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Investigating the Clinical, Radiological and Histopathological Effects of Androgens in Bone Formation and Fracture Healing

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Abstract:-

➢ ***Background and Purpose:***

How to use steroid hormones as a solution and indicator in bone fractures and healing in sterilized or unsterilized male animals and even in female animals and animals that have a deficiency and disorder of steroid hormones.

➢ ***Research Method:***

Ten apparently healthy adult male rabbits were selected from the laboratory and were sterilized by scrotal method, and four holes with diameters of 1, 2, 3, and 4 mm were inserted on the tibia from the lateral side, and then into two The group was divided. Regarding the time evaluation of radiographs, which had a normal distribution, variance analysis tests were used at a significant level of 0.05. About the status of the steps that were in the ranking scale. Kruskal-Wallis test was used and statistical calculations were done using SPSS statistical program.

➢ ***Results:***

The gait status of rabbits in both groups improves significantly from day one to day 60. On the other hand, there is no significant difference between the two groups at different times and between different times in each group. Except for the first and seventh day, this difference is completely normal. In relation to the amount of callus formed in the two groups, there is a significant difference at some times. From the point of view of pathology, the assessment of the first and second groups indicated the occurrence of restoration and bone callus formation in both groups, but in comparison, the first group had a wider and more voluminous callus. The whole restoration process had more advanced stages.

Keywords:- *Nandrolone, Cyproterone, Bone, Healing.*

I. INTRODUCTION

In the last few decades, significant advances in our understanding of how sex steroids affect skeletal growth and gaining bone health during puberty are necessary and necessary. Estrogen deficiency is the main factor in the development of osteoporosis.

The mechanisms of sexual skeletal steroid effects are not yet fully known (22, 31, and 57). But in recent years, there have been significant advances in our knowledge about estrogens and to a lesser extent androgens in bone regeneration (31). New insights about estrogen receptors, recent discoveries in the field of increasing the activity of osteoclasts and lessons learned from genetic mutations in humans and animals are all important in increasing our understanding of the skeletal effects of estrogen in males and females (30 and 33). On the other hand, bone fracture repair is generally followed in an orderly manner with suitable mechanical and biological components that are currently available. Improved surgical techniques and grafting surgeries allow surgeons to treat relatively complex bone fractures with a successful outcome. However, some complications following bone fractures occur, such as delayed bone fusion, non-union, and malunion. Eating a broken bone leads. The purpose of this study is to improve and increase the mechanical strength and action of bone for better and faster weight gain, preventing the delay in fusion and lack of fusion and finally returning the efficiency of the damaged bone.

II. WORK METHOD

In this study, after the surgery, the rabbits were completely randomly divided into two groups of five and under the same maintenance and nutrition conditions, including carrot, lettuce and plate.

- Group One: Rabbits received nandrolone decanoate injection after surgery.
- Group Two: Rabbits received oral cyproterone acetate tablets after the operation.

A. Preparation of Rabbits

In order to carry out the plan, two weeks before the experiment, after confirming the clinical health, the rabbits were kept in a standard condition and injected with rabies vaccine.

B. Anesthesia and Surgical Preparation

On the day of the operation, the rabbits were transferred to the surgery room and were examined again. After placing the rabbit on the surgical table with an intramuscular injection of a mixture of aspromazine (0.1 mg per kilogram of body weight) and Vectamine (30 mg per kilogram of body

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weight), the animal was anesthetized and the animal's right leg was completely amputated. Shaved and disinfected with betadine, and after the area was dry, grafting was done so that the middle area of the right tibia was exposed. Method of surgery.

An incision of about 7 cm was made in the middle surface of the tibia with a scalpel blade, after cutting the skin, fascia, tendons and muscles around the bone were slowly removed without cutting or damaging them. It was easily visible.

Next, four holes with a diameter of 1, 2, 3, and 4 mm are made at a distance of one centimeter from each other along the length of the bone to pierce the opposite cortex.

The holes start with a one-meter drill from the bottom of the tibia and end with a four-millimeter drill at the top of the tibia.

After making sure that the tibia is not cracked, the area is washed with Ringer's solution and the remaining bone particles from the created holes are removed by suction, and then the muscles are returned to the first place and under the skin with nylon thread all over. And the skin is stitched individually with nylon thread.

In the next stage, the suture area of the animal, which was shaved before, was disinfected and sterilized and the animal was sterilized scrotally.

➢ *Radiography*

Radiography of the tibia was done in the same way in both groups, so that two perpendicular radiographs were taken immediately after the operation (day zero) and also on the 15th, 30th, 45th and 60th days after the operation.

➢ *Post-Operative Care*

Intramuscular injection of penicillin 3:3:6, one injection before the operation and three injections after the operation, every 48 hours. Sutures were pulled 10 days after the operation.

