

## Rapid Communication

# The Effect of Nandrolone Decanoate on Bone Mineral Density, Muscle Mass, and Hemoglobin Levels in Elderly Women With Osteoporosis: A Double-Blind, Randomized, Placebo-Controlled Clinical Trial

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**Methods.** In a randomized, double-blind, placebo-controlled clinical trial, we evaluated the effect of a 2-year treatment with nandrolone decanoate (ND) on bone mineral density (BMD) of lumbar spine, femoral neck, and trochanter and on vertebral fracture rate, muscle mass, and hemoglobin levels. Sixty-five osteoporotic women older than 70 years were studied. Thirty-two patients received injections of 50 mg ND, and 33 received placebos every 3 weeks. All patients received 500 mg calcium tablets daily.

**Results.** Compared to baseline, ND increased the BMD of the lumbar spine ( $3.4\% \pm 6.0$  and  $3.7\% \pm 7.4$ ;  $p < .05$ ) and femoral neck ( $4.1\% \pm 7.3$  and  $4.7\% \pm 8.0$ ;  $p < .05$ ) after 1 and 2 years, respectively. The BMD of trochanter increased significantly only after the first year ( $4.8\% \pm 9.3$ ,  $p < .05$ ). Compared to the placebo group, the ND group presented with significantly increased BMD of the trochanter and neck. ND significantly reduced incidence of new vertebral fractures (21% vs 43% in the placebo group;  $p < .05$ ). ND showed a significant statistical increase in lean body mass after the first ( $6.2\% \pm 5.8$ ;  $p < .01$ ) and second years ( $11.9\% \pm 29.2$ ;  $p < .01$ ). In addition, a 2-year treatment with ND significantly increased hemoglobin levels compared to baseline ( $14.3\%$ ;  $p < .01$ ) and placebo ( $p < .01$ ).

**Conclusions.** ND increased BMD, hemoglobin levels, and muscle mass, and reduced the vertebral fracture rate of elderly osteoporotic women.

THE world population is aging, and the rate is particularly significant in developing countries where the number of elderly persons is expected to increase over 9 times by 2050, from 171 million to 1.6 billion (1). Osteoporosis is highly prevalent in elderly women (2–4) and is one of the chief factors related to hip fractures, high morbidity, and mortality (5).

A number of factors are associated with the etiology of osteoporosis in elderly women: the reduction in hormone levels stimulating bone formation, such as dehydroepiandrosterone sulfate (DHEAS) (6), insulin-like growth factor type I (IGF-I) (7), growth hormone and androgens (8–12), and the reduction in muscle mass (sarcopenia).

Authors have published studies showing the anabolic effect of growth hormone (13,14), dehydroepiandrosterone (DHEA) (15), and artificial and natural androgens on bone formation and muscle mass. Nandrolone decanoate (ND), a weak androgen, has been studied since the end of the 1960s as an option of treatment for osteoporosis in women. Some studies (16–18) have associated the anabolic action of ND with the increased production of IGF-I.

Although many clinical trials, with small samples of postmenopausal osteoporotic and osteopenic women, have

demonstrated the positive action of ND on bone mineral density (BMD) of the lumbar spine (19–23); only one (24) has been able to show significant improvement in BMD of the proximal femur, with 50 mg every 4 weeks. There are no data available on the action of ND on the muscle mass of elderly women or on the proximal femur of elderly osteoporotic women with a dose of 50 mg every 3 weeks.

In our study, we evaluated the effects of 50 mg of ND every 3 weeks, over a 2-year period, on total body muscle mass; BMD of lumbar spine, neck, and trochanter of proximal femur; and vertebral fracture rates of elderly osteoporotic women 70 years old or older.

## METHODS

### Study Design

*Prospective, randomized, double-blind, placebo-controlled clinical trial.*—This study was designed to assess efficacy of ND on BMD of lumbar spine, neck, and trochanter of femur, and muscle mass. The assessment of efficacy was based only on eligible patients. Patients were considered

eligible if they received a total of 26 injections of ND during the period of study.

