

Nandrolone (17-Nortestosterone) And Glucose Metabolism: From Ugly Duckling To Handsome Swan

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Abstract

Glucosarcopenia, or sarcopenia coexisting with diabetes, is a common condition. Caused by various factors, including poor glucose control, as well as some glucose-lowering therapies, sarcopenia negatively impacts quality of life and long-term health. Nandrolone, or 19-nortestosterone, is a selective anabolic receptor modulator (SARM), classified as an anabolic-androgenic steroid (AAS). A review of its pharmacological properties suggests that it may be used as therapy for sarcopenia, along with medical nutrition therapy and resistance exercise training. This review suggests a practical and pragmatic approach towards ensuring safe and smart usage of nandrolone in glucosarcopenia management.

Keywords: Anabolic steroid, androgenic steroid, diabetes, glucosarcopenia, muscle health, musculoskeletal health, sarcopenia

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Introduction

Sarcopenia, a major health challenge, is more common in persons living with diabetes.¹ Apart from factors such as age, physical inactivity, and associated comorbidities, which hamper exercise, poor glycaemic control, as well as some drugs used for diabetes management, may lead to sarcopenia. These multifaceted aspects of pathophysiology may be grouped under the term glucosarcopenia.

Anabolic Steroids

At the same time, multiple anabolic drugs are available for use. Categorized under the umbrella of anabolic-androgenic steroids (AAS), these are structurally related

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to testosterone. AAS usage increases the risk of CVD, even though AAS users usually maintain high levels of physical activity. The increase in the risk of sudden cardiac death may be due to cardiac remodelling, leading to cardiac hypertrophy and resulting in abnormal cardiac function. Polycythaemia reduced left ventricular and diastolic function, and accelerated atherosclerosis has been reported in chronic AAS prescribers. An increase in blood pressure and low-density lipoprotein cholesterol (LDL-C), as well as decreased high-density lipoprotein cholesterol (HDL-C), also contribute to the higher risk.²

All Aas Are Not The Same

However, due to negative connotations associated with AAS in sports, the pharmacokinetic and dynamic differences between various AAS are sometimes not appreciated. While lower insulin sensitivity and higher levels of visceral adipose tissue have been reported with usage, there is no definite evidence that AAS causes dysglycaemia.

Nandrolone, or 19-nortestosterone, is a selective anabolic receptor modulator (SARM) with a high myotrophic: androgenic ratio.³ This allows it to exert anabolic effects without causing virilization. This suggests that nandrolone may be used, along with nutritional therapy and resistance exercise training, in the management of sarcopenia. It may also be useful in glucosarcopenia, as it helps improve glucose levels.

We review animal and human studies that have explored the effect of nandrolone on glucose metabolism and suggest pragmatic usage of this drug in glucosarcopenia. While reiterating that this compound has the potential for abuse, we call for scientific research in this field to ensure safe and smart usage of the molecule in the promotion of musculoskeletal health in diabetes.

Animal Studies

In a preclinical study to determine the impact of supraphysiological doses of nandrolone decanoate on rat glucose metabolism during fasting, male Wistar rats were treated with intramuscular injections of vehicle, low dose (0.016 mg/100 g body weight) or high dose nandrolone decanoate (1 mg/100 g body weight)-SD group, once a week for 8 weeks. After 12 h fasting, high dose group had

increased serum insulin levels, a blunted response to insulin regarding glucose uptake in skeletal muscle, and lower Fasting serum glucose, pyruvate tolerance and liver glycogen content.⁴

This may be explained by the effect of nandrolone decanoate on adenosine monophosphate-activated protein kinase (AMPK) activation. Albino CF1 mice at 3 and 18 months of age were separated into 4 groups that received daily subcutaneous injections of either nandrolone decanoate (15 mg/kg) or vehicle for 15 days. The drug was found to promote hypothalamic AMPK activation while leading to metabolic connectivity rearrangements in the brains of adult and aged mice.⁵ It is noteworthy that metformin is also an AMPK activator.

