1. Introduction

Rheumatoid cachexia, a consequence of chronic inflammation, is a common feature of rheumatoid arthritis (RA) [1]. It is characterised by reduced muscle mass and increased, predominantly truncal, adiposity, which in turn both contribute to physical weakness and disability [2,3]. Additionally, as in other catabolic conditions, these adverse changes in body composition exacerbate risk of falls and fracturing, contribute to impaired physical disability and reduced quality of life, and increase morbidity and mortality [e.g. 4-6]. In RA, again as in other chronic conditions, these outcomes are most marked in severe forms of cachexia where there is frank weight loss with reductions in both lean and fat mass. This overt wasting has been estimated to occur in up to 10% of RA patients and is associated with a three-fold higher mortality [7].

There is evidence that rheumatoid cachexia is established early in the course of the disease [8], and that it is resistant to antirheumatic drug treatment. This non-responsiveness to standard treatment is highlighted by the high prevalence of significant muscle wasting (approximately 67%) and the even higher incidence of obesity (approximately 80%) observed in patients with stable, controlled disease [9-13]. Despite the fact that TNF-α is considered to be a major factor driving rheumatoid cachexia, even anti-TNF treatment fails to reverse or attenuate these perturbations to body composition [8,14,15]. In fact, evidence is emerging that anti-TNF therapy increases fat mass, particularly trunk adiposity, relative to standard DMARDs [14,15]. Consequently, specific potential anabolic interventions need to be as-
sessed as adjuncts to antirheumatic drug therapy. The most efficacious means of improving body composition and physical function in RA patients is regular, high-intensity exercise [9,10,16,17]. However, uptake of this mode of therapy is extremely low amongst RA patients [e.g. 18] as it is for the general population.

During recent years there has been a dramatic increase in the clinical use of testosterone and its synthetic derivatives, anabolic-androgenic steroids (AAS), to improve body composition; in particular, for treatment of muscle loss due to age-related sarcopenia, HIV-related muscle wasting, and hypogonadism in men [19-21]. In support of this treatment strategy, studies utilising either replacement or supraphysiologic doses of testosterone or AAS have been shown to elicit significant increases in lean/muscle mass and reductions in fat mass in healthy, young, middle-aged and old androgen-deficient men [20,21,22-29], frail elderly men [30], glucocorticoid-treated men [31], and men with heart failure [32], HIV [33-38], chronic renal failure [39-41], and COPD [42]. Surprisingly, given the profound positive effects on body composition, the effects of testosterone or AAS therapy on physical function are moderate at best [20], with many of the studies cited above failing to detect improvements in objectively or subjectively assessed function [26,28,29,37-39,41,42].

In the past, trials of testosterone or AAS in RA have mainly focused on improving bone mineral density and general wellbeing [43-45], rather than effects on body composition. Although in one controlled study [43] in which postmenopausal women with RA received 50mg nandrolone decanoate (ND) every 3 weeks for 2 years, whilst there was no effect of treatment on bone density (the primary outcome measure of the investigation), it was incidentally reported that there were significant increases in total body nitrogen and total body potassium, two proxy measures of muscle mass. However, other aspects of body composition, such as adiposity, were not assessed. Nor were the consequences of increased muscle mass on physical function investigated.

Given its anabolic effects, and its relatively reduced androgenic effects compared to testosterone (testosterone has an anabolic:androgenic ratio of 1, whereas the ratio for ND is 10 [19]), ND, an esterified form of the minimally aromatizable testosterone analog, nandrolone, would appear to be a suitable potential anabolic intervention for RA. A reduction in androgenic effects is a vital consideration when proposing potential therapies for RA as the incidence of this disease is three times higher in women than in men [46].

Thus, in the present pilot study we assessed the efficacy of 24 weeks of ND (100mg/week) administration in reversing muscle loss and decreasing fat mass in male patients with established RA. As secondary outcomes, we assessed safety and the effects on physical function of ND treatment.
2. Methods

2.1. Subject recruitment and eligibility

This was a randomised, placebo-controlled, double-blind trial, approved by the North West Wales NHS Research Ethics Committee. Sample size was determined by power calculations for the principal outcome variable: appendicular lean mass (ALM). This calculation was based on the results of a study conducted by our group investigating the efficacy of ND (@ 100mg/week) in increasing ALM in male haemodialysis patients [41]. Thus, we used a mean change in ALM of 1.40kg (SD = 0.46kg), assumed normal distribution, two groups, equal variance, no change in the control group, α = 0.05, and power = 0.80. Calculations resulted in the requirement of 5 participants per group to identify a significant change in ALM. To account for potential dropouts, we aimed to recruit 12 participants per group (i.e. a total of 24 participants).