The primary endpoint of efficacy analyses was the increment of at least 7.5% in BMD of the neck, trochanter, or lumbar spine. The secondary endpoints were reduction of vertebral fracture rate and increased muscle mass.

Sample size was calculated for the primary outcome of this study, using the following parameters: a) increase of 7.5% in the mean BMD of femoral neck in the intervention group after 2 years, while holding mean BMD constant in the placebo group; b)  $\alpha = 0.05$  (two-sided); c) power = 0.80; d) correlation between baseline and follow-up femoral neck measures = 0.80. Estimated sample sizes were 25 for the placebo group and 25 for the ND group.

#### *Patients and Randomization*

Patients were selected from the Rheumatology and Geriatrics outpatient clinics of the Federal University of São Paulo, and were randomized into two groups. Of each group of 10 people, 5 received ND and 5 a placebo, at random. The medical board of Organon/AKZO-Nobel carried out randomization independently with a list of all studied patients prior to study start. Patients and principal investigator were blinded. The list of randomization was revealed only 2 weeks after the last patients received the injection.

Inclusion criteria were: age of 70 years or older, Caucasian race, having no difficulty walking, having no bilateral hip prosthesis, and having no disease which might limit movement. All patients had at least one bone site (lumbar spine, trochanter, or neck) with BMD equivalent to or lower than  $-2.5$  standard deviations (*SD*) at T score when compared to that of a healthy young Caucasian woman. The diagnosis of osteoporosis was based on the 1994 criteria of the World Health Organization (25).

Exclusion criteria were: determination of being mentally disabled by the Mini-Mental State Examination (for persons with 0–4 years of education, we used the threshold of 19 and below; for 5–8 years of schooling, 23 and below; for 9–12 years of schooling, 27 and below; and for college level and beyond, 29 and below); use, during the previous 6 months or at time of evaluation, of drugs that may interfere with bone remodeling (calcitonin, bisphosphonate, fluoride, growth hormone therapy, estrogens and/or progesterone therapy replacement, calciferol, calcitriol, raloxifen); having any chronic disease that might interfere with study follow-up, such as psychiatric or neurological diseases, uncontrolled hypertension, heart failure, active gastrointestinal or liver disease, recurrent renal calculi, chronic obstructive pulmonary disease, or severe osteoarthritis of hip or knees; use, during the previous 6 months or at time during evaluation, of systemic corticosteroid therapy (furosemide, phenytoin); a history of previous allergy or intolerance to ND or its excipients; having a disease that may affect bone metabolism, such as hyperparathyroidism, hyperthyroidism, hypercortisolism, chronic renal failure (serum creatinine  $> 1.5$  mg/dl), Paget's disease, lower limb paresis or plegia, anorexia nervosa, multiple myeloma and other neoplastic diseases, rheumatoid arthritis, granulomatous diseases, or gastrointestinal diseases; being bedridden for more than

3 months; smoking more than 20 cigarettes/day; alcohol consumption of more than two drinks (two shots of liquor, two glasses of wine, two beers) a day; and a history of any kind of cancer disease over the past 10 years. All patients signed a previously informed consent approved by the Medical Ethics Committee of Federal University of São Paulo.

#### *Physical Examination*

All patients underwent the same standardized physical examination, which was conducted by a physician blinded to treatment allocation. Every 3 months, patients were systematically examined for hirsutism, acne, and edema. Hoarseness was systematically evaluated by the following question: "Have you noted any change in your voice in the last 3 months?" In addition, all patients were advised to call the medical doctor if they noted hoarseness and/or hirsutism. Anthropometric measurements (weight and height) were taken every 12 months.

#### *Medications*

ND (Deca-Durabolin; Organon/AKZO-Nobel, São Paulo, Brazil) has 50 mg/ml ND in arachis oil and is pharmacologically classified as an anabolic steroid and weak androgen. The chemical name is  $17\beta[(1\text{-Oxodecyl})\text{oxy}]\text{-est-4-en-one}$  (C<sub>28</sub>H<sub>44</sub>O<sub>3</sub>). The placebo injections contained arachis oil with 10% benzyl alcohol, and were indistinguishable from the active medication supplied by Organon/AKZO-Nobel. Organon supported the placebo and ND injections. There was no interference of Organon in any part of the study.