Another study has evaluated the independent and associated effects of nandrolone decanoate and resistance exercise on hormones related to energy balance in male rats. Over eight weeks, four groups were exposed to vehicle 3x/wk; resistance exercise 5x/wk and vehicle 3x/wk; nandrolone decanoate (5 mg/kg) 3x/wk, and resistance exercise 5x/wk with nandrolone decanoate (5 mg/kg) 3x/wk. The gastrocnemius muscle was larger in both exercise groups. Body weight was reduced in the exercise group, while total fat mass decreased in both the exercise and exercise + nandrolone groups. The exercise group experienced an increase in prepro-orexin, while both exercise and exercise + nandrolone groups had a reduction in mesenteric fat leptin expression. Serum leptin concentrations fell in all three active groups, while orexin-A increased in the nandrolone group. Overall, resistance exercise related to central and peripheral changes in energy metabolism, while nandrolone changed only peripheral components.⁶

Clinical Studies

Eleven healthy men enrolled in a randomized, double-blind cross-over study and completed two treatment cycles consisting of two weekly injections of placebo followed by six weekly injections of either testosterone ester (300 mg/week) or \pm nandrolone decanoate (300 mg/week), with both treatment periods separated by a 4-week washout. A tolbutamide-modified, frequently sampled, intravenous glucose tolerance test was used to assess glucose disposal. Nandrolone decanoate improved noninsulin-mediated glucose disposal as expressed by glucose effectiveness at basal insulin (SG), and glucose effectiveness at zero insulin (GEZI). In nandrolone-treated men, SG ($\times 10^{-2}$ min⁻¹) rose from 2.4 ± 0.2 to 3.7 ± 0.6 after treatment ($P < 0.05$), whereas GEZI ($\times 10^{-2}$ min⁻¹) increased from 1.8 ± 0.2 to 3.1 ± 0.6 ($P < 0.01$).⁷

Nandrolone has also been postulated to favourably

influence diabetic neuropathy and postherpetic neuralgia by improving amino acid and protein metabolism in nerve cells, neuronal supporting tissues, and myelin; stimulating nerve growth factor; altering nerve transmission by an influence on neuromodulators, acetylcholinesterase or choline acetylase, and calcium or potassium metabolism; increasing tissue oxygenation; and changing the physical nature of axoplasm elaborated by the nerve cell body.⁸

Specific Situations

Thirty human immunodeficiency virus (HIV)--infected men were randomized to a high dose of nandrolone decanoate weekly or nandrolone plus resistance training for 12 weeks. Fasting glucose, fasting insulin, and homeostasis model assessment improved in ($P < 0.05$). These beneficial metabolic effects lasted only 2 months after the interventions were completed.⁹

From ugly duckling to handsome swan

All anabolic-androgenic steroids have conventionally been studied as one homogenous group. This, however, is not correct. Nandrolone decanoate is a selective anabolic receptor modulator that has potentially advantageous effects on glucose metabolism. It, therefore, has the potential to be used as therapy for persons with diabetes and sarcopenia, i.e., glucosarcopenia (Table).

Table: Management of glucosarcopenia.

Nutrition
• Macronutrition-protein, energy
• Micronutrition-vitamin D calcium
Exercise
• Flexibility and balance
• Resistance exercise
Glucose control
• As per standard of care
Anabolic therapy
• Selective anabolic receptor modulation
Targetted anabolic therapy, if indicated
• Testosterone
• Menopausal hormonal therapy

Pragmatic Posology

A course of 50mg to 100mg at 3-4 weekly intervals, for 5 doses, should improve muscle function and strength. This will also serve as positive motivation and encourage persons living with diabetes to adopt a healthy lifestyle. Maintenance therapy may be offered through lower doses (25 mg) at 1-2 monthly intervals, dosage at less frequent intervals, or regular cycles of therapy every 6-12 months. The optimum course of action needs to be

studied in clinical trials. A person-centred approach will probably offer maximal dividends, keeping the patient's priorities and preferences in mind.

Summary

Nandrolone viewed as an ugly duckling by some, is actually a handsome swan. It can help improve muscle health and overall health in persons with sarcopenia, including those with diabetes. One must be aware of the contraindications (hormone-sensitive cancers) and caveats (watch for sexual dysfunction and mild fluid retention). Through rational and responsible presentation, nandrolone can help persons with glucosarcopenia achieve their full health potential and emerge as handsome swans.

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