Nandrolone Potentiates Arrhythmogenic Effects of Cardiac Ischemia in the Rat

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Anabolic steroid abuse has been associated with thrombosis and arteriosclerosis, both of which predispose to myocardial ischemia and infarction. However, there are reports of sudden cardiac death in the absence of thrombus and atheroma following anabolic steroid use. Although treatment with the commonly abused steroid, nandrolone, has been shown to decrease recovery of systolic function following ischemia in isolated rat hearts, it is unknown whether anabolic steroids can increase the incidence of fatal arrhythmia associated with cardiac ischemia. Anesthetized male Sprague–Dawley rats were administered vehicle or nandrolone (10–160 μg/kg/min iv) 10 min prior to 15-min occlusion of the left anterior descending coronary artery followed by 10-min reperfusion. Nandrolone, in this dose range, did not significantly change heart rate, blood pressure, or cardiac rhythm in the absence of ischemia. However, the fraction of rats surviving ischemia was significantly (p < 0.05) decreased by nandrolone at both 40 and 160 μg/kg/min, while survival time during ischemia was decreased significantly (p < 0.001) by nandrolone 160 μg/kg/min. An increase (p < 0.05) in the duration of ventricular fibrillation was noted at the highest compared to the lowest dose of nandrolone, corresponding to a significant increase in the fraction of rats experiencing ventricular fibrillation (p < 0.01). Nandrolone had no effect on the frequency or duration of ventricular fibrillation or survival time during reperfusion. Although the mechanisms underlying these effects are currently unclear, they indicate that exposure to anabolic steroids in combination with transient reductions in coronary blood flow may explain some reports of sudden cardiac death in anabolic steroid users.

Key Words: nandrolone; cardiac; ischemia; arrhythmia; ventricular fibrillation.

There is a growing body of epidemiological evidence indicating an increasing prevalence of the abuse of anabolic steroids in both image-conscious, sedentary, teenage males, and power athletes. In the United States up to 12% of young males have been shown to use steroids (DuRant et al., 1994, 1995; Handelsman and Gupta, 1997; Kindlundh et al., 1998; Radakovich et al., 1993; Scott et al., 1996; Tanner et al., 1995). This trend has been associated with a number of adverse cardiovascular events including sudden cardiac death (Dickerman et al., 1995; Fineschi et al., 2001; Hausmann et al., 1998; Luke, 1990).

A number of athletes, known to be current anabolic steroid users, and dying from sudden cardiac death, have been found to have coronary arteries free from thrombus or atheroma (Kennedy and Lawrence, 1993; Luke, 1990). Likewise, anabolic steroid abusing athletes, admitted to hospital for infarction have displayed angiographically normal arteries (Ferenchick and Adelman, 1992). In contrast, some case reports have linked anabolic steroids to atherosclerosis (Mewis et al., 1996) and thrombosis (Fisher et al., 1996; Nieminen et al., 1996) both of which significantly increase the risk of cardiac ischemia.

Limited studies in animal models have attempted to identify underlying mechanisms and establish a cause/effect relationship between anabolic steroid use and cardiac function but these relationships remain largely unresolved. In general, the cardiovascular consequences of anabolic steroid administration to rats reported to date have been moderate. Nandrolone is a steroid commonly abused by humans (Committee on Sports Medicine and Fitness, 1997; Parkinson and Evans, 2006). When administered chronically to rats nandrolone has been associated with a significantly heightened heart rate response to cocaine (Phillis et al., 2000), with accelerated development of hypertension in developing, spontaneously hypertensive rats (Tseng et al., 1994), and with left ventricular hypertrophy (Trifunovic et al., 1995; Tseng et al., 1994) in sedentary rats. More recently an increase in myocardial susceptibility to ischemia/reperfusion injury has also been shown in isolated hearts prepared from rats treated chronically with nandrolone (Du Toit et al., 2005).

Changes in gene expression as a result of the interaction of steroids with nuclear receptors cannot explain all the observed effects of anabolic steroids. For example, it has been demonstrated that testosterone can block the vasodilator effect of adenosine in isolated perfused rat hearts (Ceballos et al., 1999).
However, this effect remained when testosterone was coupled to a large macromolecular complex, which prevented transport into the cytosol indicating the site of action was likely to be on the cell membrane.

