

PATHOLOGICAL EFFECT OF DEXAMETHASONE ON HEALING OF RABBIT WOUND

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ABSTRACT

In this study 15 rabbits were divided into three groups ,each group contain five rabbit were submitted to surgical section in the skin layer 3-5 cm long after anasesthesia and cleaning the part from the hair by sheaving . The surgical section was made by scable and then the wound sutured by silk band 2.5 cm and then administrated the dexamethasone 1 mg / Kg body weight of animals of second and third groups of this study . After that the skin spicemen were taken for histopathological sections to preperd slid.

The first group was considered as control with no administrated of dexamthasone , the second group treated as 1 mg / Kg body weight dexamthasone and sections were taken after 7th days , the third group were also treated with dexamthasone at the 1 mg /Kg and the skin sample were taken after 14 th days.

The present study it was found that dexamthasone have no effect on the wound healing after 7th days or 14th days but the collagenization , epithelization and fibroblast content were less in the dexamthasone group compered with control group . The vascularity and the degree of inflammatory cells were more intense in the dexamthasone group compared with control group.

INTRODUCTION

Dexamethasone is a synthetic glucocorticosteroid which has minimal mineralocorticoid activity it is potent anti-inflammatory drug with 25-50 times .The potency of hydrocortisone and is up to sixteen times as potent as prednislone [1]. In the Knockout mice the dexamethasone exhibit immune suppression due to T cell and thymocyte impairment [2, 3]. The mechanism of action of this effect is un clear but believed to be related to the use of a phosphate ester of the steroid dexamethasone effectivity, decrease the incidence of postoperative nausea and vomiting remains a common distressing problem after anesthesia and surgery . The dexamethasone

therapy increased or decreased appetite, stomach bloating, nausea ,vomiting ,hiccups and heart burn [4].

Dexamethasone and hydrocortisone both displayed dose dependent relationships for impairment of healing, while over comparative doses, methylprednisolone failed to affect healing significantly[20].

Glucocorticoids are believed to hinder healing process causing decreased cell proliferation and revascularization and matrix production [8]. In addition to their anti-inflammatory and Immunosuppression effects ,another important glucocorticoid property is the ability to induce apoptotic cell death which has been described in many cell lines (e.g. epithelial and lymphoid) . Keratocyte apoptosis is probably an initiating factor in wound – healing response after refractive surgical procedure . The effect of dexamethasone on keratocyte apoptosis and proliferation were investigated . Because it's well established that glucocorticoid exert their biologic action by binding to specific intracellular receptors[9].

The aim of this study is know the effect of administration of dexamethasone on the skin healing in rabbits and appearance the efficiency of drug in the tissue repair .

MATERIAL AND METHOD

The study was done on 15 rabbits weighting (375-400) g ,in temperature controlled and ventilated room. Animals were housed for least 10 days before experiments for accumulation and they were given unlimited access to food and water during experiment .

Rabbits were randomly assigned to three groups of five animals they were anesthetized with Ketamine (15 ml /kg) and Xylazine (5ml/ kg) by subcutaneous injection .The hair was closely shaved with manual razor , and the surgical area disinfected with povidone –iodine. All surgical procedures performed under aseptic conditions by the same surgeon. A dorsal midline of abdomen incision measuring approximately 3-5 cm made through the skin of each animals until the muscular fascia was exposed . The dorsal wound margins were apposed an absorbable interrupted suture.

The first group of animal and the second group were administrated dexamethasone 1mg / Kg body weight IM. Histopathological examination was done by taking 1 cm³ of wound obtained from the caudal part on 7th days of first group and on 14th days of second group while the third group administrated physiological saline as control group ,the sections placed in 10% formalin ,embedded in paraffin ,sectioned and stained with Haematoxylin and Eosin stain for examined by light microscope.

RESULT

The observation period , no animals died in the control or dexamethasone groups . There was sever purulent inflammation on the third days after wound induction of control animals ,the principle constituent of the exudates is neutrophils which were the first line of cellular defense accumulates in the area of skin(Fig. 1) . There are hyperplasia of basal layers cells on 7th days (Fig. 2). But on the third days of treated animals with dexamethasone there was a large subcutaneous area of inflammation , large area of ulceration (Fig 3) ,and scar formation .

In the 7th days of administration of dexamethasone there was thickened epidermis (Fig. 4) , and there was fibrinous deposit in the dermis an area of ulceration (Fig. 5) and either area of purulent or suppurative inflammation compared with control animals that showed massive area of purulent inflammation with marked fibrinous deposit skeletal muscle as well as fibrinous materials in dermis with thickened epidermis (Fig. 6). In the (Fig. 7) there were marked dermal fibrinous inflammation and epidermal thickening on the 14th days .

There are a less changes in the healing of skin between the control animals and treated animals .