#### *Therapeutic Plan*

Every 3 weeks, for at least 2 years, patients received 22 tablets containing 500 mg of elementary calcium for daily consumption and an intramuscular injection of 50 mg of ND or a placebo.

#### *Imaging Examinations*

*Thoracic-lumbar spine X-rays.*—Using standardized procedures, X-rays of thoracic and lumbar spine were taken of all participants at baseline and after 2 years of treatment. The tube-to-film distance was 101 cm. Ideally, the X-ray beam was centered at T8 for X-rays of the thoracic spine and at L3 for those of the lumbar spine (26).

A new deformity, or radiographic vertebral fracture, was defined as a 20% decrease and 4 mm or more in any vertebral height from baseline to the end of the study, and was confirmed by a repeated measurement of the involved vertebral body (26). The vertebrae T4 to L4 were analyzed. Upon X-ray reading, osteophytes of the lumbar vertebra (L2–L4) and the presence of calcification of the abdominal aorta in the lumbar section were evaluated. Two nonradiologist medical doctors, unaware of the treatment given, were trained to read the X-rays of the vertebra. The coefficient of variation between the two readers was  $3\% \pm 1.8\%$ , as determined by independent readings of 10 participants.

**Bone densitometry.**—The participants underwent bone densitometry examination of total body, lumbar spine, femoral trochanter, and neck at baseline, after 12 months, and after 24 months. The DXA machine used was the bone densitometer with an X-ray source (DPX-L; GE/Lunar) (supplied by the Federal University of São Paulo). The coefficient of variation of the device used was: for the BMD of the lumbar spine, 2.9%; for the trochanter, 3.2%; for the neck, 1.8%. The coefficient was obtained through tests and retests of 10 participants.

**Lean body mass and total body fat.**—The lean body mass and total body fat was determined with an X-ray source (DXA machine, DPX-L) at the same time as the BMD measurements. The 2.3% coefficient of variation was obtained through tests and retests of 10 participants.

### Laboratory Examinations

At baseline, the following hematological and biochemical parameters were determined: complete blood count, total cholesterol and subfractions, glutamic-oxaloacetic transaminase (GOT) and glutamic-pyruvic transaminase (GPT), alkaline phosphatase, total calcium, protein electrophoresis, and thyroid stimulating hormone. Assessments were repeated at 12 and 24 months, except for those of thyroid stimulating hormone and protein electrophoresis.

### Statistical Analysis

The variables of this study were analyzed with the Mann-Whitney nonparametric *U* test, for comparison between groups, and with the Wilcoxon signed rank test, for comparison against the initial value within each group. A significance level of 5% was used in all the tests.

Weighted kappa was calculated using Stata Statistical software (release 7.0; Stata Corporation, College Station, TX) to compare agreement between raters. Agreement between observers at baseline and at the end of the study was, respectively, 95% and 97%. Weighted kappa calculated to compare the agreement between the readers of lumbar/thoracic spine X-ray above and beyond chance alone were 0.84 (baseline), and 0.89 (end of the study), indicating excellent reliability.

### RESULTS

Of the 154 four women initially interviewed, 89 were considered eligible, of which 65 accepted the study conditions. The main reason for nonparticipation in the study was the possibility of hirsutism and hoarseness with the use of ND. After randomization, the participants were divided into two groups, with 32 participants in the ND group and 33 in the placebo group. The groups were comparable with respect to height and weight, but participants in the placebo group were older (Table 1). At baseline, the two groups were also homogeneous regarding hematological, biochemical parameters, total body muscle mass, total body fat, and BMD of the total body and of specific skeletal sites (lumbar spine, trochanter, and femoral neck) (Table 2).

