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# Effect of Nandrolone Decanoate on Some Biochemical Markers When Used as Adjuvant Therapy for Healing of Facial Muscle Wound

# Tamarah M. Al-Abdullah<sup>1</sup>, Faehaa A. Al-Mashhadane\* <sup>2</sup>

- <sup>1</sup>Master student, Department of Dental Basic Sciences, College of Dentistry, Mosul University / Iraq.
- <sup>2</sup> Department of Dental Basic Sciences, College of Dentistry, Mosul University / Iraq.

# **Article information**

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## \*Correspondence:

E-mail: faehaaazher@uomosul.edu.iq

## **Abstract**

Aims: to distinguish if the nanodrolone decanoate has any effect on the healing of facial muscular wounds which are one of the issues that dentists face, and it is a challenge to find a useful treatment for this condition. This study explores the idea that, when used in conjunction with surgical repair. The steroid Nandrolone-Decanoate, when injected locally to the masseter muscle, improves healing. Materials and Methods: The study comprised twenty-five healthy rabbits, were sorted into three equal groups at random. The animals were classified randomly into 3 groups (5 rabbits/group). Group I: (control negative/5 rabbits) the rabbits were not undergoing surgical procedure and not receive any treatment. Group II: (control positive/10 rabbits) the rabbits were undergoing surgical procedure and receive distilled water injection. Group IIA: contained 5 rabbits that were euthanized on the 3<sup>rd</sup> day of the surgical procedure. Group IIB: contained 5 rabbits that were euthanized on the 7th day of the surgical procedure. Group III: (treatment/10 rabbits) the rabbits were undergoing surgical procedure, and each rabbit, treated once daily with nanodrolone deconate (10 mg/kg) using Mantoux syringe via intramuscular injection from the first day of the surgical procedure to the euthanizing day. Group IIIA: contained 5 rabbits that were euthanized on the 3rd day of the surgical procedure. Group IIIB: contained 5 rabbits that were euthanized on the 7th day of the surgical procedure. Results: There are highly significant differences in the serum aspartate aminotransferase (GOT) and Alanine aminotransferase (GPT). The results demonstrate an increase (both enzymes) in the treatment group on the seventh day of the trial as compared to the control group and the 3<sup>rd</sup> day. There is a decrease in the LDH (lactate dehydrogenase) level in the 7<sup>th</sup> day of the treatment as compared with 3rd day of treatment group and with the control group. C -reactive protein (CRP) serum results show a highly significant decrease in its level in 7th day as compared to the 3rd day and the control group. Conclusions: Nanodrolone Decanoate may be used as an adjunctive therapy in the healing of intramuscular wounds.

# تأثير ديكانوات الناندرولون على بعض العلامات البيوكيميائية عند استخدامه كعلاج مساعد لشفاء جرح عضلات الوجه

لملخص

الأهداف: تهدف الدراسة الى التمبيز بين ما إذا كان ديكانوات النانودرولون له أي تأثير على التنام جروح عضلات الوجه التي تعد واحدة من المشكلات التي بواجهها أطباء الأسنان ، ومن الصعب العثور على علاج مفيد لهذه الحالة. تستكشف هذه الدراسة فكرة أنه عند استخدامها جنبا إلى جنب مع الإصلاح الجراحي. السنيرويد الناندرولون-ديكانوات ، عند حقنه محليا في العضلات الماضغة ، يحسن الشفاء. المعواد وطرائق المعمل: ضمت الدراسة خمسة وعشرين أرنبا سليما ، تم فرزها إلى ثلاث مجموعات متساوية عشوائيا. تم تصنيف الحيوانات بشكل عشوائي المعموعات (5 أرانب/مجموعة). المجموعة الأولى: (تحكم سلبي / 5 أرانب) لم تكن الأرانب تخضع لعملية جراحية وتثلقى حقن الماء المقطر. المجموعة إيا: الواردة 5 المجموعة الثانية: (مراقبة إيجابية / 10 أرانب) كانت الأرانب تخضع لعملية جراحية وتثلقى حقن الماء المقطر. المجموعة إيا: الواردة 5 الأرانب التي تم الموت الرحيم في اليوم 3 من العملية الجراحية. المجموعة الثانية: احتوي على 5 أرانب تم القتل الرحيم. المجموعة الثانية: تحتوي على 5 أرانب تم التخلص منها في اليوم 3 من العملية الجراحية. المجموعة الثانية: تحتوي على 5 أرانب تم التخلص منها في اليوم 3 من العملية الجراحية. المجموعة الثانية: احتوي على 5 أرانب تم التخلص منها في اليوم 3 من العملية الجراحية. المجموعة الثانية: احتوي على 5 أرانب تم التخلص منها في اليوم 5 من العملية الجراحية. المجموعة الثانية: احتوي على 5 أرانب تم التخلص منها في اليوم 5 من العملية الجراحية. المجموعة الثانية: احتوي على 5 أرانب تم التخلوب المتابع من التجربة مقارنة بالمجموعة المينوتر انسفيراز (غت). النتائج: الخبرت النتائج زيادة (كلا الإنزيمين) في مجموعة العلاج في اليوم 1 السابع من التجربة مقارنة بالمجموعة المحلوم 5 الصابطة. الاستنتاجات: يمكن استخدام ديكانوات النانودرولون كعلاج مساعد في التنام الجروح العضلية. والمجموعة الصابطة. الاستنتاجات: يمكن استخدام ديكانوات النانودرولون كعلاج مساعد في التنام الجروح العضلية.

