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(54) METHODS OF TREATING ANDROGEN DEFICIENCY IN MEN USING CLOMIPHENE

VERFAHREN ZUR BEHANDLUNG VON ANDROGENDEFIZIENZ IM MÄNNER MIT CLOMIPHEN

METHODES DE TRAITEMENT D'UNE CARENCE ANDROGENIQUE CHEZ DES HOMMES AU MOYEN DU CLOMIFÈNE

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Description

Background of the invention.

[0001] The invention relates to the new use of CLOMIPHENE for the production of a pharmaceutical agent for treating a disorder related to male menopause in men.

[0002] In men, increasing age leads to a reduction of testicular androgen production and androgen concentration in the organism. In contrast to the situation in women, in whom estrogen production drops to castration values within a comparatively short period, this takes decades in men and involves a gradual drop. The total concentration of testosterone in the serum in the older age group is significantly reduced compared to the values in young men. Because of the increase in steroid hormone-binding globulin (SHBG) that coincides with the aging process, moreover, the proportion of free, unbound, and thus biologically active testosterone drops. In addition, the serum levels of estrogens, although they are produced from androgens by direct conversion, do not drop in the same way as a function of age. As a result, the hormonal environment is significantly altered.

[0003] In men, the hormonal environment is characterized by a significant preponderance of androgens over estrogens. While the circulating main component of androgens, testosterone, is detected in the serum in units in the range of nmol/l, the estrogen antagonist, estradiol, can be measured only in the range of pmol/l. This considerable preponderance of androgen can be detected basically in the entire late puberty period of life , but there is a clearly different intensity of this androgen dominance as a function of age. With increasing age and particularly as in those over the age of 60, there is a less pronounced emphasis of the androgen preponderance.

[0004] In older men there are relative decreases in the preponderance of testosterone by 30-50% compared to the previous values found in young men.

[0005] The relative testosterone deficiency per se can be regarded as responsible for a number of age-related disorders. Reduction of muscle mass accompanied by limitation of body performance capacity, reduction of bone density and in individual cases even osteoporosis, an increase in prostate size referred to as benign prostatic hyperplasia, reduction of libido and potency, and psycho-vegetative disorders such as depression and a decline in cognitive functions, which are disorders that are often generically referred to as Male Menopause and are caused by relative androgen deficiency in men. Libido is the desire to obtain an erection, while potency is the ability to have that erection.

[0006] It is known that in younger men, testosterone values are also effectively increased by daily treatment with antiestrogens to treat male infertility. Treatment of Male Infertility, Springer-Verlag Berlin, Heidelberg, New York 1982; Fuse, H. et al., Archives of Andrology 31 (1993) 139-145; Nonsurgical Treatment of Male Infertility, Jarow, J. Infertility in the Male, pp.410-422. However, it has been thought that antiestrogens do not seem well suited for treatment of a relative androgen deficiency in men. Thus, for example, US Patent 5.861.389 proposes the use of at least one aromatase inhibitor for the production of a pharmaceutical agent for treating a relative androgen deficiency in men.

Summary of the invention.

[0007] The object of the present invention is to treat the specific disorders related to male menopause by the use of clomiphene according to claim 1. The disorders preferably comprise reduction of libido, reduction of potency.

[0008] The use of clomiphene in treating a relative androgen deficiency in older men results surprisingly in a long-term increase in the androgen level.

[0009] By gradually stimulating the body to produce testosterone, the clomiphene results in an endogenic rebalancing of the testosterone/estrogen ratio in men. As a result, the relative androgen deficiency is compensated for.

[0010] For the purposes of this invention, clomiphene is the compound that competes with estrogen for estrogen-receptor-binding sites and may delay replenishment of intracellular estrogen receptors.

[0011] Suitable, for example, is clomiphene citrate which is 2[p-(2-chloro-1,2-diphenylvinyl) phenoxy] triethylamine citrate (1:1). It has the molecular formula C2-6H2 8ClNO·C6H8O7 and a molecular weight of 598.09 and is sold under the trademark Clomid.

[0012] A pharmaceutically effective dosage of clomiphene is administered in older men for an effective time period, preferably continuously. For example, a dose of 10-25 mg of clomid daily or every other day and up to 100 mg is administred to obtain the mid-normal levels. Measuring the serum concentration of testosterone and estradiol can thus give early indication of whether the desired hormone balance was achieved and optionally whether dose adjustment can be undertaken.

[0013] In general, 5 to 1000 mg, preferably 10 to 100 mg clomiphene citrate is used daily or every other day to treat a relative androgen deficiency in men.

[0014] Clomiphene can be administered, e.g., orally, parenterally or transdermally by a patch for example.

[0015] For the preferred oral administration, suitable means are especially tablets, coated tablets, capsules, pills, suspensions, or solutions that can be produced in a way that is commonly used and familiar to one skilled in the art, with the additives and vehicles that are commonly used for formulations that are to be administered orally.

[0016] The pharmaceutical agent that is produced according to the invention contains an active ingredient per dosage unit of clomiphene at a daily or every other day dosage of 5-100 mg in addition to the commonly used additives, vehicles and/or diluents or other antiestrogens at biologically equieffective dosages.

[0017] When clomiphene is used for treating male menopause, the estrogen concentration is effectively lowered. The easy controllability of the treatment distinguishes treatment with an antiestrogen.

[0018] Clomiphene citrate tablets is a mixture of two geometric isomers [cis (zuclomiphene) and trans (enclomiphene)] containing between 30% and 50% of the cis-isomer. A standard commercially available tablet contains 50 mg clomiphene citrate and the following inactive ingredients: corn starch, lactose, magnesium stearate, pregelatinized corn starch, and sucrose. The current tablets are used primarily for treating female infertility. Treatment according to the present invention contemplates a redosing to accommodate the lower dosages specified herein.

[0019] It is also contemplated that combinations of antiestrogens with clomiphene can be administered or combinations with other testosterone producing drugs can be used.

Claims

1. Use of clomiphene or clomiphene citrate in the preparation of a pharmaceutical composition for treating a disorder related to male menopause in men, wherein said disorder is selected from the group of reduction of libido and reduction of potency.

2. The use according to claim 1, wherein the disorder is reduction of libido.

3. The use according to claim 1, wherein the disorder is reduction of potency.

Patentansprüche

1. Verwendung von Clomiphen oder Clomiphen Citrat zur Herstellung eines pharmazeutischen Präparats zur Behandlung einer Störung im Zusammenhang mit der Menopause bei Männern, wobei diese Störung eine solche aus der Gruppe Verminderung der Libido und Verminderung der Potenz ist.

2. Verwendung nach Anspruch 1, wobei die Störung eine Verminderung der Libido ist.

3. Verwendung nach Anspruch 1, wobei die Störung eine Verminderung der Potenz ist.

Revendications

1. Utilisation de Clomiphene ou Clomiphene citrate pour la préparation d'une composition pharmaceutique pour la traitement d'une dérangement en connection avec la menopause d'homme, cette dérangement est de la groupe de carence de libido et carence de puissance.

2. Utilisation à revendication 1 cette dérangement est la carence de libido.

3. Utilisation à revendication 1 cette dérangement est la carence de puissance.

REFERENCES CITED IN THE DESCRIPTION

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