➢ *How to Prescribe Medicine in Two Groups*

- First Group: nandrolone decanoate drug was injected intramuscularly in a muscle in the amount of 2 mg/kg at intervals of 0, 7, 14, 21, 28, 35, 42, 50 and 57 days.
- Second Group: spirotron acetate tablets were fed to rabbits daily until day 57 at the rate of 5 mg/kg. Evaluation methods.

➢ *Assessing the Situation of Step 1*

- Step evaluation was done based on Smith's advanced method. In this way, the walking condition of animals and hind legs was divided into grades 0 to 4 as follows:
- Grade Zero: Inability to bear weight on the operated limb completely.
- First Degree: the animal put the tip of the paw on the ground.
- Second Degree: the animal put the tip of the claw and part of the fingers on the ground.
- Grade 3: The animal was fully weight bearing but with lameness.
- Fourth Grade: The animal could bear weight without the slightest limp.

The gait status of the animals after the operation was evaluated by one person on different days until the end of a 60-day period to examine the gait status of each group, on days 0, 7, 14, 21, 28, 35, 42, 50, and 60 with groups Others were compared.

In this evaluation, the process of filling the holes created in the tibia bone in terms of callus formation was evaluated on days zero, 15, 30, 45 and 60 on the radiographs prepared. In this way, the amount of callus formation was determined on different days after the operation.

➢ *Histopathological Evaluation*

In this study, 60 days after the operation, all animals were killed by intra-abdominal injection of barbiturates with a high dose, and the areas of the bone where callus was formed. The surrounding tissues were separated and removed from the adhesion site. The samples were placed in 10% formalin solution and transferred to the laboratory for microscopic studies. In order to accurately evaluate the healing effect, the samples were first limed with a 5% citric acid solution that was fixed with a 1% urea solution, and then the bone tissue was stained using the usual method of hematoxylin and eosin (H8E).

III. RESULTS

A. Results Related To Step Condition

In table No. (1), the mean and standard deviation of scores related to the state of step subsidence in two groups have been recorded. If it is clear, the gait status in each group improves significantly from day one to 60 days. ($P < 0.05$). On the other hand, there is no significant difference between the two groups at different times and between different times in each group ($P>0.05$).

Except for day one and day seven, there is a significant difference in both groups ($P<0.05$), which is completely normal.

For example, the condition of gait in both groups shows 80% improvement on the seventh day and almost 100% improvement from the fourteenth day onwards.

B. Radiographic Results

In table number (2-4) and (pict Figures 1-10) the mean and standard deviation of the amount of callus formed within 60 days after the operation has been recorded. There is a meaning. ($P<0.05$).

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Thus, there is no significant difference in the amount of callus formed in the two groups until the 30th day. (P>0.05).

But there is a significant difference between the 30th day and the 45th day and the 45th day to the 60th day in both groups.

So that in the group, one hole with a diameter of 1 and 2 mm was filled (Figure 4) and sixty holes with a diameter of 3 and 4 mm were filled in a day. (Figure 5). In the second group, the callus is formed by the 30th day (Figure 6-8).

On the 45th day, the hole with a diameter of 2 mm was filled (Fig. 4-9), and there is a significant difference from the 30th day to the 60th day (Fig. 4-10) in both groups (P<0.05). . But there is no significant difference from day 0 to day 30 (P>0.05).

Sometimes there is a significant difference between the two groups (P<0.05) and sometimes there is no significant difference (P>0.05). So that there is no significant difference between the two groups on days 0, 15 and 30, but there is a significant difference between the two groups on days 45 and 60. (P < 0.05).

C. Pathology Results

The histological evaluation of the sections prepared from the rabbits of the first and second groups indicated the occurrence of bone healing and callus formation in both groups. Although comparing the cross-sections obtained from these two groups, it showed that in terms of quality, the bone callus formation in the rabbits of the first group was wider and more voluminous, and basically the whole process of bone repair showed a more advanced stage compared to the animals of the second group. In the histological study of soft tissues, the observed changes were all non-specific and not of special importance.

Table 1: The Mean and Standard Deviation of the Gait Condition within 60 Days after Smith's Surgery

	Day									
	60	50	42	35	28	21	14	7	1	Group
*	0±4	0±4	0/1±3/8	0/2±3/7	0/2±3/7	0/4±3/5	0/2±3/5	0/2±3/1	0	I
*	0±4	0±4	0/1±3/8	0/2±3/7	0/1±3/7	0/2±3/5	0/2±3/5	00/2±3	0	II
	NS	NS	NS	NS	NS	NS	NS	NS	NS	

Table 2: The Mean and Standard Deviation of the Radiographic Callus Formed During 60 Days after the Operation in Millimeters