Accordingly, 24 consenting adult males with established rheumatoid arthritis from the Gwynedd Hospital Rheumatology Department were recruited into the study and randomized for treatment with either ND or placebo [41]. Eligibility criteria for subjects were: a diagnosis of RA according to the American Rheumatism Association 1987 revised criteria [47]; aged 18 years or older; functional class I or II; and stable antirheumatic drug therapy for at least 3 months. Patients were excluded if they: were cognitively impaired; had other reasons for cachexia; were taking drugs or nutritional supplements known to affect muscle mass; were engaged in regular, high intensity exercise; or had a contraindication to receiving anabolic steroids. The intervention was either 200mg nandrolone decanoate (Deca-Durabolin, Organon Laboratories Ltd., Cambridge, UK) or matched placebo (vehicle only) given by deep intramuscular injection every two weeks for 24 weeks.

2.2. Outcome measures

All study outcome measures were assessed at baseline and at 24 weeks. To monitor treatment safety, an additional blood sample was taken at 12 weeks. For each assessment, subjects presented at approximately the same time of day, fasted, and having refrained from strenuous exercise for 24 hours.

2.2.1. Body composition

Body composition was assessed by whole-body pencil-beam dual x-ray absorptiometry (DXA; Hologic, QDR1500, software version V5.72). This measurement provides estimates of total and regional lean, fat and bone masses. Subsequently, appendicular lean mass (ALM; i.e. total arms + legs soft-lean mass), a proxy measure of total body skeletal muscle mass [48], was determined [49]; relative skeletal muscle index (RSMI) was calculated (ALM (kg)/height (m)^2) [50]; and percent body fat (%BF) estimated. RSMI and %BF were then used to determine whether patients were “cachectic”, “obese”, and if both, “cachectic-obese”, according to the definitions of Baumgartner et al. [50].
Immediately following DXA scanning, bioelectrical impedance spectroscopy (BIS; Hydra ECF/ICF 4200, Xitron Technologies, San Diego, Calif., USA) was used to estimate extracellular water (ECW), intracellular water (ICW), and total body water (TBW). Checking these is necessary since ND treatment has been associated with oedema which impairs interpretation of DXA measures of body composition.

2.2.2. Muscle strength and physical function

Maximal voluntary isometric knee extensor strength (at a fixed joint angle of 90°) was measured by a Kin-com isokinetic dynamometer (Chattanooga, Tennessee, USA). Physical function was additionally measured by objective tests from the “Senior Fitness Test” [51]: 30-seconds sit-to-stand chair stand, the 30-seconds arm curl, and 50-foot walk. Subjective patient reported physical disability was assessed with the multidimensional Health Assessment Questionnaire [52].

2.2.3. Disease Activity and inflammation

Disease activity was evaluated by the Disease Activity Score in 28 joints (DAS28-ESR) [53], and systemic inflammation by erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level.

2.2.4. Harms

Guidelines for reporting harms where taken from the extended CONSORT statement [54]. Proformas (templates with information completed by the lead researcher following a set pattern) were completed detailing expected adverse ND effects including androgenic effects, sodium/fluid retention, alterations to dry weight causing cramps/hypotension, haematoma at injection site, blood data including liver function tests (alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (Alk Phos)), lipid profiles (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides), haemoglobin (Hb), hematocrit (Hct), and prostate specific antigen (PSA). Unexpected (not reported on medication information sheets) and serious (fatal, life threatening, or resulted in hospitalization) adverse events were collected passively as they occurred during the trial period. Decisions about whether events should be attributed to the intervention were made unblinded by the lead clinician. Decisions about whether to withdraw patients from the trial following harms were made following discussion between the patient and the lead clinician. Adverse events with ambiguous definitions were defined as follows: hypotension (fainting and concomitant low blood pressure); fluid retention (clinical signs including oedema, breathlessness, high blood pressure, and increased hydration of the lean body mass); carpal tunnel syndrome (tingling/numbness associated with medial nerve and positive Phalen’s test); fitting (seizures or convulsions); heart attack (myocardial infarction), and acne and hair loss (self-reported and defined by patients). Potential drug-related adverse events such as fluid retention were monitored clinically each month of the intervention, and blood analyses i.e. liver function tests, serum lipid profile, Hb, Hct and PSA were assessed every 12 weeks. All blood analyses were performed in hospital laboratories by automated analysers using routine methods.
2.3. Statistical Analysis

