Use of Androgens in Postmenopausal Women

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Abstract
During menopause, women may experience greater loss of bone mineral density, leading to a high risk of fractures. Estradiol has great importance in the maintenance of bone microarchitecture and estradiol and testosterone combination have high effectiveness in preventing osteoporosis and fractures in postmenopausal women. There is an actual trend of using testosterone combined with estradiol in order to improve the hypo androgen symptoms with an important improvement in the quality of life of these women. The behavior of the lipid profile in women using this combination is not well defined once the results of the studies already made are very controversial. This review article aims at evaluating the studies made in the last years that evaluated the impact of the use of androgens in postmenopausal women over a bone mineral density and the lipid profile. Searches of articles were made on Pubmed from 1980 to 2011. The searches were made with the use of the keywords ‘testosterone’ or ‘androgens’ and ‘postmenopausal women’ and ‘bone density’ and ‘hormone replacement therapy’. In its second phase the ‘testosterone’ or ‘androgens’ and ‘postmenopausal women’ and ‘lipoprotein’ and ‘hormone replacement’. A total of 67 articles were found. After reading their whole content, 09 original articles were included in this review, prospective that evaluated bone mineral density or the lipid profile in patients using hormone therapy in postmenopause. The benefits of the use of androgens have been demonstrated in publications resulting from studies with a reduced number of patients, in non-probabilistic samples, and most of them observational. On the other hand, the results converge towards an improvement of the lipid profile and increase in the bone mineral density in the patients in post-menopause. The greater limitation of these results lies on the difficulty on determining the isolated effects of the androgens once the studies showed results obtained through HT with estradiol and androgens. Clinical rehearsals in comparison between the use of isolated estradiol and estradiol + testosterone shall clarify the impact of this combination under the lipid profile and bone protection in postmenopausal patients.

Keywords: Testosterone; Postmenopausal women; Lipoprotein; Hormone replacement therapy; Androgens; Bone mineral density

Introduction
Due to the increase in number of women who survive on average one-third of their lives after menopause, osteoporosis has become a condition of high cost to society. During menopause, women may experience greater loss of bone mineral density, leading to a high risk of fractures and their consequences for patients in this stage of life. Estradiol (E) has great importance in the maintenance of bone microarchitecture and E and testosterone (T) combination have high effectiveness in preventing osteoporosis and fractures in postmenopausal women [1].

Women at menacme have a natural protection against cardiovascular diseases [2-5]. Until the middle of the last decade, hormone therapy (HT) was indicated for cardiovascular protection and many observational studies showed an improvement in the lipid profile and reduction in cardiovascular risks among users of HT [6-9].

In the last decade studies suggest that HT in post-menopause with a combined scheme of estrogen and progestogen not only does not show any protection against cardiovascular diseases, but also seems to promote the increase on the risk of acute myocardial infarction and cerebrovascular accident [10-12]. Whereas some studies show that menopause causes a worsening in the lipid profile of women, the use of E combined with progesterone has shown a worsening in the lipid profile with an increase in the LDL cholesterol (LDL) and...
in the cardiovascular risk [13, 14]. There is an actual trend of using T combined with E in order to improve the hypo androgen symptoms with an important improvement in the quality of life of these women [15-18]. Studies have already shown that this combination offers endometrial protection, without the use of progestogens needed [19]. The behavior of the lipid profile in women using the combination E and T is not well defined once the results of the studies already made are very controversial [20-25].

Subjects and Methods

Objectives

This review article aims at evaluating the studies made in the last years that evaluated the impact of the use of androgens in HT on women in post menopause over a bone mineral density and the lipid profile.

Review methods

In July, 2011 searches were made on Pubmed and the articles searched were the one published between 1980 and 2011. The searches were made with the use of the keywords ‘testosterone’ and ‘postmenopausal women’ and ‘bone density’ and ‘hormone replacement therapy’ and 12 articles were found. The search was made exchanging the term ‘testosterone’ for ‘androgens’ and 19 more articles were found.

In its second phase the ‘testosterone’ and ‘postmenopausal women’ and ‘lipoprotein’ and ‘hormone replacement therapy’ were used and 14 articles were found. The search was made exchanging the term ‘testosterone’ for ‘androgens’ and 22 more articles were found.

