COMPARISON OF DEPRESSIVE-LIKE SYMPTOMS AND SEXUAL BEHAVIOR IN RAT MODEL TREATED WITH ANTI-ANDROGEN (BICALUTAMIDE VS. GOSERELIN) AND SURGICAL CASTRATION

Hypothesis / aims of study
Androgen-deprivation treatment, termed as chemical castration, has been used as the supportive measure in addition to psychotherapy for treatment of sex offenders. Chemical castration using luteinizing hormone-releasing hormone (LHRH) agonists and anti-androgens is alternative method to the surgical castration. Goserelin and bicalutamide are drugs used for chemical castration. Goserelin is a synthetic long-acting agonist of gonadotropin-releasing hormone (GnRH), and it is used for the treatment of malignant neoplasms of the prostate, uterine fibromas, and metastatic breast cancer. Bicalutamide is an inhibitor of the androgen receptor, and it is used for the treatment of advanced prostate cancer. These drugs produce similar effects as surgical castration. LHRH agonists have a number of deleterious adverse events, such as the loss of libido, erectile dysfunction, depression, and osteoporosis, as well as decreased erections and reduced sexual desire. So, we investigated the effects of anti-androgen (Goserelin and Bicalutamide) and surgical castration on depressive-like symptoms and sexual behavior in rat model treated with anti-androgen.

Study design, materials and methods
A total of 40 adult male Sprague-Dawley rat weighing 300 ± 10 g was used. The animals were randomly assigned to the following four groups (n = 10 in each group); Group 1: transscrotal sham-operated, Group 2: transscrotal orchietomized, Group 3: subcutaneous goserelin (goserelin acetate 3.6 mg housed in a 5-mm-long × 1-mm-wide biodegradable cylinder) injected once every 4 weeks (total 12 weeks), Group 4: oral bicalutamide (10 mg/kg daily for 12 wks) administrated, respectively. Total testosterone levels were checked and the modalities of analyses included forced swimming test, open field test, sexual behavioral test, and immunohistochemistry, western blot.

Results
Complete suppression of total testosterone was observed through goserelin and and orchietomy. In the forced swimming test, the rats in the goserelin injected group, bicalutamide administrated group and orchietomized group showed significantly higher time of immobility, lower number of climbing and swimming, decreased 5-HT, TPH, 5-HT1A expressions in the dorsal raphe nuclei, but bicalutamide administrated group not showed suppressive effect on the sexual behaviors compared to the rats in the control group (P < 0.05).

Interpretation of results
In this study, chemical castration and surgical castration showed depression-like and serotonin depletion in the dorsal raphe nuclei.

Concluding message
We revealed that chemical castration and surgical castration can exert depression-like symptoms.

References

Disclosures
Funding: None Clinical Trial: No Subjects: ANIMAL Species: Rat Ethics Committee: This study was performed in accordance with the guidelines of the National Institutes of Health and the Korean Academy of Medical Sciences (Seoul, Korea), and approved by Kangbuk Samsung Hospital Institutional Animal Care and Use Committee (Seoul, Korea).