Baseline differences between the groups were examined using multiple independent t-tests. When no difference was confirmed, treatment effects were assessed by multiple, 2-way (2x2; treatment by time (baseline and at 24 weeks)) ANOVAs. When baseline differences were revealed, the effects of ND were determined by ANCOVAs. Assumptions of sphericity were verified by Mauchly’s Test, and the between subjects effect size for group was calculated as eta squared ($\eta^2$), with thresholds for small, moderate, large and very large effects set at 0.1, 0.08, 0.26 and 0.50, respectively. Data were analysed using SPSS version 14 (Chicago, IL), and are presented as mean±SD. P values <0.05 were considered statistically significant, whilst p values from 0.05-0.10 were considered a trend.

3. Results

Of the 24 participants who were randomised, there were three dropouts in the ND group. Logistical failure meant two did not receive their injections and one developed fast atrial fibrillation after the first ND injection; the latter was thought to be unrelated to the treatment but resulted in withdrawal from treatment. The remainder (9 on ND, 12 on placebo) completed the study and provided the data used for the analysis. As shown in Table 1, there were no significant differences between the two groups at baseline in age, disease duration, functional class, DAS 28, ESR and CRP, and serum testosterone levels, and for both groups, there were no significant changes in DAS28, ESR and CRP at follow-up (data not shown). At baseline, 7 of the 9 ND subjects and 9 of the 12 placebo subjects had low serum testosterone (T) levels as defined by being below the 50th percentile for healthy males aged 60-80 years (i.e. <13.7 mmol/L) [26]. As anticipated, at 24 weeks serum concentrations of T, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) were significantly reduced (p’s=0.002, 0.005, 0.041, respectively) in subjects receiving ND treatment, and unchanged in those receiving placebo (data not shown). There were also no differences in serum sex hormone binding globulin (SHBG) levels between the groups at baseline (p=0.522), but in contrast to T, LH and FSH, SHBG levels were unaffected by treatment and remained similar for both groups at 24 weeks (p=0.943) (data not shown).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nandrolone (n = 9)</th>
<th>Placebo (n = 12)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>56.9 ± 12.4</td>
<td>64.4 ± 8.5</td>
<td>0.100</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>9.7 ± 8.0</td>
<td>15.8 ± 11.4</td>
<td>0.270</td>
</tr>
<tr>
<td>Functional class</td>
<td>1.60 ± 0.52</td>
<td>1.70 ± 0.89</td>
<td>0.360</td>
</tr>
<tr>
<td>HAQ (0-3)</td>
<td>0.85 ± 0.64</td>
<td>1.18 ± 0.93</td>
<td>0.390</td>
</tr>
<tr>
<td>DAS 28 score</td>
<td>3.50 ± 1.54</td>
<td>5.29 ± 3.48</td>
<td>0.167</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>22.11 ± 27.59</td>
<td>28.91 ± 26.40</td>
<td>0.573</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>24.33 ± 27.32</td>
<td>13.50 ± 6.31</td>
<td>0.197</td>
</tr>
<tr>
<td>Testosterone (mmol/L)</td>
<td>11.70 ± 6.04</td>
<td>11.82 ± 6.20</td>
<td>0.967</td>
</tr>
</tbody>
</table>

Table 1. Baseline characteristics of study participants. Data are presented as means ± SD.
The effects of ND on body composition are summarised in Table 2. At baseline there were no significant differences in body composition variables, and a similar proportion of subjects in the ND (6 of 9) and placebo (9 of 12) groups were initially classified as cachectic (RSMI ≤7.26kg/m^2) and/or obese (7 of 9, and 10 of 12, respectively; %BF ≥27% for males [50]). In the ND group, there were substantial mean increases in both total lean mass (TLM) and ALM (a surrogate measure of muscle mass) at 24 weeks (4.24kg and 2.39kg, respectively; i.e. 8.4% and 12.1% increases versus baseline, respectively), whereas these remained stable in the controls. ND also induced large reductions in total fat mass (FM) (mean of 2.16kg; -8.6% versus baseline) and in truncal FM (mean of 0.97kg; -7.1% versus baseline). By contrast, both mean total and truncal FM increased in the control group (by 1.93kg and 0.90kg, respectively). Thus, post intervention, percent body fat was significantly different between the two groups. Body mass increased slightly in both groups following the intervention period, but remained similar as increased muscle mass in the ND group corresponded with increased FM in the controls. As a consequence of the respective treatment effects, at 24 weeks there were reductions in the number of subjects classified as either cachectic or obese in the ND group (6 of 9 to 4/9, and 7/9 to 4/9, respectively), but not the placebo group (9/12 to 9/12, and 10/12 to 11/12, respectively).