	Day					
	60	45	30	15	0	Group
*	4	2	0	0	0	I
*	2	1	0	0	0	II
	*	*	NS	NS	NS	

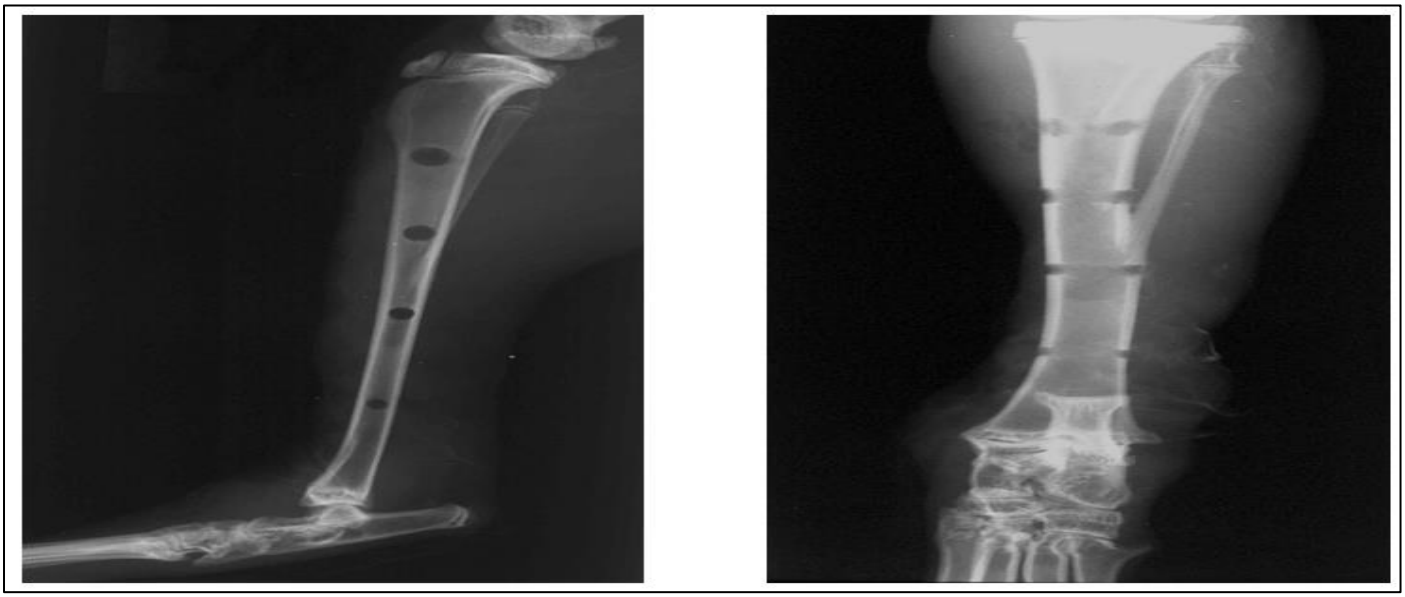

Fig 1: Radiography of Group One on Day 0

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Fig 2: Radiography of Group One on Day 15

