Sexual dimorphism in airway responsiveness to sex hormones in rabbits

Vassiliki Kouloumenta,1,2 Apostolia Hatziefthimiou,1 Efrosyni Paraskeva,1 Konstantinos Gourgoulianis,2 and Paschalis Adam Molyvdas1

Departments of 1Physiology and 2Respiratory Medicine, Medical School, University of Thessaly, Larissa, Greece

TO THE EDITOR: Recently, Massaro and Massaro (4) demonstrated a sexual dimorphism of alveolar size in male and female adult rats and mice and that estrogen receptor (ER)-α and ER-β are required for this sexual dimorphism.

Our group recently showed that a similar phenomenon of sexual dimorphism presents in airway responsiveness to sex hormones in rabbits. We studied the direct effect of sex hormones (testosterone and 17β-estradiol) on airway smooth muscle (ASM) at rest and precontracted with acetylcholine or carbachol. Testosterone induced a concentration-dependent (10^{-12} \text{ M} \text{ to} \text{ 10}^{-4} \text{ M}) contraction of ASM at rest and a concentration-dependent (10^{-12} \text{ M} \text{ to} \text{ 10}^{-4} \text{ M}) relaxation of ASM precontracted with 10^{-5} \text{ M} acetylcholine or carbachol (3). This action of testosterone was observed only in male rabbits, whereas testosterone had no effect in female rabbits. Mechanical removal of the airway epithelium abolished significantly ($P < 0.05$) the relaxing effect of testosterone (10^{-7} \text{ M} \text{ to} \text{ 10}^{-4} \text{ M}). In contrast to testosterone, 17β-estradiol had an epithelium-independent relaxing effect on ASM from male rabbits precontracted with acetylcholine, only in the concentration of 10^{-6} \text{ M} ($P = 0.005$). Similar results have been obtained in a previous study demonstrating that in male rabbits, β-estradiol caused an epithelial-independent relaxation of tracheal muscle strips precontracted with either acetylcholine or KCl (5). Indirect immunofluorescence with an anti-human androgen receptor (AR) monoclonal antibody revealed that ASM cells express AR. However, in culture of epithelium-intact ASM, the presence of testosterone (10^{-8} \text{ M} \text{ or} \text{ 10}^{-4} \text{ M}) for 24 or 48 h did not alter their responsiveness to acetylcholine. Besides, the testosterone effect was not influenced by the presence of the specific AR antagonist flutamide or the inhibitor of DNA transcription actinomycin D in the perfusing medium.

Nevertheless, there are not many studies in airways. There are studies on vessels suggesting this phenomenon of sexual dimorphism. Many clinical and epidemiological studies show a bigger frequency of cardiovascular diseases in men than in pre-menopause women (1), whereas studies in rabbits demonstrated a different effect of testosterone in male and female animals in the development of athiromatic plaque (2).

The results above suggest that in our experiments, sexual dimorphism was not due to classic steroid receptors. It remains to be investigated whether the action of testosterone on rabbit trachea is mediated by nonclassic membrane receptors that also exist in tracheal smooth muscle cells.

REFERENCES