Decanoato de Nadrolona para osteoporose pós-menopausa: revisão com busca sistemática

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Introdução

As fraturas osteoporóticas, em especial, as que ocorrem em decorrência das alterações pós-menopausa, têm a projeção de liderar as causas de dor, incapacidade, institucionalização e aumento da morbimortalidade até o ano de 2025; com expectativa de despender USD 25 bilhões. Visando o aumento da densidade óssea, diversas medicações estão sendo utilizadas: uma delas é o Decanoato de Nandrolona (DN). Apesar de evidências científicas prévias para o uso dessa droga, um esteróide anabólico, esta não está incluída nas opções de tratamentos recomendados. O Decanoato de Nandrolona (DN) age no aumento da densidade mineral óssea ao aumentar a atividade osteoblástica e diminuir atividade dos osteoclastos.

Objetivos

Realizar uma revisão narrativa com busca sistemática da literatura referente ao uso do DN para o tratamento da osteoporose pós-menopausa.

Métodos

Busca sistemática realizada nas bases de dados Medline, Lilacs, Central, tripdatabase, Scielo e Opengrey. Foram utilizados estruturadamente, descritores DeCS e MeSH, combinados com palavras chave, buscando apenas estudos randomizados controlados em humanos, sem limite de data. Para a extração dos dados, a estrategia PICO (paciente, intervenção, comparação e outcomes) foi realizada: P: pós-menopausa em mulheres, I: nandrolona ou decanoato de nandrolona; C: placebo, tratamento preconizado e O: densidade mineral óssea, fraturas, marcadores bioquímicos do metabolismo ósseo.

Resultados e Discussão

Da busca, foram selecionados 11 estudos incluídos para tabulação, e todos apresentaram algum resultado positivo relacionado a manutenção ou aumento de massa óssea em diferentes regiões, melhora de marcadores de reabsorção óssea, aumento de massa muscular e, redução do número de fraturas. Nestes, foi realizada a administração de DN 50mg, a cada 2 a 4 semanas, por período de 12 a 36 meses. Os resultados estão sumarizados no Quadro 1. Foram também observados efeitos adversos nos estudos citados, incluindo alterações bioquímicas e relacionadas a androgenização, no entanto, foram considerados de leve a moderados, e clinicamente aceitáveis na maioria dos casos. Os resultados estão sumarizados no Quadro 2.

Quadro 1. Estudos incluídos

Author / Year	Study / Type	Population / Age	ND Intervention / Duration	Main efficacy outcomes
Need AG et al.[1] 1987	CO	52 PMWO (66±1y)	ND 50mg; IM, every 2wk 6 mo aprox.	ND group: Increased BMC (right forearm) (+0.793 to +0.821 g/cm); higher BMC mean rate change in ND group vs control (+ 0.053 vs -0.016 g/cm/year)
Johansen JS et al.[2] 1989	RCT	39 PMWO (55-75y)	ND 50mg; IM, every 3wk 12 mo	ND group: increased proximal part of the distal forearm BMC (+3%)
Gennari C et al.[3] 1989	RCT	20 PMWO (55-65y)	ND 50mg; IM, every 3wk 12 mo	ND group: Increased lumbar spine BMC (+9.8% vs placebo -3.2%); + 3.5% increase in femural diaphysis (vs -3.3% in placebo group); reduced urinary excretion of hydroxyproline; increased intestinal calcium absorption; reduction in bone pain; increased TBV % and OS%
Szücs J et al.[4] 1992	RCT	45 PMWO (49-69y)	Norandrostenolona Decanoate; IM, 50mg every 4wk; 36 mo	ND group: no significant bone loss at 24mo; combination with calcitonin extended treatment efficacy (BMC) up to 36 months (no bone loss, distal radius); increased metacarpal índices; no decrease in lumbar biconvavity indices; height maintenance during 36mo; reduced bone pain; no new crush or other fractures
Birkenhäger JC et al.[5] 1992	RCT	36 PMWO or osteopenia (50-70y)	ND 50mg; IM, every 4wk; 24mo	ND group: increased proximal and distal forearm BMC (1y: +3.2%; 2y: +4.5%), increased lumbar BMC (1y: +9.2%; 2y: +12.2%), QCT: increased by 29% (at 6mo), no increase of newly deformed vertebrae (2y)
Passeri M et al.[6] 1993	RCT	46 PMWO (46-68y)	ND 50mg; IM, every 3wk 18 mo	ND group: increased (4%, 6-12 mo) distal radius BMD (vs placebo: -4%, 18mo); increased (2.9%, 18mo) vertebral BMD (vs placebo: -2.3%); reduced urinary excretion of hydroxyproline; reduced bone pain; no new fractures
Need AG et al.[7] 1993	RCT / CO	45 PMW with low BMD (age: NR)	ND 50mg; IM, every 4wk; 6 mo	ND group: increased FMD and FMC (+8.3 ± 3.7 mg/cm), and decreased forearm fat (-12.3 ± 1.44 mg/cm); reduced plasma and urinary phosphate (-0.082 ± 0.020 mmol/L)
Erdtsiek RJ et al.[8] 1994	RCT	33 PMWO or osteopenia (50-70y)	ND 50mg; IM, every 4wk; 36mo	ND group: increased lumbar BMC (+3.5%); maintenance of results for 1 additional year after ND cessation; 1 less fracture after 3y (also a lower estimate fractures for ND group)
Lyritis GP et al.[9] 1994	RCT	88 PMWO (46-68y)	ND 50mg; IM, every 3wk 12 mo	ND group: 69% of patients with reduction in pain intensity (-1.08 ± 0.16; 1-5 scale); increased mobility (+0.47 ± 0.10); increased (5%) BMC corrected for soft tissue (vs Vitamin D group: -2.5%)
Flicker L et al.[10] 1997	RCT	123 PMWO or osteopenia (60-88y)	ND 50mg; IM, every 4wk; 40wk + 24wk off ND + 40wk	ND group: increased lumbar spine BMC (+4.7 ± 1.9%); increased proximal femur BMD (+3.8 ± 1.8%); maintenance of results for 24wk off ND
Frisoli A Jr et al.[11] 2005	RCT	65 PMWO (>70y)	ND 50mg; IM, every 3wk 24 mo	ND group: increased lumbar spine BMD after 12 and 24 mo (+3.4 ± 6.0% and 3.7 ± 7.0%); increased trochanter BMD after 12 mo (+ 4.8 ± 9.3%); increased femoral neck BMD after 12 and 24 mo (+4.1 ± 7.3% and 4.7 ± 8.0%); reduced new fractures at 24 mo (8 vs 16 placebo); increased muscle mass (2 kg/y); less drop out (4 vs 12 placebo)