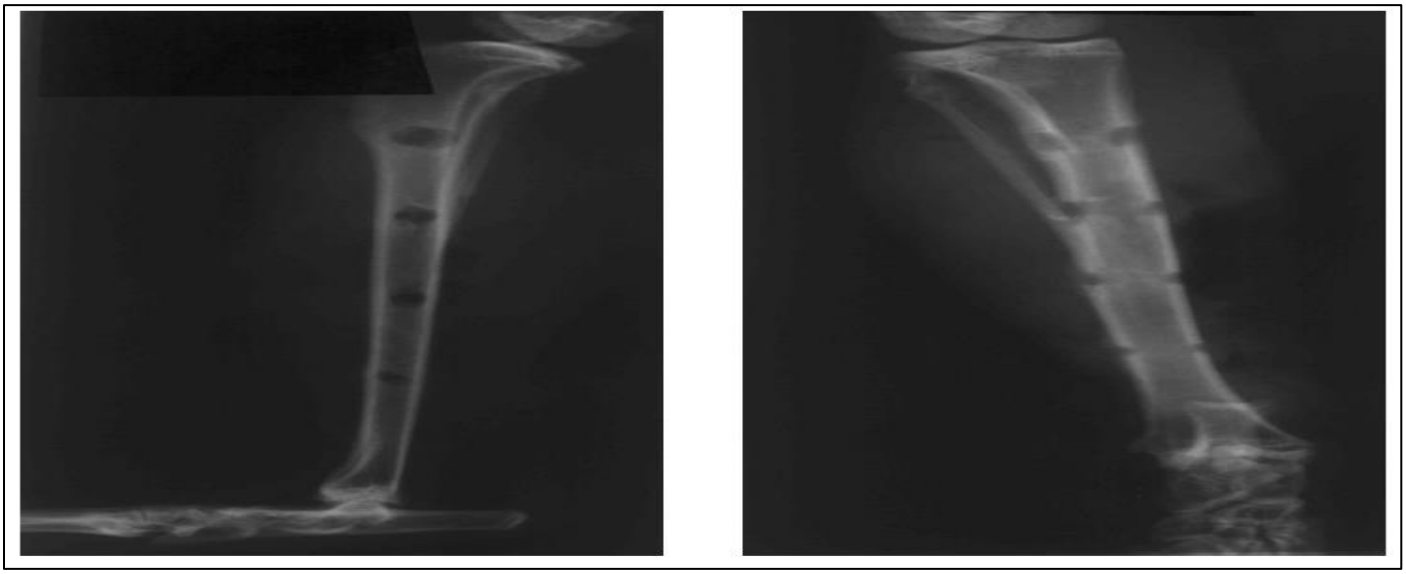

Fig 3: Radiography of Group One on Day 30

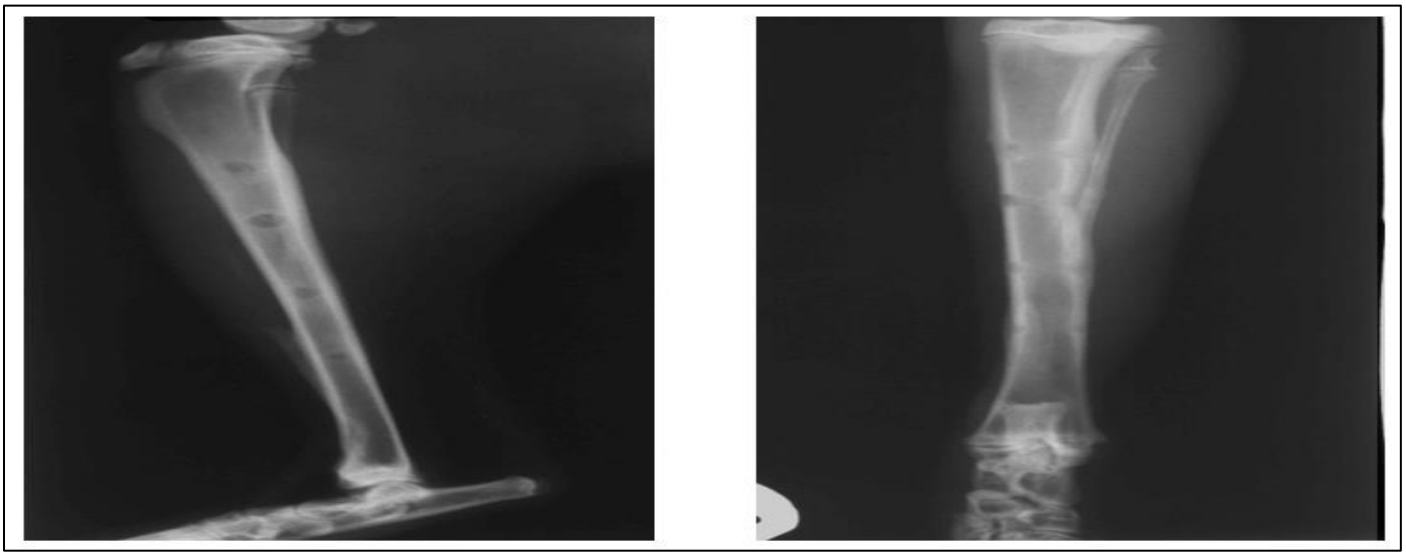

Fig 4: Radiography of Group One on Day 45

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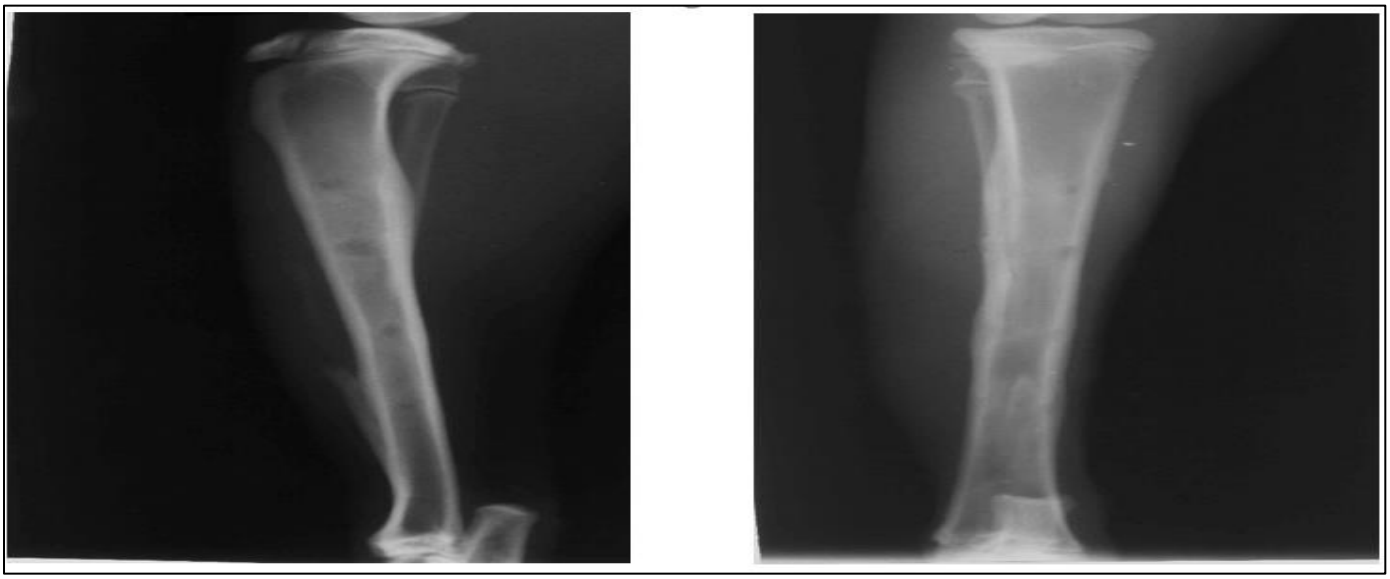