There was no significant change in bone density for either group (data not shown).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nandrolone (n = 9)</th>
<th>Placebo (n = 12)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass (kg)</td>
<td>78.45 ± 16.21</td>
<td>77.32 ± 11.59</td>
<td>0.650</td>
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<tr>
<td>Baseline</td>
<td>81.13 ± 15.05</td>
<td>79.14 ± 12.33</td>
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</tr>
<tr>
<td>Total lean mass (kg)</td>
<td>50.39 ± 7.39</td>
<td>48.65 ± 6.44</td>
<td>0.001</td>
</tr>
<tr>
<td>Baseline</td>
<td>54.63 ± 7.99</td>
<td>48.37 ± 6.88</td>
<td>0.002</td>
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<tr>
<td>Appendicular lean mass (kg)</td>
<td>22.10 ± 4.28</td>
<td>18.48 ± 3.10</td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>19.71 ± 3.64</td>
<td>18.54 ± 3.03</td>
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</tr>
<tr>
<td>Total fat mass (kg)</td>
<td>25.47 ± 11.02</td>
<td>26.88 ± 8.50</td>
<td>0.005</td>
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<tr>
<td>Baseline</td>
<td>23.29 ± 10.26</td>
<td>28.81 ± 8.06</td>
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</tr>
<tr>
<td>Trunk fat mass (kg)</td>
<td>13.58 ± 6.06</td>
<td>15.13 ± 5.78</td>
<td>0.074</td>
</tr>
<tr>
<td>Baseline</td>
<td>12.61 ± 6.02</td>
<td>16.03 ± 4.94</td>
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<tr>
<td>% Body fat</td>
<td>31.33 ± 8.41</td>
<td>34.44 ± 7.03</td>
<td>0.001</td>
</tr>
<tr>
<td>Baseline</td>
<td>28.20 ± 7.72</td>
<td>36.22 ± 6.26</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Effects of 24 weeks of nandrolone (200mg every two weeks) or placebo on body composition in male patients with rheumatoid arthritis
As a consequence of randomization, mean objectively assessed physical function at baseline was generally significantly lower for the placebo group than for the ND group (e.g. knee extensor strength, \( p = 0.010 \); chair stand test, \( p = 0.005 \); arm curls, \( p < 0.001 \)). As expected, physical function of both groups was reduced relative to that of age- and sex-matched, sedentary, healthy individuals (i.e. mean performances in the objective measures were 31-32% less for the ND group and 47-51% less in the placebo group than the 50\(^{th}\) percentile levels for healthy 60-64 year old males [51]). Increased muscle mass and reduced fat mass following ND treatment, however, was not accompanied by significant improvements, by ANCOVA, in knee extensor strength or performance in the 30sec chair stand or 50 foot walk tests. In contrast, a significant improvement in the arm curl test was observed in the ND group following 24 weeks treatment, albeit the effect size was only moderate (Table 3).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nandrolone (( n = 9 ))</th>
<th>Placebo (( n = 12 ))</th>
<th>( p ) value ( \eta^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee extensor strength (newtons)</td>
<td>403.50 ± 113.99</td>
<td>287.96 ± 76.01</td>
<td>0.012</td>
</tr>
<tr>
<td>Baseline</td>
<td>420.21 ± 155.61</td>
<td>293.45 ± 81.78</td>
<td>0.622 0.014</td>
</tr>
<tr>
<td>Post-intervention</td>
<td>360.55 ± 31.53</td>
<td>338.19 ± 26.65</td>
<td></td>
</tr>
<tr>
<td>Adjusted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 sec chair stand test (reps)</td>
<td>11.11 ± 1.96</td>
<td>7.83 ± 2.55</td>
<td>0.005</td>
</tr>
<tr>
<td>Baseline</td>
<td>12.77 ± 3.23</td>
<td>9.25 ± 2.99</td>
<td>0.873 0.001</td>
</tr>
<tr>
<td>Post-intervention</td>
<td>10.86 ± 0.78</td>
<td>10.68 ± 0.65</td>
<td></td>
</tr>
<tr>
<td>Adjusted</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>30 sec arm curl test (reps)</td>
<td>14.89 ± 1.90</td>
<td>10.08 ± 2.57</td>
<td>0.001</td>
</tr>
<tr>
<td>Baseline</td>
<td>16.56 ± 2.65</td>
<td>10.83 ± 2.41</td>
<td>0.034 0.227</td>
</tr>
<tr>
<td>Post-intervention</td>
<td>15.27 ± 1.00</td>
<td>11.80 ± 0.82</td>
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<tr>
<td>Adjusted</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>50 foot walk (secs)</td>
<td>9.50 ± 2.24</td>
<td>12.34 ± 3.97</td>
<td>0.070</td>
</tr>
<tr>
<td>Baseline</td>
<td>8.22 ± 1.92</td>
<td>11.27 ± 2.98</td>
<td>0.112 0.134</td>
</tr>
<tr>
<td>Post-intervention</td>
<td>9.02 ± 0.72</td>
<td>10.67 ± 0.62</td>
<td></td>
</tr>
<tr>
<td>Adjusted</td>
<td></td>
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</tbody>
</table>