Participants in the ND group presented significantly increased BMD of the lumbar spine (L2–L4) after the first and second year ( $3.4\% \pm 6.0$  and  $3.7\% \pm 7.4$ , respectively;

Table 1. Age, Weight, Height, Laboratory, and Densitometry Characteristics of the Nandrolone Decanoate (ND) and Placebo Groups at Baseline

| Characteristic                                         | ND<br>(N = 32) | Placebo<br>(N = 33) | p Value |
|--------------------------------------------------------|----------------|---------------------|---------|
| Age, y                                                 | 74.0 ± 3.8     | 76.8 ± 4.0          | .005*   |
| Weight, kg                                             | 54.6 ± 8.0     | 56.3 ± 7.1          | .361    |
| Body mass index height, cm                             | 149.1 ± 6.2    | 149.1 ± 7.2         | .571    |
| Hemoglobin, g/dL                                       | 12.9 ± 1.2     | 12.8 ± 0.8          | .893    |
| GOT, U/L                                               | 22.5 ± 8.3     | 24.9 ± 7.0          | .133    |
| GTP, U/L                                               | 16.6 ± 6.6     | 18.0 ± 7.4          | .394    |
| A. phosphatase, U/L                                    | 177.2 ± 53.6   | 184.4 ± 46.1        | .963    |
| Creatinine, mg/dL                                      | 0.75 ± 0.21    | 0.8 ± 0.2           | .321    |
| Total cholesterol, mg/dL                               | 221.8 ± 33.6   | 226.7 ± 31.3        | .667    |
| High density lipoprotein, mg/dL                        | 51.8 ± 10.3    | 58.5 ± 12.8         | .149    |
| Low density lipoprotein, mg/dL                         | 137.6 ± 36.3   | 136.5 ± 30.4        | .984    |
| Calcium, mg/dL                                         | 9.2 ± 0.7      | 9.3 ± 0.6           | .789    |
| Bone mineral density (L2–L4), g/cm <sup>2</sup>        | 0.81 ± 0.11    | 0.8 ± 0.2           | .816    |
| Bone mineral density (trochanter), g/cm <sup>2</sup>   | 0.55 ± 0.08    | 0.5 ± 0.1           | .919    |
| Bone mineral density (femoral neck), g/cm <sup>2</sup> | 0.7 ± 0.1      | 0.6 ± 0.1           | .664    |
| Bone mineral density (total body), g/cm <sup>2</sup>   | 0.9 ± 0.1      | 0.9 ± 0.1           | .716    |
| Total body muscle mass                                 | 33.9 ± 5.1     | 34.3 ± 3.2          | .775    |
| Total body fat                                         | 17.3 ± 7.4     | 18.6 ± 5.3          | .381    |

Notes: Data are expressed in mean ± standard deviation.

\**p* < .05.

GOT = glutamic-oxaloacetic transaminase; GTP = glutamyl transpeptidase.

*p* < .05); significantly increased BMD of the trochanter only at the end of the first year ( $4.8\% \pm 9.3$ ; *p* < .05); and significantly increased BMD of the femoral neck after 1 and 2 years of treatment ( $4.1\% \pm 7.3$  and  $4.7\% \pm 8.0$ , respectively; *p* < .05) compared to baseline (Table 3). Compared to the placebo group, the participants in the ND group presented significantly increased BMD of the trochanter after 1 and 2 years and significantly increased BMD of the femoral neck after 2 years, but increased BMD of the lumbar spine was not significant during the study period (Table 2 and Figure 1A–C). No significant differences were found in total body BMD between the ND and placebo groups during the study period.

Vertebral fractures were diagnosed in 19 (67.8%) of 28 participants in the ND group at baseline, and in 12 (52.4%) of 21 participants in the placebo group. After 2 years of study, 8 participants in the placebo group presented new fractures. Three of these participants had no vertebral fractures at baseline. In the ND group, eight participants presented with new vertebral fractures. All of them had presented vertebral fractures at baseline. The number of new vertebral fractures in the placebo group was greater than that of the ND group (respectively, 16 vs 8; *p* = .028) (Table 3).

