

**EFFECT OF SYSTEMIC ADMINISTRATION OF TWO GLUCOCORTICOIDS ON THE DIURNAL VARIATION OF THE URINARY LEVELS OF CORTICOSTEROIDS, ANDROGENS AND ESTROGENS.**

**Mazzarino M.**, 3° anno di corso del Dottorato di Ricerca in Farmacologia, Farmacognosia e Tossicologia XV ciclo. Durata del Corso in anni: 3. Sede di servizio: Università degli Studi "La Sapienza" P.le Aldo Moro, 5 00185 ROMA.

Glucocorticoids are a wide class of biologically active steroids endowed with several pharmacological effects, including alteration of carbohydrates, proteins and lipids metabolism. Unlike other steroid classes, glucocorticoids receptors are distributed in various organs and tissues [1].

Apart from their use for the pharmacological treatment of various pathologies and/or diseases, glucocorticosteroids, especially when administered systemically, are illicitly used for the non-physiological enhancement of sport performance. Glucocorticosteroids are indeed abused by some athletes and are therefore included in the list of doping substances and methods.

The goal of the present work is to verify whether the systemic administration of glucocorticosteroids can affect the urinary steroid profile, and especially the levels of corticosteroids, androgens, estrogens and their metabolites.

Two different corticosteroids (Triamcinolone; Betamethasone - oral administration 1-2mg/day), selected among the most widely used, have been studied. Experiments have been carried out on healthy, adult volunteers (blanc group) and on patients with pathologies and/or diseases treated with corticosteroids (treated group). Both group are from both sexes and various ages. Baseline circadian variability of the endogenous steroid profile [2-5] was assessed in the blanc group, and in the treated group, before and after pharmacological treatments, by collecting urine samples for male and female separately. Urine samples were collected for two months, five times per day every two days for women and four time per day twice in a week for men.

The determination of the urinary levels of corticosteroids, estrogens and androgenic steroids was carried out by a specifically developed analytical technique based on the combination of gas chromatography with mass spectrometry detection (GC-MS) [2,3,6]. Briefly, the GC-MS analysis of tetramethylsilyl (TMS) derivatives was carried out following pretreatment (pre-purification on C18 cartridges; enzymatic hydrolysis by beta-glucuronidase, liquid-liquid extraction and derivatization by TMSJ) of an aliquot of 3 ml of urine; the injected volume of the derivatized extract was 1 µL. Data obtained on the urines of the treated (patients) group were evaluated taking into account the baseline individual variability, and compared with values obtained on the blanc group.

The results confirmed significant differences in the steroids metabolites excretion profiles between men and women. The circadian variability of the steroid profile is the same for both sexes, showing a maximum during the morning. After treatment with betamethasone the profile of corticosteroids and androgens and their metabolites significantly decreased.

### References

1. Hardman J.G Limbird L. (Eds). Goodman & Gilman's. *The pharmacological basis of therapeutics*. X Edizione., Mc Graw-Hill, N.Y.
2. M. Donike, H.Geyer, A Gotzmann and Mareck-Engelke. *Stability of steroid profiles (2)*; Proceeding of the 11<sup>th</sup> Cologne Workshop on Dope Analysis 7<sup>th</sup> to 12<sup>th</sup> March 1993; pag. 85-90
3. M. Donike, H.Geyer, A Gotzmann and Mareck-Engelke. *Stability of steroid profiles (4)*; Proceeding of the 12<sup>th</sup> Cologne Workshop on Dope Analysis 10<sup>th</sup> to 15<sup>th</sup> April 1994; pag. 135-156
4. Lee S.H., Nam S.Y., Chung B.C. *Altered profile of endogeneous steroids in the urine of patients with prolactinoma*. *Clinical Biochemistry* (1998), 31:529-539
5. Cooke B.A., King R.J.B., van der Molen H.J. (Eds.): *Hormones and their Actions. Part I. New Comprehensive Biochemistry*. Elsevier (1988) Vol. 18A, 3-38; 197-215.
6. Honour J.W. *Urinary steroid profile analysis*. *Clinica Chimica Acta* (2001), 313: 45-50.
7. Ayotte C., Goudreault D., Charlebois A. *Testing for natural and synthetic anabolic agents in human urine*. *J. Chromatography B* (1996), 687: 3-2550.