Review Results

A total of 67 articles were found. There were 25 duplicated articles and those were excluded. From these results after reading the title, 19 articles, which did not deal with postmenopausal patients using HT, were excluded. 02 articles were the result of studies in vitro with the use of sexual hormones. 09 were review articles. 03 dealt with sexual steroid analysis in men and women. 01 study was about rheumatoid arthritis in the post menopause. 01 article talked about obesity and the sexual hormones. 01 article evaluated the action of HT upon the hippocampus and 01 article was about the action of hormones on the cerebral vessels. 01 article evaluated the risk of breast cancer while using HT.

After reading the abstract the 23 remaining articles, 09 were excluded for not dealing with articles evaluating HT in postmenopausal women. 03 articles evaluated the risk of diabetes and resistance to insulin in postmenopausal women. 03 articles evaluated the use of non-hormonal therapy in post menopause. And 03 others dealt with the use of Raloxifeno, smoking and bone density and aromatase in patients in post menopause.

Among the 14 remaining articles, after reading their whole content, 09 original articles were included in this review, prospective that evaluated bone mineral density or the lipid profile in patients using hormone therapy in post menopause.

Discussion

The benefits over bones were demonstrated in some recent studies with the increase of bone mineral density among users of the combination E + T [26, 27]. The use of T seems to increase even more the bone mineral density in relation to the isolated use of E [28, 29].

Britto, et al studied 61 Brazilian patients in prospective cohort study using implants of E and T. BMD assessment through Dual energy X-ray absorptiometry showed addition of 1.87% in the lumbar spine and 3.8% in the neck of femur BMD in women using implants, and decrease in BMD lumbar of 5.92%, and 5.06% in the neck of femur, without implants, after 1 year [1].

In a study taken in London with 364 women in post menopause, Garnett et al showed difference in the digital radiography of 1123 grams of hydroxyapatite (gHa/cm²) in the group treated with 75 mg of E and 100 mg of endodermic T versus 0.951 gHa/cm² in the control group [26].

Studd et al studied 213 patients using E implants of E (75 mg) and T (100 mg) and showed an increase of 8.3% and 2.8% in bone density and lumbar spine and femoral neck after 1 year [27].

Davis et al showed that use of T potentialized the effects of E on bone density in prospective study of 2 years with 34 Australian women in post menopause using implants of 50 mg of E or E + T (50 mg). A bone densitometry (DEXA) was carried out with an increase of 10% and 8.8% in bone density in the femur and lumbar spine (L1-L4) in the group using E + T, compared to 2.4% and 3.5 % in the group using isolated E [29].

Savvas et al studying 20 Londoner women using oral E in post menopause, inserted implants of E + T in 10 patients and observed an increase of 5.7% of bone density in lumbar spine and 5.2% in femoral neck of these women, through the bone mineral densitometry (DEXA) after 1 year. In women who kept using oral isolated E there were no changes in bone density [28].

Castelo-Branco et al studied 120 patients in Barcelona, Spain, using the E valerate 4 mg and 200 mg of intramuscular enanthate of dihydroepiandrosterone month and after 1 year an increase of 16.9% was found in the total cholesterol (TC), 8% in the LDL, 6.5% in the triglycerides (TG) and
reduction of 2.7% in HDL cholesterol (HDL) [30].

Zang, H. et al published a Swidish study taken on 63 patients, followed for 3 months using E valerate 2 mg/day or valerate E 2 mg/day + T undecanoate 40 mg/day. They showed that TG did not suffer any change in any of the groups, whereas HDL suffered reduction in both users of E and T and increase in the users of only E [20].

Farish et al studying 14 oophorectomized women treated with 50 mg implants of E and T (50 and 100 mg respectively) during 6 months showed that the LDL reduced in both groups and LDL did not suffer modifications in the group E and T [31].

Sity six surgically menopausal women were followed during two years in Aalatte, U.S.A. by Watts et al. The group that used oral estrogen and metiltestosterone (2.5 mg/day) had TC, HDL and TG reduced significantly [32].

The benefits of the use of androgens have been demonstrated in publications resulting from studies with a reduced number of patients, in non-probabilistic samples, and most of them observational. On the other hand, the results converge towards an improvement of the lipid profile and increase in the bone mineral density in the patients in post menopause. The greater limitation of these results lies on the difficulty on determining the isolated effects of the androgens once the studies showed results obtained through HT with E and androgens. Clinical rehearsals in comparison between the use of isolated E and E + T shall clarify the impact of this combination under the lipid profile and bone protection in postmenopausal patients.

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