Table 3. Effects of 24 weeks of nandrolone (200mg every two weeks) or placebo on objective strength and physical function in male patients with rheumatoid arthritis. Differences between groups at baseline were tested by paired t tests. Pretest and posttest scores are presented as means ± SD. Adjusted scores (posttest scores adjusted for pretest scores) are presented in italics as means ± SEM. Differences between groups in the adjusted scores were tested by ANCOVA. Thresholds for small, moderate, large and very large effects (\( \eta^2 \)) were set at 0.01, 0.08, 0.26 and 0.50, respectively.

ND taken fortnightly for 24 weeks at a dose of 200mg was generally well tolerated. One participant complained of mood swings which were attributed to the intervention. An increase in ECW (mean of 0.99kg; \( p = 0.003 \)) was associated with ND treatment but there was no change in the ECW:ICW ratio between groups following treatment (ANOVA interaction \( p = 0.791 \); data not shown). Supporting this finding, no clinical indication of fluid overload
was evident in the ND treated subjects. As anticipated, ND treatment elicited a significant increase in Hb (pre- vs post-treatment: 13.9 ±1.8 vs 15.9±1.4, respectively; p=0.004) and Hct (41.7 ± 5.4 vs 48.0 ± 4.2, respectively; p<0.001). ND treatment also resulted in increased levels of transaminases (p=0.002), but these remained within the normal range except in three participants in whom there was a minimal elevation of AST above normal (less than 1 SD in each case). Serum levels of total, LDL and HDL cholesterol, triglycerides and PSA remained unchanged throughout the treatment period (data not shown). No serious adverse events occurred, and no other adverse events were reported, in either group.

4. Discussion

The main finding in this randomised control trial was that 24 weeks of 100mg/week nandrolone decanoate improved body composition; with mean increases in TLM and ALM (=4.2kg and 2.4kg, respectively, or gains of 8.4% and 12.1%, respectively, relative to baseline) accompanied by reductions in fat mass (=2.2kg; -8.6% versus baseline) including truncal adiposity (=1.0kg; -7.1% versus baseline). This was not unexpected since dose responsiveness of body composition to ND has been well established in healthy young and older adults and in patients with a variety of catabolic conditions [31,35,38-42,55]. The mechanism for testosterone and its synthetic analogs’ effects on body composition is thought to be via enhanced differentiation of multipotent mesenchymal stem cells into the myogenic lineage and concomitant inhibition into the adipogenic lineage [56]. Such preferential differentiation results in hypertrophy of both type I and type II muscle fibres and an increase in myonuclear number [57]. This anabolic effect could potentially reduce morbidity and mortality, particularly in extreme cases of cachexia. Indeed, anabolic steroids have been used therapeutically in catabolic states such as HIV/AIDS and severe age-related sarcopenia.