The prevalence of osteophytes was 63% in the ND group and 52.3% in the placebo group. Aorta calcification was observed in 40.7% of the ND group and in 47% of the placebo group. Approximately 30% of the participants in the ND group and 28.5% of the placebo group demonstrated both changes.

Table 2. Effects of Nandrolone Decanoate (ND) and Placebo on Bone Mineral Density (BMD)

| Site of BMD Measurement | No. of Participants and Variation in BMD (%) |             |         |              |               |            |         |             |
|-------------------------|----------------------------------------------|-------------|---------|--------------|---------------|------------|---------|-------------|
|                         | ND After                                     |             |         |              | Placebo After |            |         |             |
|                         | 1 Year                                       |             | 2 Years |              | 1 Year        |            | 2 Years |             |
|                         | N                                            | BMD         | N       | BMD          | N             | BMD        | N       | BMD         |
| L2-L4 lumbar spine      | 28                                           | 3.4 ± 6.0*  | 28      | 3.7 ± 7.4*   | 21            | 2.2 ± 7.1  | 21      | 4.3 ± 11.2  |
| Trochanter              | 28                                           | 4.8 ± 9.3*† | 28      | 3.1 ± 10.2*† | 21            | -1.4 ± 5.1 | 21      | -2.2 ± 4.3* |
| Femoral neck            | 28                                           | 4.1 ± 7.3*  | 28      | 4.7 ± 8.0*†  | 21            | 2.1 ± 7.5  | 21      | 1.2 ± 6.5   |
| Total body BMD          | 28                                           | 0.6 ± 3.0   | 28      | 0.3 ± 2.6    | 21            | 0.5 ± 2.5  | 21      | 0.8 ± 2.5   |

Notes: \**p* < .05 compared to baseline; †*p* < .05 compared to corresponding placebo group. N = number of patients.

Compared to the baseline and to placebo treatment, significant increases in muscle mass were observed after the first and second years of treatment with ND (Table 4 and Figure 2). The absolute increase of muscle mass was approximately 2 kg, per participant, per year. No changes were found in the placebo group, compared to baseline. The total body fat in the ND group had significantly decreased after 1 year, but increased after 2 years. The placebo group showed no significant change (Table 4).

The hemoglobin levels in the ND group significantly increased in both the first year (7.8%; *p* = .0007) and the second year (14%; *p* = .00002), compared to those in the placebo group and at baseline. No significant changes, compared to the baseline and the placebo, were found for GPT, GOT, alkaline phosphatase, total calcium levels, and total cholesterol.

Adverse effects were described in four participants in the ND group. All four reported hoarseness, two had soft facial hirsutism, and two of them dropped out of the study. In the placebo group, two participants developed soft hirsutism and one hoarseness; only one patient who developed hirsutism dropped out of the study. There were no reports of significant leg edema in either group. A number of participants complained of stomach discomfort due to the use of calcium tablets.

The dropout rate of the groups differed. The ND group had four participants drop out, and the placebo group had

12. Of the ND group, one participant dropped out due to hirsutism, one due to hoarseness, and two due to Paget's disease and vaginal cancer. Reasons for placebo group dropouts were lack of compliance to study (*n* = 1), long hospitalization due to sepsis (*n* = 1), development of bronchitis and use of high dose corticosteroids (*n* = 1), malaise attributed to injected medication (*n* = 1), change of address far from the medical center (*n* = 2), fear of hirsutism (*n* = 2), car accident with hip fracture (*n* = 1), husband's dissatisfaction with wife's participation (*n* = 1), hoarseness (*n* = 1), and domestic responsibilities for health support to family (*n* = 1).

DISCUSSION

This is the first prospective randomized, double-blind, placebo-controlled clinical trial showing that ND treatment (50 mg/3 weeks for 2 years) of women aged 70 or over significantly increases BMD of the lumbar spine, trochanter, and femoral neck. ND significantly reduces the fracture rates of the lumbar spine and also significantly increases muscle mass and hemoglobin levels.

