thyroid hormones, which are cleaved out by various processing enzymes from the modified tyrosine residues of the Tg molecule. Although Tg is currently recognized as no more than a scaffold protein for thyroid hormone synthesis, our group has shown that Tg stimulates the proliferation of rat thyroid follicular FRTL-5 cells via PI3K pathway. The signaling pathways underlying various functions of thyroid cells have been extensively investigated but some discrepancies still exist, depending on the experimental model systems and the types of cells used. Recently, our group discovered that Tg may directly regulate the synthesis of thyroid hormones in thyroid cells. In this study, we performed suspension culture of porcine thyroid cells and aimed to elucidate the mechanism of the effect of Tg on thyroid cells. Porcine thyroid epithelial cells were prepared from thyroid gland by enzymatic digestion and cultured in monolayer or in suspension culture. Various concentrations of Tg were added to the medium and cultured for several days. Then, the conditioned medium was collected and the amount of thyroid hormone was measured by reversed phase chromatography; the cells were harvested and mRNA levels of hormone-processing enzymes, cathepsin B, K, L and dipeptidyl peptidase I, II (DPP I, II), were measured by quantitative PCR. The amount and activation of cell signaling molecules were also evaluated by western blotting. Tg stimulated the secretion of thyroid hormone, thyroxine, from porcine thyroid cells in suspension culture, however, no stimulation by Tg was observed in monolayer culture. The expression of mRNAs of cathepsin B, K and L were reduced and that of DPP II was increased by the treatment of Tg in suspension culture. Tg increased the amount of NF-κB p52 and Rel B dose dependently. On the other hand, TSH had little effects on the amount of these proteins. Tg and TSH both activated PDK1 and MAPK p44/42 but not Akt. These results suggest that Tg regulates thyroid hormone synthesis in totally different way from TSH by altering the expression levels of hormone-processing enzymes in thyroid cells. This stimulatory effect might be mediated by NF-κB signaling pathway, whereas the proliferative effect of Tg under these conditions might be exerted via MAPK signaling pathway. The detailed mechanisms of these effects of Tg on thyroid cells are under investigation.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

Acceptability of Oral 11β-Methyl-19-Nortestosterone Dodecylcarbonate (11β-MNTDC) as a Potential Hormonal Male Contraceptive Pill: Results From a Randomized, Placebo-Controlled Trial

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***Background*:** Injectable hormonal male contraceptives (HMC) injectables appear safe and are effective in clinical trials, but global surveys suggest men would prefer an oral pill. 11β-methyl-19-nortestosterone dodecylcarbonate (11β-MNTDC) is orally bioavailable and well-tolerated. When taken daily with food for 28 days, the drug decreases serum gonadotropins and testosterone without significant impact on mood. If ongoing studies demonstrate that daily 11β-MNTDC consistently suppresses spermatogenesis to <1 million/mL in healthy men, oral 11β-MNTDC could be an effective HMC pill. Surveys of participant satisfaction and method acceptability for promising HMC pill prototypes, like oral 11β-MNTDC, are needed.

Objective: To determine satisfaction with and acceptability of a daily oral 11β-MNTDC HMC pill

***Study Design*:** In a double-blind, randomized, placebo-controlled trial of a 28-day regimen of daily oral 11β-MNTDC at two academic medical centers, healthy male volunteers completed baseline and end-of-treatment surveys assessing their experience, satisfaction with, and willingness to use daily oral 11β-MNTDC.

***Results*:** Of 42 participants, 40 (30 11β-MNTDC, 10 placebo) completed end-of-treatment surveys. Respondents were primarily college-educated, sexually active white men between 21-40 years old. Less than 20% of participants cited initial concerns about safety and missing doses. Following treatment, nearly 90% of participants affirmed that taking the pill was easy to remember and did not interfere with their daily routine. Although one-third (37% 11β-MNTDC vs. 20% placebo, p=0.45) reported bothersome side effects, and 28% (30% 11β-MNTDC vs. 20% placebo, p=0.66) reported potential concerns about safety, these rates were neither statistically different in those taking active drug versus placebo nor associated with method satisfaction. The majority of participants reported satisfaction with the method (73% 11β-MNTDC vs. 70% placebo, p=0.84), that they would recommend it to others (90% 11β-MNTDC vs. 100% placebo, p=0.56), and that they would use the drug regimen as their primary contraceptive even if having to pay (67% 11β-MNTDC vs. 50% placebo, p=0.35). Half of participants (50% 11β-MNTDC vs. 67% placebo, p=0.51) affirmed that the method exceeded initial expectations. Respondents who reported being more likely to miss a dose were also more likely to report dissatisfaction with the study drug (p=0.03).

***Conclusion*:** The majority of participants in a 28-day trial of daily, oral 11β-MNTDC pills were satisfied with the regimen, would recommend the drug to others, and would pay to use the drug even when adverse or off-target effects (e.g. changes in libido and/or mood) were considered. If 11β-MNTDC is demonstrated to suppress spermatogenesis uniformly to very low levels, it would be acceptable to men desiring reversible contraception.