However, despite the significant improvement in muscle mass in particular, there were no obvious corresponding improvements in physical function at 24 weeks. A similar observation has been made in numerous trials of ND and testosterone [26,28,29,31,37-42]. Even in healthy individuals, the dose-response relationship between anabolic steroid administration and physical functioning is not as clear as that with increased muscle mass. Indeed, in reported studies, the correlations between the increment in muscle mass and measures of strength are not particularly strong [e.g. 20,22]. It has been suggested by Sattler et al. [27] that threshold increments of 1.5kg in LBM and 0.8kg in ALM need to be achieved if improvements in physical function following testosterone treatment are to be realized. However, in our study, 7 of the 9 ND subjects exceeded both these threshold increases, yet all failed to achieve consistent improvements in function. Additionally, there was no correlation between increases in either LBM or ALM and gains in function.

Perhaps the results of our study reflect a physiological delay in adaptation following muscle hypertrophy, although it is clear that factors other than muscle size influence strength and physical function. To illustrate this, we observed substantial improvements in the same objectively assessed measures of physical function used in the current study (17-30% relative
to baseline; p’s = 0.027-0.001) in RA patients following 24 weeks of high intensity progressive resistance training (PRT; i.e. strength training), despite the increases in LBM and ALM (1.54kg and 1.21kg, respectively, relative to baseline) being substantially less than those observed following 24 weeks ND treatment [9]. Interestingly, in the PRT study, increases in LBM correlated significantly with gains in function – and this relationship is characteristic of anabolic exercise interventions [58]. All of which suggests that, in addition to muscle hypertrophy, neural, circulatory, endocrine and biochemical adaptations, as observed following exercise training, are prerequisites for improving strength, power and endurance. There is also evidence from both experimental animal studies and treating people with chronic catabolic disorders that physical activity is an important adjunct to anabolic steroids in improving physical functioning. Thus, the dose-response effects of ND appeared to be attenuated in inactive rat models [59], and combining ND therapy with resistance exercise training in CKD patients on haemodialysis resulted in improvements in both muscle mass and physical function [40], whereas ND alone only increased muscle mass in these patients. We would predict the same effects in people with RA.

Although our conclusions regarding the effects of ND (and testosterone therapy generally) on function are compromised by our study’s lack of power, it is clear that the dose effect of testosterone and AAS on physical function is considerably less evident than that on body composition, and that the correlation between changes in muscle mass and function following treatment with either testosterone or AAS is at best moderate [20,22]. It is also notable that numerous studies which feature much larger subject numbers (i.e. up to n=120 in the treatment group) [26,28,29,37,38,42], higher doses of testosterone or ND (i.e. up to 1120 mg testosterone undecanoate/week) [26,37], and longer treatment periods (i.e. up to 3 years) [28,29,31] failed to demonstrate improved function. Interestingly, Ottenbacher et al [20] in their meta-analysis, having concluded that the effects of androgen therapy on strength in elderly men are mixed and inconclusive, also noted that reported effect sizes were smaller in trials rated as high quality than in those designated as being of lower quality.

As reported by others [26,43], ND had a negligible effect on total bone density in the current study. There was, however, a significant increase in haemoglobin, probably due largely to direct androgen stimulation of erythropoiesis. This is a well reported consequence of androgen therapy [32,60,61], and could be an additional benefit should ND be used in rheumatoid cachexia, since anaemia is a common accompaniment of this condition. ND at a dose of 200mg every two weeks for twenty four weeks appeared to be well tolerated. Mood changes in one participant were attributed to the anabolic steroid but, apart from a clinically insignificant elevation of serum transaminases, there were no serious or non-serious observed side effects. An increase in extracellular water with ND treatment was demonstrated by BIS, but there were no clinical manifestations associated with this. As previously reported [38,42,62], ND treatment reduced serum T, LH and FSH levels in our subjects. However, this effect is transient and reversible with cessation of androgenic therapy [62]. These apparently benign treatment effects are consistent with those reported by systematic reviews and meta-analyses on testosterone and AAS therapy [19,32,60,61].
We restricted recruitment of participants to males with RA to avoid the potential virilising effects of ND. However, we have observed in our studies of CKD [41] that in women in order to produce significant muscle mass increase without virilising effects, the nandrolone dose should not exceed 50mg/week.

In conclusion, we have demonstrated that male patients with established RA respond to 100mg/week ND for 24 weeks with a considerable increase in muscle mass and decrease in fat mass. However, these improvements in body composition were not accompanied by general improvements in strength or physical function, which probably requires an additional intervention such as exercise. This treatment was well tolerated and might be appropriate for extreme cases of rheumatoid cachexia.

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References