CO: cross over; RCT: randomized controlled trial; PMWO: post menopausal women with osteoporosis; y: year; ND: nandrolone decanoate; wk: week; mo: months; BMC: bone mineral content; TBV%: trabecular bone volume; OS%: osteoid surface área; QCT: cancellous bone density of L3; FMD: forearm mineral density; FMC: forearm mineral content; NR: not reported

Quadro 2. Efeitos adversos

Author / Year	ND dose / time	Adverse Events
Need AG et al.[1] 1987	ND 50mg; every 2wk 6 mo aprox.	25/52 some voice alteration (after 4mo ND stop: 4 normal voice and 15 improved, 2 no improvement; 19/52 complained of increased facial hair
Johansen JS et al.[2] 1989	ND 50mg; every 3wk 1 year	not described
Gennari C et al.[3] 1989	ND 50mg; every 3wk 12 mo	2/20 increased hair growth and voice changes (mild, not sufficient to stop ND); biochemical analysis without liver enzymes changes
Szücs J et al.[4] 1992	Norandrostenolona Decanoate; 1x mo, 50mg; 36 mo	Rare and minimal side effects (few minutes flushes after injections, mainly in chin and ear; mild nausea, disappeared spontaneously)
Birkenhäger JC et al.[5] 1992	ND 50mg; IM, every 4wk; 24mo	higher percentage of patients complained os voice changes (timbre, unsteadiness, voice lowering and loss of high frequencies), and decreased HDL (1.38 ± 0.29 to 1.22 ± 0.18 mM). Liver enzymes panel without changes. No complaints of increased hair growth (facial or elsewhere)
Passeri M et al.[6] 1993	ND 50mg; IM, every 3wk; 18 mo	7/25 mild well toleratd side effects, such as facial hair (n=4, most common), weigth gain (less than 2kg), hoarseness, blood pressure (n=2, 5-15mmHg)
Need AG et al.[7] 1993	ND 50mg; IM, every 4wk; 6 mo	8/37 minimal voice changes (only noticed when questioned); 19/37 hair growth (facial, body) or increased loss (scalp) (mild and of little or no significance to the patients). All symptoms remitted 6 mo later
Erdtsiek RJ et al.[8] 1994	ND 50mg; IM, every 4wk; 36mo	5 (of all 9 patients who stopped treatments; ND or control/HRT) stopped due to voice changes (timber, loss of high frequencies, instability); no signs or complaints of increased hair growth in different sites; no changes on lipid (HDL, Total cholesterol) or liver enzymes panel
Lyritis GP et al.[9] 1994	ND 50mg; IM, every 3wk; 12 mo	no changes in biochemical panel (HDL, LDL, total cholesterol, triglycerides, total phospholipids, apolipoproteins, SGOT, SGTP, alkaline phosphatase, albumin, total protein), no changes in blood parameters
Flicker L et al.[10] 1997	ND 50mg; IM, every 4wk ; 40wk + 24wk off ND + 40wk	at 104wk: 7% increase in SBP and 10% increase in DBP; 15% increase in aspartate aminotransferase (no liver toxicity); 6% increase in haemoglobin; 4/52 leg oedema; 25/52 some dregree of voice hoarseness (all mild, except for 2 moderate); 6/52 increased hair growth (all mild)
Frisoli A Jr et al.[11] 2005	ND 50mg; IM, every 3wk; 24 mo	increased haemoglobin at 12 and 24 mo (7% and 14%); 2/32 hoarseness; 2/32 soft facial hirsutism; 2 drop out (1 hoarseness, 1 hirsutism); no oedema; no changes in GPT, GOT, alkaline phosphatase, total calcium and cholesterol levels

Conclusão

Em mulheres menopausadas, o DN mostrou-se eficaz em promover anabolismo ósseo e muscular, reduzir marcadores de reabsorção óssea e número de fraturas. Também, segundo os autores dos estudos selecionados, apresentou-se com segurança clínica aceitável. Assim, sugere-se que deva ser sistematicamente analisado como potencial droga auxiliar no tratamento da osteoporose.

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