Concern has been raised over increased male reproductive disorders in the Western world, and the disruption of male endocrinology has been suggested to play a central role. Several studies have shown that mild analgesics exposure during fetal life is associated with antiandrogenic effects and congenital malformations, but the effects on the adult man remain largely unknown. Through a clinical trial with young men exposed to ibuprofen, we show that the analgesic resulted in the clinical condition named "compensated hypogonadism," a condition prevalent among elderly men and associated with reproductive and physical disorders. In the men, luteinizing hormone (LH) and ibuprofen plasma levels were positively correlated, and the testosterone/LH ratio decreased. Using adult testis explants exposed or not exposed to ibuprofen, we demonstrate that the endocrine capabilities from testicular Leydig and Sertoli cells, including testosterone production, were suppressed through transcriptional repression. This effect was also observed in a human steroidogenic cell line. Our data demonstrate that ibuprofen alters the endocrine system via selective transcriptional repression in the human testes, thereby inducing compensated hypogonadism.
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