Journal of Andrology, Vol 18, Issue 4 352-358, Copyright © 1997 by The American Society of Andrology

JOURNAL ARTICLE

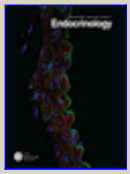
Pharmacokinetics of 7 alpha-methyl-19-nortestosterone in men and cynomolgus monkeys

N. Kumar, J. Suvisaari, Y. Y. Tsong, C. Aguillaume, C. W. Bardin, P. Lahteenmaki and K. Sundaram

Center for Biomedical Research, Population Council, New York, New York 10021, USA.

Testosterone and its esters are widely used for androgen replacement therapy. In the prostate, testosterone ins 5 alpha-reduced to dihydrotestosterone (DHT), which leads to an amplification of its stimulatory activity in this and other tissues that have significant 5 alpha-reductase activity. While this amplification is essential during fetal development, it has potentially undesirable consequences during adult life. 7 alpha-Methyl-19-nortestosterone (MENT) is a potent synthetic androgen that does not undergo 5 alpha reduction and is therefore being investigated for long-term clinical use because it is expected to be less stimulatory to the prostate. Since we anticipate using MENT acetate (MENT Ac) rather than MENT as the form of this androgen in humans, the bioavailability of MENT following the administration of MENT and MENT Ac was investigated in cynomolgus monkeys. Equimolar concentrations of MENT or MENT Ac were administered as a continuous subcutaneous infusion via Alzet osmotic pumps. Serum MENT levels were measured by radioimmunoassay (RIA) in blood samples collected daily for 4 days during steady state. The serum MENT levels were not significantly different in the two groups (11.3 +/- 1.6 vs. 13.1 +/- 1.2 nmol/L). This suggested that MENT Ac was rapidly converted to MENT in circulation. The hydrolysis of MENT Ac to MENT was confirmed by the in vitro incubation of MENT Ac with blood or plasma and the demonstration of MENT in products following separation by high-performance liquid chromatography (HPLC). Following the demonstration of the safety of MENT Ac in subchronic toxicity studies in rats and rabbits, a pharmacokinetic study was performed in men. In normal men, a single intravenous bolus of 500 micrograms of MENT led to peak serum MENT levels at 3 minutes after dosing (when the first samples were collected), followed by an exponential decline, reaching undetectable levels by 180 minutes. The average terminal half-life and the metabolic clearance rate (MCR) were calculated to be 40 minutes and 2,360 L/day, respectively. The results of the pharmacokinetic studies show that in both men and monkeys, the MCR of MENT is much faster than the values reported for testosterone. The faster MCR can be attributed, in part, to the finding that, in contrast to testosterone, MENT showed no binding to sex hormone binding globulin (SHBG).

This article has been cited by other articles:



Endocrinology HOME

B. J. Attardi, S. A. Hild, and J. R. Reel
Dimethandrolone Undecanoate: A New Potent Orally Active Androgen with Progestational Activity
Endocrinology, June 1, 2006; 147(6): 3016 - 3026.
[Abstract] [Full Text] [PDF]

THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM HOME

S. von Eckardstein, G. Noe, V. Brache, E. Nieschlag, H. Croxatto, F. Alvarez, A. Moo-Young, I. Sivin, N. Kumar, M. Small, *et al.*
A Clinical Trial of 7{alpha}-Methyl-19-Nortestosterone Implants for Possible Use as a Long-Acting Contraceptive for Men
J. Clin. Endocrinol. Metab., November 1, 2003; 88(11): 5232 - 5239.
[Abstract] [Full Text] [PDF]

THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM HOME

R. A. Anderson, A. M. Wallace, N. Sattar, N. Kumar, and K. Sundaram
Evidence for Tissue Selectivity of the Synthetic Androgen 7{alpha}-Methyl-19-Nortestosterone in Hypogonadal Men
J. Clin. Endocrinol. Metab., June 1, 2003; 88(6): 2784 - 2793.
[Abstract] [Full Text] [PDF]

ENDOCRINE REVIEWS HOME

R. A. Anderson and D. T. Baird
Male Contraception
Endocr. Rev., December 1, 2002; 23(6): 735 - 762.
[Abstract] [Full Text] [PDF]

THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM HOME

R. A. Anderson, C. W. Martin, A. W. C. Kung, D. Everington, T. C. Pun, K. C. B. Tan, J. Bancroft, K. Sundaram, A. J. Moo-Young, and D. T. Baird
7{alpha}-Methyl-19-Nortestosterone Maintains Sexual Behavior and Mood in Hypogonadal Men
J. Clin. Endocrinol. Metab., October 1, 1999; 84(10): 3556 - 3562.
[Abstract] [Full Text] [PDF]

HUMAN REPRODUCTION HOME

G. Noe, J. Suvisaari, C. Martin, A.J. Moo-Young, K. Sundaram, S.I. Saleh, E. Quintero, H.B. Croxatto, and P. Lahteenmaki
Gonadotrophin and testosterone suppression by 7{alpha}-methyl-19-nortestosterone acetate administered by subdermal implant to healthy men
Hum. Reprod., September 1, 1999; 14(9): 2200 - 2206.
[Abstract] [Full Text] [PDF]