To our knowledge, the favorable effects in BMD of the trochanter have never been reported before, whereas increases in BMD of the lumbar spine have been observed

Table 3. Effects of Nandrolone Decanoate (ND) or Placebo on Vertebral Fractures

|                                                                                                         | ND         |               | Placebo    |               |
|---------------------------------------------------------------------------------------------------------|------------|---------------|------------|---------------|
|                                                                                                         | Baseline   | After 2 Years | Baseline   | After 2 Years |
| No. of patients (%) with one or more vertebral fractures                                                | 19 (67.8%) | 19 (67.8%)    | 12 (52.4%) | 15 (71.4%)    |
| No. of patients without vertebral fracture at baseline (%) who developed a vertebral fracture after 2 y | —          | 0             | —          | 3 (14%)       |
| No. of vertebral fractures                                                                              | 38         | 46            | 35         | 51            |
| No. of new vertebral fractures in each group after 2 y                                                  | —          | 8             | —          | 16*           |

Note: \**p* < .05, Wilcoxon paired test.

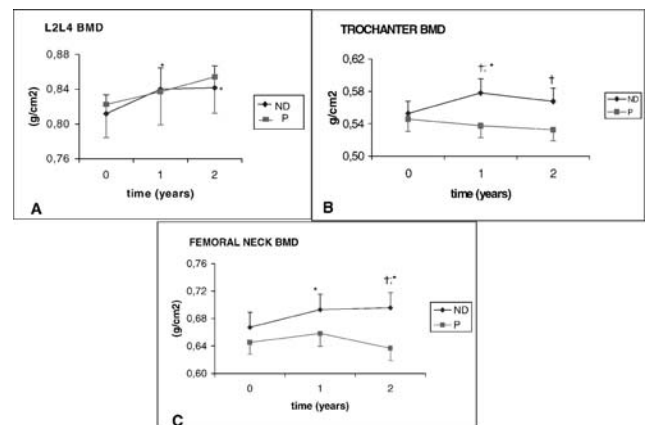


Figure 1. Effect of nandrolone decanoate (ND) or placebo (P) on lumbar spine (L2-L4) bone mineral density (BMD) (g/cm<sup>2</sup>) (A), femoral neck BMD (g/cm<sup>2</sup>) (B), and over trochanter BMD (g/cm<sup>2</sup>) (C) after 1 and 2 years of treatment, compared to baseline and between the groups. Data are expressed in mean ± standard deviation. \**p* < .05 compared to baseline; †*p* < .05 compared to corresponding placebo group.

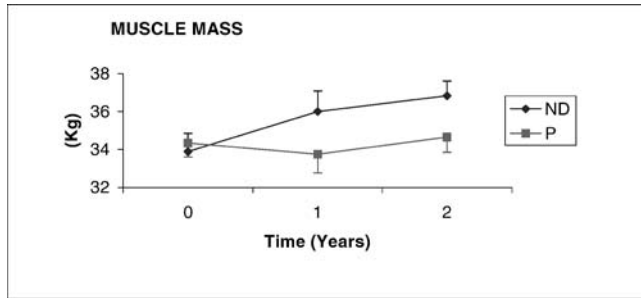


Figure 2. Effect of nandrolone decanoate (ND) or placebo (P) on muscle mass (kg) after 1 and 2 years of treatment, compared to baseline and between the groups. Data are expressed in mean  $\pm$  standard deviation (\* $p < .05$  compared to baseline;  $p < .05$  compared to corresponding placebo group).

