d, 5d
CT5	Cetrorelix acetate + Triptorelin	each drug, 30㎍/d, 5d
CT3	Cetrorelix acetate + Triptorelin	C 30㎍/d 5d, combination with T 30㎍/d for 3d

Luteinizing Hormone (LH)



Follicle Stimulating Hormone (FSH)



Estradiol (E2)

RESULTS

Rats treated with danazol showed significant advancement in vaginal opening compared with wild type rats(p= 0.000, respectively). LH and FSH inhibition was strongest after 2-d treatment with antagonist alone (LH 1.07 ±0.04 versus 1.25 ± 0.08 ng/mL in controls, p = 0.004; FSH 0.39±0.03 versus 0.55 ± 0.09 ng/mL in controls, p = 0.006). Antagonist for 2-d followed with combined agonist/antagonist had the second lowest levels of LH and FSH, though not statistically significant (after 5-d treatment, LH 1.09 ± 0.05 versus 1.17 ± 0.04 ng/mL in controls, p = 0.33; FSH 0.46 ± 0.04 versus 0.47 ± 0.07 ng/mL in controls, p = 0.7). Agonist only group showed significant increase of LH and FSH after 5-d of treatment (LH 2.27 ± 0.08 versus 1.17 ± 0.04 ng/mL in controls, p < 0.0001; FSH 2.91 ± 0.65 versus 0.47 ± 0.07 ng/mL in controls, p = 0.0008)

CONCLUSIONS

Combination of GnRH agonist with antagonist, and especially treatment with antagonist alone seems to suppress gonadotropin levels most sufficiently. The danazol treated rat model proved to be a model of true precocious puberty; further related studies involving this animal model should be considered.

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Aram Yang
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