In view of potential nongenomic effects of anabolic steroids, this study aimed to determine whether acutely administered nandrolone can increase the incidence of cardiac arrhythmia during ischemia resulting in increased mortality following in vivo coronary artery ligation/reperfusion in the rat model of cardiac ischemia and sudden cardiac death. In contrast to the previous report of Du Toit et al. (2005), where an ex vivo model after chronic nandrolone treatment was used, we employed an in vivo model and iv infusion of nandrolone to investigate the direct acute effects of nandrolone on the incidence and frequency of ventricular arrhythmia during cardiac ischemia.

**MATERIALS AND METHODS**

**Animals.** Male Sprague–Dawley rats (11 weeks of age) weighing 358 ± 4 g on the day of experiment were purchased from Central Animal Supplies (University of Adelaide) and were fasted overnight before surgery to induce ischemia, and were randomly assigned to receive either vehicle or nandrolone (10–160 µg/kg/min). The experiments were conducted in strict accordance with the guidelines of the Australian Code of Practice for the care and use of animals for scientific purposes of the National Health and Medical Research Council. Experiments were approved by the Animal Ethics Committees of the University of Adelaide andCSIRO, Health Sciences and Nutrition.

**Surgery.** Induction of ischemia and reperfusion was conducted using the methodology described previously by McLennan et al. (1985, 1988). Following induction of anesthesia (pentobarbital sodium, 60 mg/kg ip), the left femoral artery and vein were exposed and catheters inserted to allow for blood pressure measurement and intravenous drug administration, respectively. The femoral artery catheter was attached to a pressure transducer (Narco Biosystems P-1000B). The femoral vein catheter was attached to a syringe pump. The femoral artery and vein were exposed and catheters inserted to allow for blood pressure and blood flow measurements.

Ischemia/reperfusion. Ischemia was induced by tightening the ligature around the left anterior descending coronary artery for a period of 15 min. The ligature was then released and reperfusion initiated for a further 10 min.

**Data analysis.** The cardiovascular response to nandrolone (heart rate, systolic pressure, and diastolic pressure) was expressed as a change from the beginning of infusion over time. These responses were analyzed with a two-way repeated measures analysis of variance (ANOVA).

Ventricular tachycardia was defined as four or more consecutive ventricular premature beats. Ventricular fibrillation was defined as a signal that changed from beat to beat in morphology and rate.

A chi-squared test with post hoc Fischer’s exact test was used to analyze differences between treatments for the total number of surviving rats responding with ventricular tachycardia or ventricular fibrillation during ischemia or reperfusion, and the fraction of rats responding with ventricular tachycardia, ventricular fibrillation, or ventricular tachycardia + ventricular fibrillation. Survival time during ischemia and reperfusion was analyzed using a single-factor ANOVA with Dunnett’s post hoc test. For rats which died of ventricular fibrillation the time of death was taken to be the beginning of the period of fatal ventricular fibrillation.

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**Average duration (s) of ventricular tachycardia or ventricular fibrillation or total dysrhythmia (ventricular tachycardia + ventricular fibrillation) during ischemia and reperfusion was calculated for each treatment. For fatal ventricular fibrillation a maximum of 120 s was recorded for a single episode. Previous data within our laboratory have demonstrated that 120 s is the maximum period of ventricular fibrillation for which a rat has survived under this procedure. Differences between treatment groups in the duration of ventricular tachycardia, ventricular fibrillation, and ventricular tachycardia + ventricular fibrillation were analyzed with a Kruskal–Wallis test with Dunn’s multiple comparisons test post hoc.

The severity of dysrhythmia observed during ischemia and reperfusion was scored using the Lambeth convention (Walker et al., 1988). The small number of rats that died without displaying arrhythmia were excluded from the score (number of rats excluded is noted in Table 1).

Differences in Lambeth arrhythmia score or duration of arrhythmia were analyzed using a Kruskal–Wallis nonparametric test, with Dunn’s post hoc test. Differences in “zone at risk” of ischemia and total survival were assessed using a one-way ANOVA with Dunnett’s post hoc test.

Blood pressure and heart rate were recorded during ischemia and reperfusion. These cardiovascular variables were recorded immediately prior to ischemia and at 5, 10, and 15 min of ischemia. The same variables were recorded prior to reperfusion and after 10 min. If ventricular tachycardia or ventricular fibrillation was present at the designated time, a blood pressure or heart rate reading was taken within 60 s before or after the designated time. If no period of normal beat was evident for 60 s before or after the designated time, a blood pressure or heart rate reading was not recorded. All data were expressed relative to the value at the beginning of ischemia or reperfusion. Between group differences were assessed using two-way ANOVA.