Fig 5: Radiography of Group One on Day 60

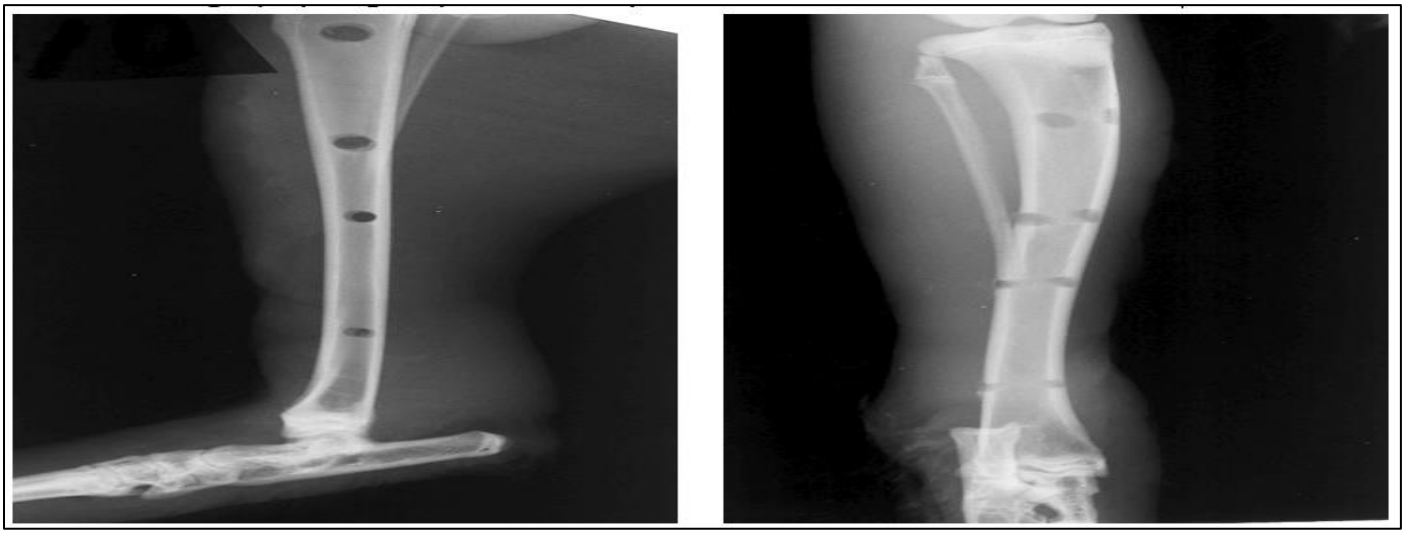

Fig 6: Radiography of group two on day 0

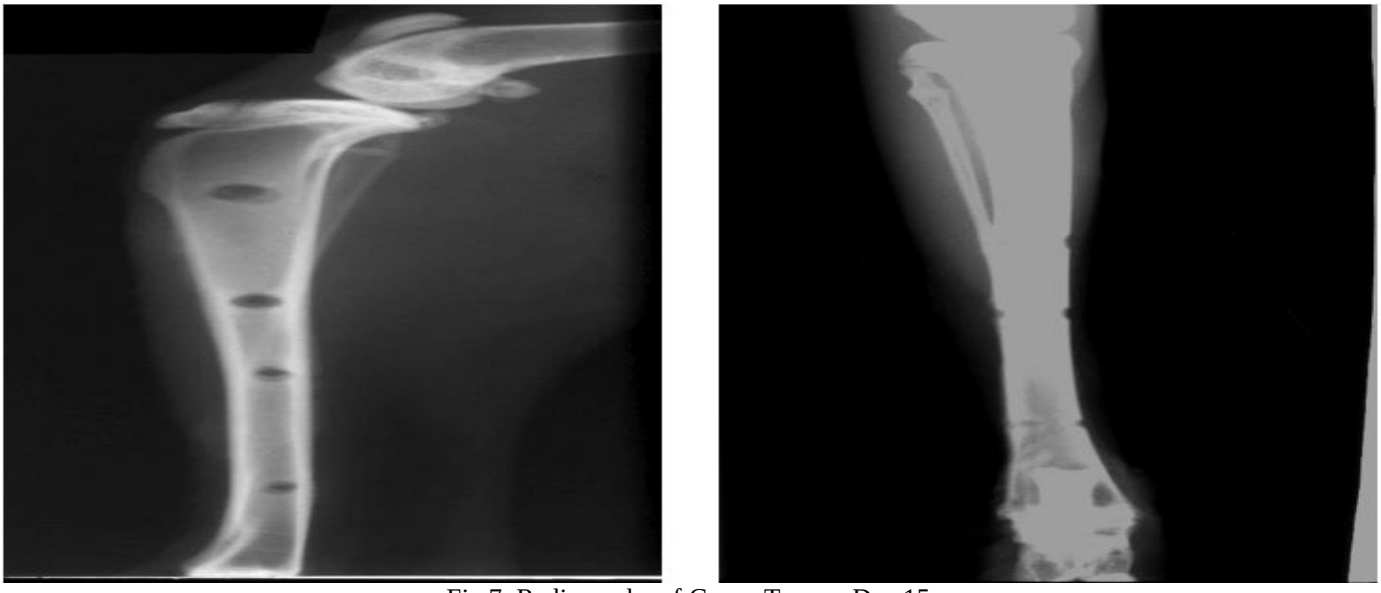

