and assessed the intrinsic electrophysiological properties as well as synaptic transmission of AVP^{PVN} neurons using whole-cell patch-clamp.

Results: We observed increased number of AVP neurons in SON, SCN, and PVN in BPA treated group compared with the control group. Lower spontaneous action potentials the frequency was found in the BPA group compared to the control group, demonstrating disruption in AVP biophysical properties. Current clamp experiments also showed that BPA treated AVP^{PVN} neurons were less responsive to current injections than control AVP^{PVN} neurons, including fewer neuronal spikes, delayed latency to the first spike, and less responsive overall were observed in the BPA group. Spontaneous excitatory postsynaptic currents frequency but not amplitude was also altered by BPA gestational exposure, while no significant changes were found for spontaneous inhibitory post-synaptic currents.

Conclusion: Collectively, our results suggest that gestational BPA expose might disturb hypothalamic AVP circuits, as indicated by increased AVP neurons in hypothalamic nuclei and disrupted excitability and synaptic transmission of/onto AVP neurons.

Endocrine Disruption

ENDOCRINE DISRUPTING COMPOUNDS: MECHANISMS OF ACTION AND CLINICAL IMPLICATIONS

Efficacy and Safety of TLANDO, A Novel Oral Easy to Prescribe and Use TRT Option

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Most widely used testosterone replacement therapy (TRT) products can be inconvenient and cumbersome topical and invasive injectable requiring dose adjustments to attain efficacy. In a pivotal study, a recently approved oral TRT only 26% of patients did not require any dose adjustment. Typically, patients start on a sub-therapeutic dose with gradual dose increases to attain efficacy resulting in additional visit(s) to clinic and pharmacy. Physician research data (N=402) suggested it typically takes 3-6 months of titrations to reach an efficacious dose for majority of patients, a significant barrier in effecting a switch without a period of "efficacy gap". The requirement of additional visit(s) presents significant challenges for new and current patients desiring to start and to switch to a convenient TRT option, especially in the current COVID-19 pandemic. Recent reports suggest increase of disease severity/mortality in men with low testosterone is possibly due to underlying co-morbidities commonly associated with male hypogonadism. There remains a need for an effective, safe, and easy to use and prescribe product that does not require dose titration. TLANDO is a "triglyceride-free" oral single strength TRT with single dose designed to lymphatically deliver effective and safe levels of testosterone regardless of meal fat content. Moreover, dose titration is prone to some inherent titration decision errors and requires understanding of often complex titration rules. The objective is to assess whether TLANDO, an oral TRT without requiring dose titration, safely restores effective testosterone (T) levels in hypogonadal men. An open-label, single-arm, multicenter study (NCT03242590) was performed with TLANDO in hypogonadal males (N=95). Subjects received orally 225 mg twice a day testosterone undecanoate (TU) for 24 days without dose adjustment. Efficacy was evaluated by % of subjects who achieved daily T Cavg within the eugonadal range. Using 450mg daily dose without dose adjustment, 80% of subjects (95% CI of 72% to 88%) achieved a T Cavg in the normal range and safely restored with mean T Cavg of 476±184 ng/dL post steady state. T restoration was comparable to other non-oral TRT products. TLANDO was well tolerated with no deaths, no drug-related severe AEs, and no hepatic AEs. In conclusion, effective T restoration using TLANDO, an easy to use and prescribe oral TRT option, was confirmed. Minimal AEs were reported with no hepatic AEs. Upon approval, TLANDO will be the first convenient TRT option without requiring dose adjustments; therefore, enabling selection of an efficacious dose from the start of therapy. TLANDO is well suited for new or existing TRT patients desiring a convenient oral option.

Endocrine Disruption

ENDOCRINE DISRUPTING COMPOUNDS: MECHANISMS OF ACTION AND CLINICAL IMPLICATIONS

Estrogen Activity of OTC Topical Medications Containing Parabens Depends on Paraben Type and Concentration

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Methylparaben, ethylparaben, and propylparaben are widely used as preservatives in food, cosmetics, and pharmaceutical products. Parabens are also known to bind the estrogen receptor and induce weak estrogen activity in laboratory bioassays. Many OTC topical medications contain one or more parabens as preservative ingredients. In this study, we surveyed the estrogen activity of extracts from OTC topical medications and tested the hypothesis that a combined threshold concentration of particular parabens is required to induce estrogen activity in human breast cancer cell bioassays. Ethanol extracts (1 gm:1 ml) were prepared from OTC topical medications containing parabens (including: Olay Quench Lotion, CeraVe Daily Moisturizing Lotion and Cortizon-10 Lotion). The estrogen agonist and antagonist activity of each extract was determined using the T47dkbluc estrogen reporter