In all statistical tests the level for statistical significance was \( p < 0.05 \).

**Drugs.** Nandrolone was dissolved in a 100% ethanol solution from which it was diluted with sterile saline. Vehicle containing the equivalent location of “zone at risk” of ischemia between the various pretreatment groups (0 µg/kg/min: 51 ± 1%, 10 µg/kg/min: 50 ± 2%, 40 µg/kg/min: 50 ± 1%, 80 µg/kg/min: 45 ± 4%, 160 µg/kg/min: 55 ± 2%).
Effect of Nandrolone on Survival During Myocardial Ischaemia/Reperfusion

<table>
<thead>
<tr>
<th>Survival time (s)</th>
<th>Fraction of rats surviving</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
</tr>
<tr>
<td>0N</td>
<td>900 ± 0 (1)</td>
</tr>
<tr>
<td>10N</td>
<td>900 ± 0</td>
</tr>
<tr>
<td>40N</td>
<td>782 ± 53 (2)</td>
</tr>
<tr>
<td>80N</td>
<td>797 ± 53 (2)</td>
</tr>
<tr>
<td>160N</td>
<td>693 ± 85*</td>
</tr>
</tbody>
</table>

Note. Left-hand columns display survival times (mean ± SE) during cardiac ischaemia (I) (n = 10–13) and reperfusion (R) (n = 10–13) in rats treated with nandrolone. 0N, 10N, 40N, 80N, and 160N indicate 0, 10, 40, 80, and 160 μg/kg/min nandrolone, respectively. Numbers in parentheses indicate the number of rats in each treatment group excluded because of death unrelated to ventricular fibrillation. Single-factor ANOVA, Dunnett’s post-hoc test. Ischaemia (I) [F(4,51) = 3.80, P < 0.01]. *P < 0.001 significantly different from 0N. Right-hand columns display the fraction of rats surviving cardiac ischaemia (I) or reperfusion (R) after treatment with nandrolone (0, 10, 40, 80, and 160 μg/kg/min); data include only those rats which obeyed the Lambeth scoring system. *P < 0.05 indicates significantly different from 0N, chi-squared test with Fischer’s exact test.

Results

Plasma Level of Nandrolone

In rats administered 160 μg/kg/min for 10 min (n = 3), the resultant plasma concentration was 915 ± 135nM which was significantly greater [t(4) = 4.686, P < 0.01] than rats infused with 40 μg/kg/min where a plasma concentration of 281 ± 15nM was observed Nandrolone was undetectable in rats administered vehicle.

Blood Pressure and Heart Rate

Small decreases in systolic and diastolic blood pressure and heart rate after coronary artery ligation were observed as reported previously for this model (McLenann et al., 1985). However, there were no effects of nandrolone observed on systolic pressure, diastolic pressure, or heart rate relative to control treatment, either prior to, during, or after ischemia.

Survival

Ischemia. Survival time decreased significantly (F(4,51) = 3.80, P < 0.01) during ischemia in rats administered the highest nandrolone dose (160 μg/kg/min) compared to vehicle-treated rats (P < 0.001) (Table 1). While no other significant decreases in survival time during ischemia were evident between treatment groups, the fraction of rats surviving ischemia was found to be significantly lower (χ² = 12.29, P < 0.05) in the 40 μg/kg/min (P < 0.05) and 160 μg/kg/min (P < 0.05) treatment groups in comparison to vehicle treated controls (Table 1). Five deaths occurred during ischemia (one in the vehicle treated group, two in each of the 40 and 80 μg/kg/min treated groups) which were not due to ventricular fibrillation and therefore could not be scored using the Lambeth convention. These were excluded from all survival calculations.

Reperfusion. No significant difference between groups was observed in the number of rats surviving reperfusion (Table 1). No statistically relevant decreases in survival time were observed in any group in comparison to control (Table 1). One death during reperfusion (in the 40 μg/kg/min group) which was not due to ventricular fibrillation and therefore could not be scored using the Lambeth convention was excluded from survival calculations (Table 1).