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## INTRODUCTION

Synthetic testosterone derivatives known as anabolic androgenic steroids (AASs) are created to increase anabolic activity while reducing androgenic side effects. They have garnered a great deal of notoriety in the last 50 years <sup>(1-3)</sup>.

There are numerous therapeutic uses for AASs. AASs' anabolic effects could be useful in the management of muscle loss caused by severe burns, as well as a number of additional long-term diseases such as malignancy, kidney damage, liver cirrhosis, lung disease, and muscle dystrophy (4-7).

There is mounting evidence that AASs have muscle mass and strength are increased. It was recently suggested that AASs have anabolic effects be studied further in muscle could improve postoperative healing and recovery after surgery including muscle injuries. Although the exact role of their administration in the mentioned processes is still inconclusive. Skeletal muscle has a well-known ability to selfrepair, despite the fact that the severity of the injury may cause delayed or incomplete healing as a result of fibrosis. Preclinical research has demonstrated a link between testosterone and muscle regeneration processes. Unfortunately, few researches have directly examined. The impact of the AASs on the growth of muscles is debatable. with contradictory evidence (8).

Ferry and colleagues investigated the impact of Nanodrolone-Deconate (ND) on the soleus and extensor digitorum longus muscles following myotoxic injection <sup>(9)</sup>, and additional

preclinical studies discovered that administering ND increased Muscle regeneration was permitted based on the number and shape of myofibers found in those muscles (10-12).

AST (GOT) and ALT(GPT) values are enzymes mainly found in liver tissues, red blood cells, muscle tissue and heart muscle and other organs, any damage in these tissues results in increase in the serum level of these two enzymes so they are particularly useful in the detection of liver disease (11, 13). Lactate-dehydrogenase is an enzyme that can be found in almost every human tissue. organ destruction and diseases cause elevation in the serum level of LDH which occurs due to significant cell death that results in loss of cytoplasm (14,15). C-reactive protein (CRP) is one of the liver enzymes that is produced in an acute -phase form, activated by TNF, IL-6, and IL-1. CRP level increase in response to inflammation. This can be proved by measuring the serum level of CRP which is increased in the 4 to 6 hours following inflammation, this level multiplying by two in 8 hours till it reaches its peak level in 36-50 hours (16).

Preclinical data may differ depending on the differential regeneration response to various forms of muscle injury, the dose and the duration of androgen treatment, as well as the outcome variables. No human research has examined the function of androgens in fostering muscle regeneration as of yet. Despite the fact that there is ongoing study on this subject, the most recent studies do not provide convincing arguments for or against the AASs uses <sup>(8)</sup>.

## MATERIALS AND METHODS

The experiment for this study was carried out with consent from the Dentistry College / Mosul University: approval of the Study Ethics Panel and the Dept. of Dental-Basic Science Educational Committee. NO. Uo.M-Dent: A.82/22.

#### Animals

The study comprised twenty local male rabbits weighing 1-1.5 kg and aged between 11-12 months. Individual animals were kept in special cages in specific circumstances (temperature of around 20-25°C with a light-dark cycle). 12:12 hr.), with left access to water and food (17).

# **Surgical processing**

An injectable dosage of xylazine hydrochloride (5mg/kg) and ketamine hydrochloride (50 mg/kg) was used to anesthetize the animals (18). The anesthetized animal was placed on the surgical board on its ventral side, and the operative region (cheek) before being cleaned with tap water and sterilized with povidone-iodine solutions. Utilizing forceps and a surgical blade no:15 (19), a 1 cm long incision in the skin and deep into the masseter muscle was carefully produced. Following that, the wounds were sutured with an absorbable suture to allow them to heal by primary purpose. The animals received both antibiotics and analgesics in the first day only.