in smaller double-blind trials or open label studies (19–24). It is, however, difficult to extrapolate an increase in BMD to increased bone strength and thus a reduced fracture rate. As in ovariectomized rats, treatment of ovariectomized cynomolgus monkeys with ND for 2 years was shown to prevent osteopenia and to inhibit bone turnover (27). Gadeleta and colleagues (28) showed in a physical, chemical, and mechanical follow-up study of lumbar vertebra that ND increased the ultimate stress compared to a nontreated ovariectomized group, indicating that the increase in BMD does indeed result in improved bone strength. Effects on fracture rates in humans have been inconclusive (20–22), although a 50% reduction in fracture rates has been observed in a double-blind controlled study (23). In a retrospective case–control study using a questionnaire in six Mediterranean countries, it was shown that the use of anabolic steroids in women was associated with the decrease in relative risk (relative risk = 0.6) of hip fracture, but not significantly. Analysis of the data in Italy, the country with the largest use of ND, showed a marked and significant reduction in hip fracture risk (relative risk = 0.20;  $p = .008$ ) (29). Our study shows, in a relatively large group of participants, that increased BMD by ND does indeed reduce fracture rate of the lumbar spine, thus indicating that increased BMD is reflected in increased bone strength. In view of the lower incidence of hip fractures, larger studies are obviously required to evaluate the effect of ND on hip fracture rates.

In 1989, Hassager and colleagues (30) also noted a 10% increase in muscle mass of 16 women, aged 45–75, who received 50 mg ND every 3 weeks for 1 year. The difference between our study and the study of Hassager and colleagues can be related to the fact that the age of our participants was more advanced. Aging is directly related to a smaller production of hormones, such as IGF-I, growth hormone, testosterone, and estrogen, which stimulate formation and maintenance of muscle mass. This association has been demonstrated in several clinical trials (21,31–34). The increase in hemoglobin levels in the ND group is due to direct stimulation of erythropoietin production or to increased sensitivity to erythropoietin that the erythroid progenitor cells in the bone marrow present (30,35–37). Variation in hemoglobin levels has also been reported in several studies with ND. Flicker and colleagues (24)

Table 4. Change From Baseline in Total Body Fat and Muscle Mass After Nandrolone Decanoate (ND) or Placebo

| Period of treatment    | After ND (29 Patients)        |                               | After Placebo (21 Patients) |                 |
|------------------------|-------------------------------|-------------------------------|-----------------------------|-----------------|
|                        | 1 y, %                        | 2 y, %                        | 1 y, %                      | 2 y, %          |
| Total body muscle mass | 6.2 $\pm$ 5.8* <sup>†</sup>   | 11.9 $\pm$ 29.2* <sup>†</sup> | -1.6 $\pm$ 9.9              | 0.9 $\pm$ 4.2   |
| Total body fat         | -9.8 $\pm$ 17.0* <sup>†</sup> | 3.6 $\pm$ 74.8* <sup>†</sup>  | -0.8 $\pm$ 10.2             | -1.7 $\pm$ 17.7 |

Notes: \* $p < .05$  compared to baseline; <sup>†</sup> $p < .05$  compared to corresponding placebo group.

reported an increase of only 6% in the hemoglobin levels of the group that received 50 mg ND during 104 weeks of therapy, whereas other authors, when applying higher ND doses (100–200 mg/week) in chronic kidney failure participants, found increases of up to 24% in 6 months (37,38).

The chief adverse reactions were due to the weak androgenic action of ND, such as hoarseness and hirsutism. Despite the lack of adequate methodology for voice evaluation, the prevalence of hoarseness was lower than the average reported in previous clinical trials, whereas the prevalence of hirsutism on patients who received ND and placebo was similar to that in the other studies. Hassager and colleagues (30) related hoarseness in 11 of the 14 women who received ND every 3 weeks for 1 year, whereas, of the 11 who received it every 4 weeks, only 4 presented changes. In another clinical study, Need and colleagues (20) reported hoarseness in 20 (48%) of the 42 women who received 50 mg ND every 2 weeks for approximately 7.2 months and in 2 (5%) of the 38 who received 50 mg ND every 3 weeks for 5.2 months. Other authors, using populations and ND doses similar to those described previously (19,23,39), also detected no significant changes in voice, body hair, or facial hair.

Our results indicate that ND is a good treatment option for osteoporosis in women aged 70 or older; ND increases BMD, decreases the number of vertebra fractures, and improves muscle mass and hemoglobin levels.

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