Arrhythmia

Arrhythmia as reflected by the Lambeth scores showed a significant increase (kw = 13.69, P < 0.01) for the three highest doses of nandrolone, compared to vehicle-treated rats (all P < 0.05) during ischemia (Table 2). Conversely, there were no differences found in Lambeth scores between nandrolone treatments and vehicle during reperfusion (Table 2).

Ischemia. A significant increase in the fraction of rats responding to ischemia with ventricular fibrillation was observed in nandrolone-treated rats (χ² = 13.66, P < 0.01) (Table 3). A significantly greater fraction of rats treated with the highest dose of nandrolone (160 μg/kg/min) responded with ventricular fibrillation compared to the vehicle control (0 μg/kg/min) (P < 0.05). Likewise, significant increases in the frequency of ventricular fibrillation were found in all doses of nandrolone in comparison to the lowest nandrolone dose of 10 μg/kg/min (40 μg/kg/min, P < 0.05; 80 μg/kg/min, P < 0.05; 160 μg/kg/min, P < 0.01). No other significant changes in the fraction of rats responding to ischemia with ventricular fibrillation were observed in any group in comparison to control (Table 3).

<table>
<thead>
<tr>
<th>TABLE 2</th>
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<tbody>
<tr>
<td>Effect of Nandrolone on Lambeth Arrhythmia Score</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>0N</td>
</tr>
<tr>
<td>10N</td>
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<tr>
<td>40N</td>
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<tr>
<td>80N</td>
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<td>160N</td>
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</tbody>
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Note. Lambeth arrhythmia scores (mean ± SE) are shown during cardiac ischemia (I) or reperfusion (R) in rats treated with nandrolone. 0–160N represent 0–160 μg/kg/min nandrolone, respectively. Kruskal–Wallis (kw = 13.69, P < 0.01), with Dunn’s post hoc comparisons. *P < 0.05 significantly different from 0N. n = 10–13 (ischemia), n = 6–13 (reperfusion).
TABLE 3
Effect of Nandrolone on the Occurrence of Arrhythmia during Myocardial Ischemia and Reperfusion

<table>
<thead>
<tr>
<th></th>
<th>Fraction with VT</th>
<th></th>
<th>Fraction with VF</th>
<th></th>
<th>Fraction with VT or VF</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>R</td>
<td>I</td>
<td>R</td>
<td>I</td>
<td>R</td>
</tr>
<tr>
<td>0N</td>
<td>11/14 (78.6)</td>
<td>3/13 (23.1)</td>
<td>3/14 (21.4)</td>
<td>2/13 (14.4)</td>
<td>11/14 (78.6)</td>
<td>4/13 (30.8)</td>
</tr>
<tr>
<td>10N</td>
<td>9/13 (69.2)</td>
<td>6/13 (46.2)</td>
<td>1/13 (7.7)</td>
<td>1/13 (7.7)</td>
<td>9/13 (69.2)</td>
<td>6/13 (46.2)</td>
</tr>
<tr>
<td>40N</td>
<td>10/12 (83.3)</td>
<td>2/7 (28.6)</td>
<td>7/12&lt;sup&gt;ab&lt;/sup&gt; (58.3)</td>
<td>1/7 (14.3)</td>
<td>11/12 (91.7)</td>
<td>2/7 (28.6)</td>
</tr>
<tr>
<td>80N</td>
<td>10/12 (83.3)</td>
<td>5/7 (71.4)</td>
<td>6/12&lt;sup&gt;bc&lt;/sup&gt; (50.0)</td>
<td>2/7 (28.6)</td>
<td>10/12 (83.3)</td>
<td>5/7 (71.4)</td>
</tr>
<tr>
<td>160N</td>
<td>9/10 (90.0)</td>
<td>2/6 (33.3)</td>
<td>7/10&lt;sup&gt;bc&lt;/sup&gt; (70.0)</td>
<td>0/6 (0.0)</td>
<td>9/10 (90.0)</td>
<td>2/6 (33.3)</td>
</tr>
</tbody>
</table>

Note. The fraction of nandrolone treated rats responding with ventricular tachycardia (VT), ventricular fibrillation (VF), or ventricular tachycardia + ventricular fibrillation (VT + VF) during a 15-min period of cardiac ischemia (I) and during 10 min of cardiac reperfusion (R) are shown in the left, middle, and right-hand panels, respectively. 0N, 10N, 40N, 80N, 160N represent 0, 10, 40, 80, 160 µg/kg/min, respectively. The percentage of rats responding with VT, VF, or VT + VF is shown in parentheses. Chi-squared test, Fischer’s exact test post hoc.