Fig 7: Radiography of Group Two on Day 15

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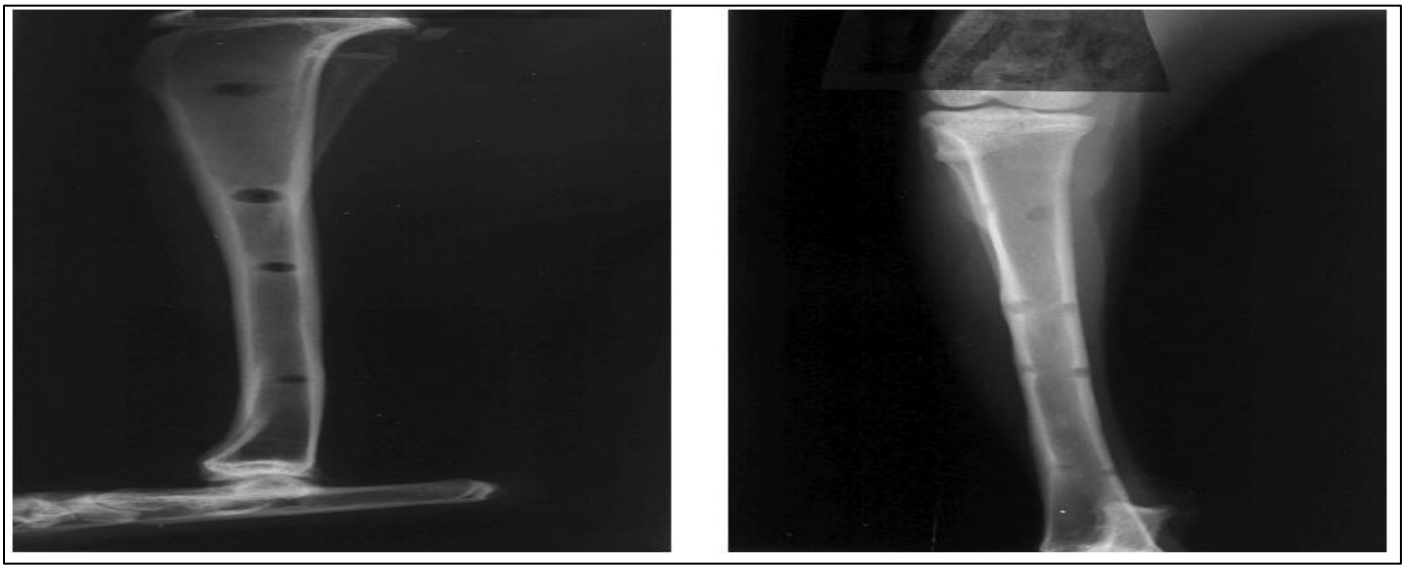