The rabbits were sorted into three equal groups at random. Group I consist of five rabbits control negative that receive nothing. Group II: Control positive group, (10 rabbits) were

subjected to a surgical procedure and injected with distilled water without receiving any treatment. Group III (10 rabbits): treatment group, rabbits were subjected to a surgical procedure and were treated once daily with Nanodrolone-Deconate (10)mg/kg) using Mantoux syringe via intramuscular injection from the first day of the surgical procedure to the euthanizing day. Five animals of each group were euthanized on the 3<sup>rd</sup> and 7<sup>th</sup> day were euthanized. Blood was collected from each rabbit The serum was separated for biochemical parameter analysis. using centrifugation and stored at (-20C°) until analysis by using BIOLABO kit for measuring AST, ALT- colorimetric method and BILLABO kit for measuring LDH SFBC modified method and CRP detection kit (SIEMENS).

## **RESULTS**

#### Clinical observations

The animals were under daily observation of veterinary doctor. During the trial period, no mortality toxicity, aberrant signs in their activity, any behavioural pattern or other clinical findings were documented in any of the groups. Except local changes in the wound area as compared with the control group.

# **Biochemical finding**

There is a highly significant difference of GOT, GPT, LDH and CRP. The results demonstrate a significant increase in GOT and GPT in the group treated with Nanodrolone-Deconate group on the

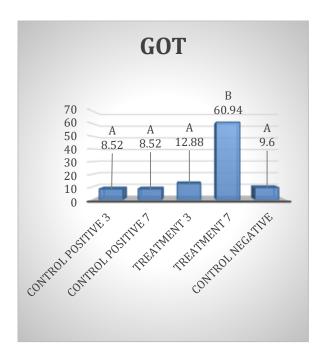
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seventh day of the trial as compared to the control group and the 3<sup>rd</sup> day of treatment (Table 1 & 2), (Figure 1 & 2). In addition, there is a decrease in the LDH level in the 7<sup>th</sup> day of the treatment as compared with 3<sup>rd</sup> day of treatment and the control groups (Table 3) (Figure 3). CRP in serum results shows a highly significant decrease in the level in 7<sup>th</sup> day group as compared to the 3<sup>rd</sup> day and the control groups (Table 4), (Figure 4).

**Table 1:** Comparison between all groups in GOT level.

	ANOVA							
		Squares	Df.	Square	F	sig		
		Sum		Mean				
GOT	Between-	10492.382	4	2623.096	17.183	0.000**		
	Groups							
	Within	3053.096	20	152.655				
	Groups							
	Total	13545.478	24					

<sup>\*\*</sup> Highly Significant at P-value ≤ 0.01



**Figure 1:** level of GOT in different groups.

**Table 2:** Comparison between all groups in GPT level.

ANOVA							
	Squares	Df.	Square	F	sig.		
	Sum		Mean				
GPT Between-	7653.761	4	1913.440	2.640	0.044*		
Groups							
Within	14495.671	20	724.784				
Groups							
Total	22149.432	24					

<sup>\*</sup> Significant at P-value  $\leq 0.05$ 

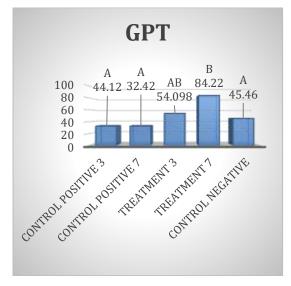
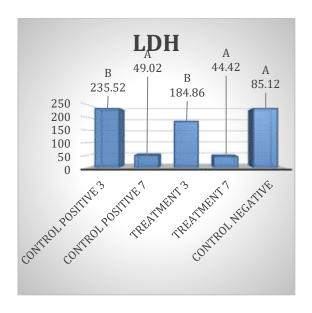


Figure 2: level of GPT in different groups.

**Table 3:** Comparison between all groups in LDH level.

	ANOVA								
		Squares Sum	Df.	Square	F	sig.			
				Mean					
LDH	Between-	147592.882	4	36898.221	24.918	0.000**			
	Groups								
	Within	29615.864	20	1480.793					
	Groups								
	Total	177208.746	24						

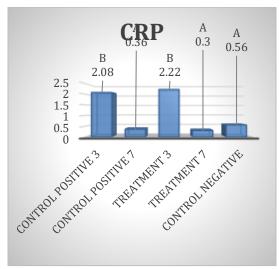
<sup>\*\*</sup> Highly Significant at P-value  $\leq 0.01$ .