<sup>a</sup><sup>p < 0.05</sup> significantly different from 0N.
<sup>b</sup><sup>p < 0.05</sup> significantly different from 10N.
<sup>c</sup><sup>p < 0.01</sup> significantly different from 10N.

responding with ventricular tachycardia, or ventricular tachycardia + ventricular fibrillation were found during ischemia (Table 3).

Rats displayed arrhythmia of longer duration during cardiac ischemia than in reperfusion. The mean duration of ventricular fibrillation during cardiac ischemia was found to increase with nandrolone dose (Fig. 1B). A statistically significant increase in mean ventricular fibrillation duration (kw = 15.19, <sup>p < 0.01</sup>) was noted in rats treated with the highest dose of nandrolone (160 µg/kg/min) compared to the lowest nandrolone dose (10 µg/kg/min) (<sup>p < 0.05</sup>). No dose-related effect was evident for mean ventricular tachycardia duration, neither were any between group differences evident (Fig. 1A). When the ventricular tachycardia and ventricular fibrillation data were combined (Fig. 1C) a dose–response relationship was seen for the doses 0, 10, 40, and 80 µg/kg/min. The slope was significantly different from zero (<sup>p = 0.004</sup>) with an <sup>r</sup><sup>2</sup> of 0.16.

Reperfusion. No significant differences were found in the fraction of surviving rats responding with ventricular tachycardia, ventricular fibrillation, or ventricular tachycardia + ventricular fibrillation during reperfusion (Table 3).

There was very little ventricular tachycardia (Fig. 1D) or ventricular fibrillation (Fig. 1E) during reperfusion in these rats, with no significant differences in the response between treatment groups. Similarly, much smaller mean durations of ventricular tachycardia + ventricular fibrillation were noted in cardiac reperfusion compared to cardiac ischemia, with no significant differences between the responses of the various treatment groups (Fig. 1F).

DISCUSSION

The main finding in this study was that acute iv administration of a high dose of nandrolone to rats potentiated ischemia-induced arrhythmia thereby decreasing the proportion of rats surviving ischemia. This occurred without nandrolone by itself causing any hemodynamic effects as measured in this model. These data suggest that synthetic steroids, such as nandrolone at high concentrations, may well have direct adverse cardiovascular effects which do not require repeated exposure to the drug. Those animals that did survive the ischemic period showed no greater susceptibility than control rats in the reperfusion period. This is an expected result as this model has been optimized to examine arrhythmias during ischemia rather than during in reperfusion (McLennan et al., 1988).

This is the first study to investigate changes in hemodynamics following nandrolone infusion in male rats. Blood pressure and ECG assessment in human volunteers administered iv testosterone at physiological and superphysiological doses have been reported with no effects on these parameters observed (White et al., 1999). However, there are two issues in interpreting these data. One, the steroid used was the endogenous compound and synthetic steroids such as nandrolone are more commonly abused. Two, the issue of appropriate dosing. For example, in the White et al. (1999) study the maximum plasma testosterone concentration achieved was only six times the endogenous level. It is probable that plasma concentrations reached with illicit use are several orders of magnitude higher than this. Nevertheless, the current study is consistent with these data in that iv high dose nandrolone by itself had no effect on ECG or blood pressure when administered acutely in the absence of myocardial ischemia.

The relevance of the plasma concentrations of nandrolone achieved in the current study to the abuse situation is difficult to assess as plasma nandrolone concentrations following an abusive cycle have not been reported. Peak plasma concentrations following a single intramuscular dose of 150 mg of nandrolone decanoate to healthy volunteers achieved peak nandrolone plasma levels of approximately 20nM (Bagchus et al., 1999).
et al., 2005). This dose is in the range used clinically for treatment of HIV induced wasting. Although the plasma concentration of nandrolone achieved with the highest dose in the current study, namely 915 ± 135nM, was approximately 45-fold greater than this level, illicit use of anabolic steroids is associated with doses 10–100 times those that would be clinically prescribed (Haupt and Rovere, 1984; Parkinson and Evans, 2006; Socas et al., 2005).