Fig 8: Radiography of Group Two on Day 30

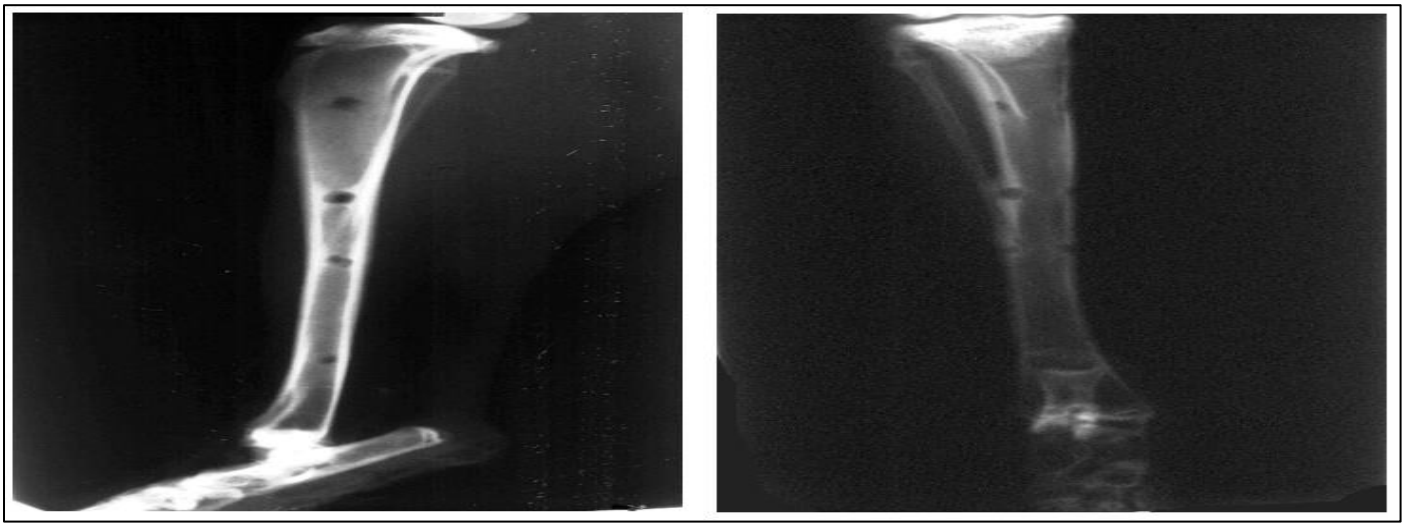

Fig 9: Radiography of Group Two on Day 45

IV. CONCLUSION

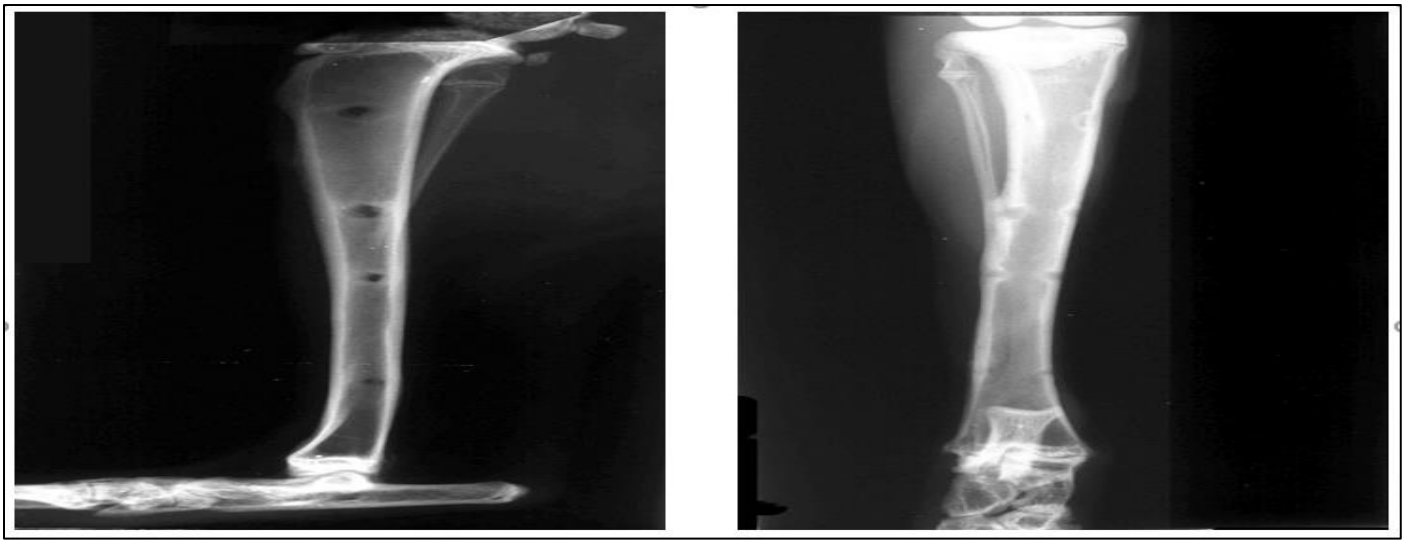

Fig 10: Radiography of Group Two on Day 60

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Nandrolone causes a significant increase in bone mineral content (IA). In a study of monkeys whose ovaries were removed, the amount of phosphate compounds and collagen in the cortical bone one or two years later was higher, but the amount of carbonate was lower. Treatment with nandrolone caused the return of most of the side effects caused by the removal of the ovaries until the amount of bone formation reached the same level as the control group, i.e. the group in which the ovaries were not removed, but the bone after the removal of the ovaries is chemically different from the healthy bone. Especially in certain areas of the bone, which reduces the quality of the bone. (6A, 3A, 5A). But in another relation, it was shown that the decrease in bone quality is not significant. (4A).