**Figure 3:** level of LDH in different groups. Table 4: Comparison between all groups in CRP.

	ANOVA							
		Squares	Df.	Square	F.	sig.		
		Sum		Mean				
CRP	Between	18.445	4	4.611	16.898	0.000**		
	Groups							
	Within	5.458	20	0.273				
	Groups							
	Total	23.902	24					

<sup>\*\*</sup> Highly Significant at P-value  $\leq 0.01$ .



**Figure 4:** level of CRP in different groups.

# **DISCUSSION**

Although the effects of anabolic steroids on skeletal muscle have been well documented, little attention has been paid to the acceleration of muscle regeneration following injury. The goal of this research was to find out if Nandrolone-Decanoate local injection improves masseter muscle regeneration and healing after incisional wound.

The muscle regeneration induced by exogenous anabolic steroids in the animal models have been examined after several types of muscle injury. In a previous study, the exogenous use of the administration of Nandrolone Decanoate to non-castrated rats proved advantageous for the regeneration of gastrocnemius muscle following crush injury. In intact rats, anabolic steroid use increases soleus muscle mass after muscular damage caused by snake venom (10,13 & 20).

Exogenous Nandrolone-Decanoate adjustment of the muscle regeneration is in need of additional search. Moreover, Nandrolone-Decanoate has also been implicated in the effective regeneration of mouse TA (tibialis anterior) muscle following muscle graft surgery <sup>(17)</sup>. Although the Anabolic steroid regulation of muscle regeneration after injury has been broadly examine <sup>(20 & 21)</sup>, their impact on these regenerative processes has not been fully recognized.

After injury, the early skeletal muscle regenerative response is comparable to wound repair in that it requires synchronized inflammation control, extracellular matrix renovation, and myofiber expansion (22 & 23).

Anabolic steroids have also an improved control the activity of immunologicalAll of these cells are required for tissue regeneration, fibroblasts, and myogenic precursor cells. Anabolic steroids also have a greater capacity to influence the activity of immunological, a fibroblast and the myogenic cell precursors, all of which are required over the repair of tissues (17-19,24 & 25).

During 5, 14, and 42 days, Nandrolone-Decanoate treatment alone boosted muscle protein expression. Nandrolone-Decanoate enhanced protein expression in injured muscle three-fold over the control after 14 days of healing. Nandrolone-Decanoate significantly increased protein expression in damaged muscle compared to Nandrolone-Decanoate alone. Androgen receptor Induction of target gene recording may be ND is important in accelerating muscle mass expansion during injury healing (26). ND (nanodrolone decanoate) has been implicated in numerous studies. functional morphological changes in the liver and kidney, resulting in increased blood levels of creatinine levels, urea, alanine transaminase, and the enzyme aspartate transaminase (27 & 28).

These findings support Hough's assertion that elevated levels of AST, ALT, and lactic dehydrogenase are prevalent among steroid-using athletes (29).

According to Vieira *et al.*, ND treatment raises serum levels of AST, ALT, and alkaline phosphatase in rats in a dose-dependent manner. Our findings suggest that sub chronic ND therapy, particularly at higher-than-clinical

doses, may be harmful to the liver, resulting in incipient fibrosis (30).

Our study found a mild increase in LDH levels on the third day and a significant decrease on the seventh day, indicating that there is minimal cellular damage. Lactate dehydrogenase (LDH) is a cytoplasmic enzyme that is found in all cells and is rapidly released into the cell culture supernatant when the plasma membrane is damaged, making LDH an important feature of apoptotic cells. Necrosis, as well as other types of cellular damage (31).

Finally, the C-reactive protein test shows a highly significant difference between the groups, these differences include an increase in the level of the CRP in the 3<sup>rd</sup> day as compared with the control positive group which is partly agreed with Grace FM and Davies B who say C reactive-protein concentrations were considerably (p0.05) greater in bodybuilders who used AAS <sup>(32)</sup> and disagree because our result shows a drop in the level of CRP in the 7<sup>th</sup> day.

The findings of the current study showed accelerating effect of ND on healing process of muscle injury within few days. There is evidence that Nandrolone-Decanoate-induced myofiber development Early in the recovery process, a muscle is injured. There are some drawbacks to this study. The tiny sample size and short duration of the study. However, we believe that the findings of local anabolic steroid use on masseter muscle healing are definitely useful. More research is needed to confirm these findings.

## **CONCLUSIONS**

The local injection of Nandrolone in the injured masseter muscle of rabbits was capable to alter the healing direction. Complementary pharmaceutical therapies may aid in the successful recovery and regeneration of face muscle after surgery.

#### **Conflict of Interest**

The authors declare that there are no conflicts of interest regarding the publication and/or funding of this manuscript.

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