A recent study reported decreased recovery of contractility after global ischemia/reperfusion in Langendorf-perfused hearts from rats treated chronically for 6 weeks with im nandrolone (Du Toit et al., 2005). However, there have been no previous reports of increased myocardial susceptibility to ischemia/reperfusion after acute nandrolone administration.

In the current study, the mechanism of the increased susceptibility to cardiac ischemia following acute nandrolone administration was not identified. Unfortunately, there are limited studies on the mechanism of action of nandrolone but consideration of the effects of other related steroids may be of help in identifying possible mechanisms for future study. Steroid hormones, chemically related to nandrolone, can acutely inhibit the reuptake of catecholamines into extraneuronal tissues (Salt, 1972) which could in turn increase catecholamine concentrations at receptor sites. Although normally responsible for reuptake of noradrenaline, during ischemia the neuronal catecholamine transporter has been shown to be responsible for nonexocytotic release of noradrenaline from sympathetic nerve terminals. Increased release of noradrenaline has been implicated in

**FIG. 1.** Effect of nandrolone pretreatment on duration of arrhythmia. Average duration (mean ± SE) of (A) ventricular tachycardia (VT), (B) ventricular fibrillation (VF), and (C) ventricular tachycardia + ventricular fibrillation (VT + VF) in cardiac ischemia, and average duration (mean ± SE) of (D) VT, (E) VF, and (F) VT + VF in cardiac reperfusion, in rats infused with nandrolone. 0N, 10N, 40N, 80N, 160N represent 0, 10, 40, 80, 160 μg/kg/min nandrolone, respectively. Kruskal–Wallis test with Dunn’s multiple comparisons test. *p < 0.05 significantly different from 10N (n = 10–14 ischemia, n = 6–13 reperfusion).
ischemia-induced arrhythmia (Du and Dart, 1993; Du et al., 1998; Richard et al., 1994; Schomig, 1990; Schomig et al., 1984, 1987). Under these circumstances it is possible that inhibitors of extraneuronal removal of noradrenaline could potentiate the effects of neurally released transmitter. However, this potential mechanism seems unlikely to account for the current data, since an unpublished study from our laboratory showed that nandrolone has a very low affinity (3.95mM) as an inhibitor of extraneuronal uptake of noradrenaline in the Langendorf-perfused rat heart when compared with other steroid inhibitors such as corticosterone (1.78µM). Therefore, the plasma concentration achieved in our rats at the highest dose of nandrolone (915nM) is unlikely to have significant effects on extracellular concentrations of catecholamines via this mechanism.

Other potential mechanisms may explain the increase in ventricular fibrillation, decrease in survival time and the increased lethality of nandrolone during cardiac ischemia. For example, nandrolone has been shown to cause the release of intracellular calcium in rat primary myotubes, in a manner which is independent of intracellular androgen receptors, but dependent on inositol tris-phosphate and the extracellular signal-regulated kinase pathway (Estada et al., 2003). If nandrolone acts to cause an increase in myocardial intracellular calcium release in a similar way to that in skeletal muscle, it is possible that this could explain proarrhythmic effects of nandrolone since intracellular calcium overload has been associated with arrhythmogenesis during myocardial ischemia (Clusin et al., 1982). The importance of calcium in the maintenance of cardiac rhythm is supported by the efficacy of calcium channel antagonists in the treatment of supraventricular tachyarrhythmias and ventricular arrhythmias (Billman, 1991, 1993; Levy, 1989). Further studies are required to explore this potential mechanism.

Finally, since the present study was conducted in vivo, it is possible that some of the effects of nandrolone were indirect. Studies in isolated perfused hearts subjected to regional ischemia may be helpful in identifying direct actions upon the heart itself.

The main finding in this study was that acute administration of a high dose of nandrolone to rats, although producing no apparent hemodynamic effects by itself, potentiated ischemia-induced arrhythmia thereby decreasing the proportion of rats surviving ischemia, reflected in a decreased survival time during ischemia. This increased mortality corresponded with an increase in the duration of ventricular fibrillation, and a significantly increased Lambeth score compared to control. These data suggest that some of the cardiovascular effects of high concentrations of anabolic steroids reported in humans may be due to the direct and immediate pharmacological actions of these drugs on the heart and could occur after a single administration of a high dose of steroid.

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