Treatment with nandrolone increases bone so that the level of bone mass is equal to that of non-sterilized animals (6A, 5A, 4A).

According to the above results, removal of the ovary along with treatment with nandrolone has no effect on the degree of bone mineralization in terms of phosphate to protein ratio, but the amount of phosphate in cortical and subchondral bone increased due to removal of the ovary and the amount of carbonate decreased in comparison with the control group. (7A, 4A). Contrary to some other theories (3A), no changes in carbonate contents were observed in the trabecular areas, and it was determined that treatment with nandrolone causes the return of the lost carbonate. (7A, 6A, 5A, 4A).

Among the other effects of Nandrolone, there is a 50% increase in weight without the effect of 25 mg every three weeks (7A).

In another study, two groups were studied, in the first group, estrogen and progesterone were used, and in the second group, estrogen and progesterone were used along with nandrolone. It was found that the cancellous bone increased by 21% in the first group and 29% in the second group after 6 months. And then it remained constant and obtained the result that the bone density in both groups has a significant increase compared to the baseline. ($P<0.55$). But there is no significant increase between the two groups. This result is contrary to some sources (A 8 and A 10).

In another study, it was shown that intramuscular injection of 50 mg of nandrolone is effective on calcium metabolism and bone density in samples that have used corticosteroids for a long time and suffered from osteoporosis with the mentioned amounts of nandrolone, which is one of the abnormal effects of corticosteroids. It has been prevented and also seems to prevent bone resorption. without stimulating bone formation. (A9).

It was also shown that bone formation clearly decreases during treatment with estrogen and progesterone, but if long-term treatment with anabolic steroids (nandrolone) is done at the same time, it does not cause bone disorders (A10). In another study, it has been shown that nandrolone treatment increases bone mineral content, which is not the result of a direct increase in bone formation, and another mechanism is involved, i.e. a combination of reducing bone resorption and increasing muscle mass, both of which have a beneficial role in maintaining They have bones (A11). Unconventional and excessive use of androgens causes the loss of sexual desire and the relationship with anti-androgens basically affects all androgen-dependent organs and its activity, for example, on the gonads, sperm production, and the skin. And pure non-steroidal anti-androgens such as Fultamide and Anandrone, there is a difference B) 1.(

Anti-androgen drugs are used in cases including androgen-dependent disorders, skin acne, alopecia, seborrhea, advanced prostate carcinoma, premature puberty and high sexual sensitivity in males. These have lipophilic properties and can penetrate around the hair follicle B) 1). In cases of treatment with these drugs, the secretion of gonadotropins and estrogen stops completely, and bone maturation slows down B) 2 and B11.(

Estrogen, progesterone, medoxyprogestone and cyproterone acetate cause changes in body composition, such as weight gain, decrease in muscle mass, increase in body fat, decrease in bone density, anemia, and hair changes B) 3 and B11.(

In another study, two groups were investigated, in the first group of males who changed the sex of the female (estradiol and cyproterone acetate were prescribed) and the second group of females who changed the sex of the male (testosterone was prescribed). The results were as follows. that estrogen and cyproterone acetate decrease bone formation, and in the second group, androgen administration increases bone formation. B) 9.(

Intramuscular administration of anti-androgens (cyproterone acetate) causes a severe decrease in the level of testosterone in the plasma and will also lead to premature and incomplete antler mineralization in deer. B) 12(

According to the studies conducted and the results obtained from this research, it seems that despite the discrepancies that exist in some cases, steroid androgens nandrolone can cause calcium deposition and faster formation of bone tissue in cases of bone defects.

REFERENCES

[1]. Abdalla, HI., Hart, DM., Lindsay, R., Leggate, I., and Hook, A., (1985). Prevention of bone mineral loss in postmenopausal women by norethi sterone. Obstet Gynecol 66:789-792, [ISI], [Medline].
[2]. Adami, S., Fossaluzza, V., (1991). The prevention of corticosteroid induced osteoporosis with nandrolone decanoate. Bone and Mineral , Volume 15, Issue 1, pp: 73-81.
[3]. Areyl, B., (1968). Human histology. A text book in outline form. 3rd ed. WB saunders co. philadelphia, London & Torento.

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[4]. Biller, BMK., Saxe V, Herzog, DB., Rosenthal, DI., Holzman, S., and Klibanski, A., (1989). Mechanism of osteoporosis in adult and adolescent women with anorexia nervosa. Jclin Endocrinol Metab 68:548-554, [Abstract].
[5]. Birkenhager, JC., Erdtsiekck, R.J., (1992).Can nandrolone add to the effect of hormonal replacement therapy in postmenopausal osteoporosis.
[6]. Bone and mineral, Volume 18, Issue 3, pp: 251-265.
[7]. Bonjour, Jp., Theintz, G., Buchs, B., slosman, D., and Rizzoli , R., (1991). Critical year and stages of puberty for spinal and femoral bone mass accumulation during adolescence. Jcline Endocrinol Metab 73:555-563, [Abstract].