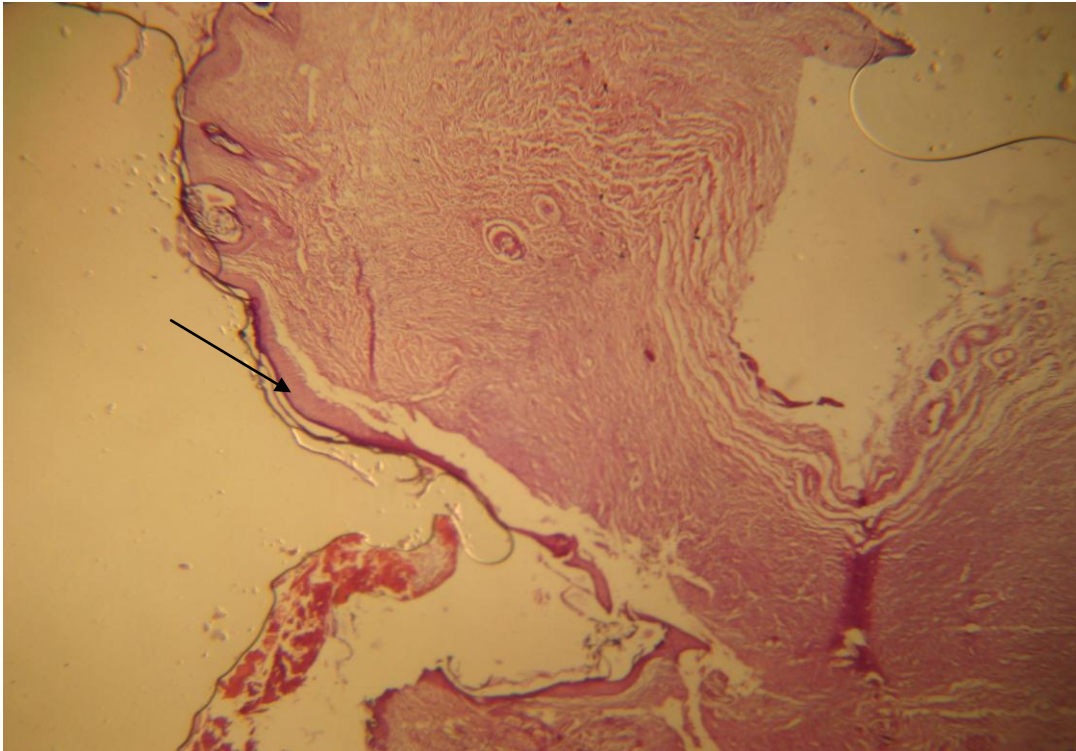


Fig. 1: section of skin rabbit in control group after 3days, note the purulent inflammation and fibrin. 4X (H&E).

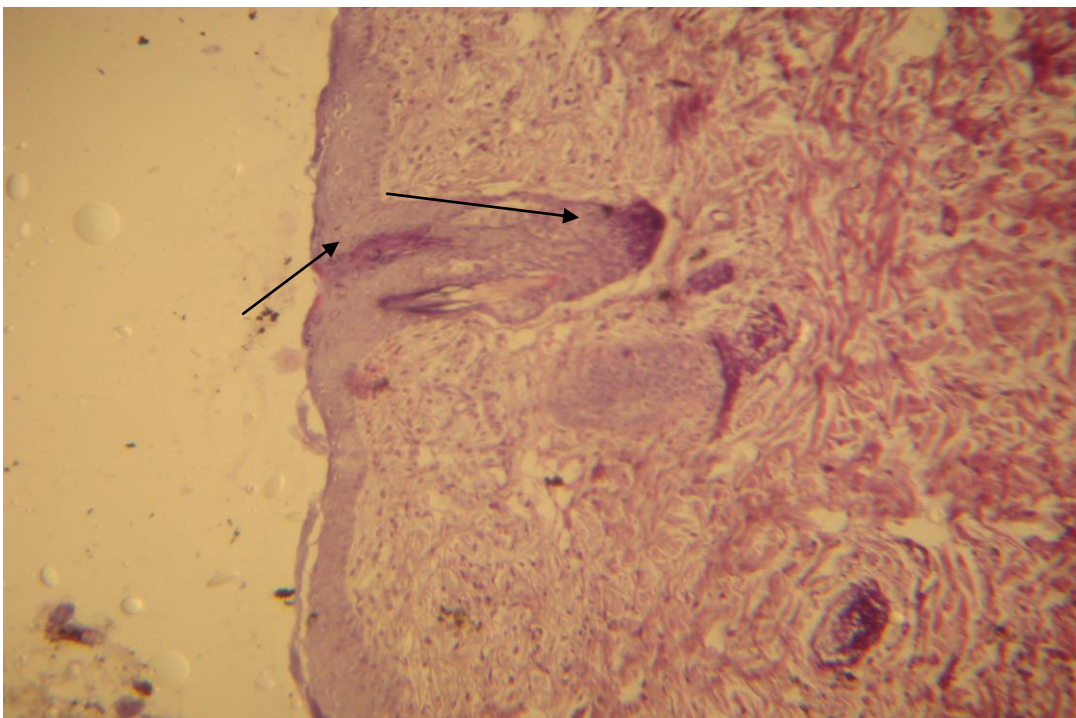


Fig. 2: section of skin rabbit in control group after 7days, note the hyperplasia of basal layer cells. 10X (H&E).

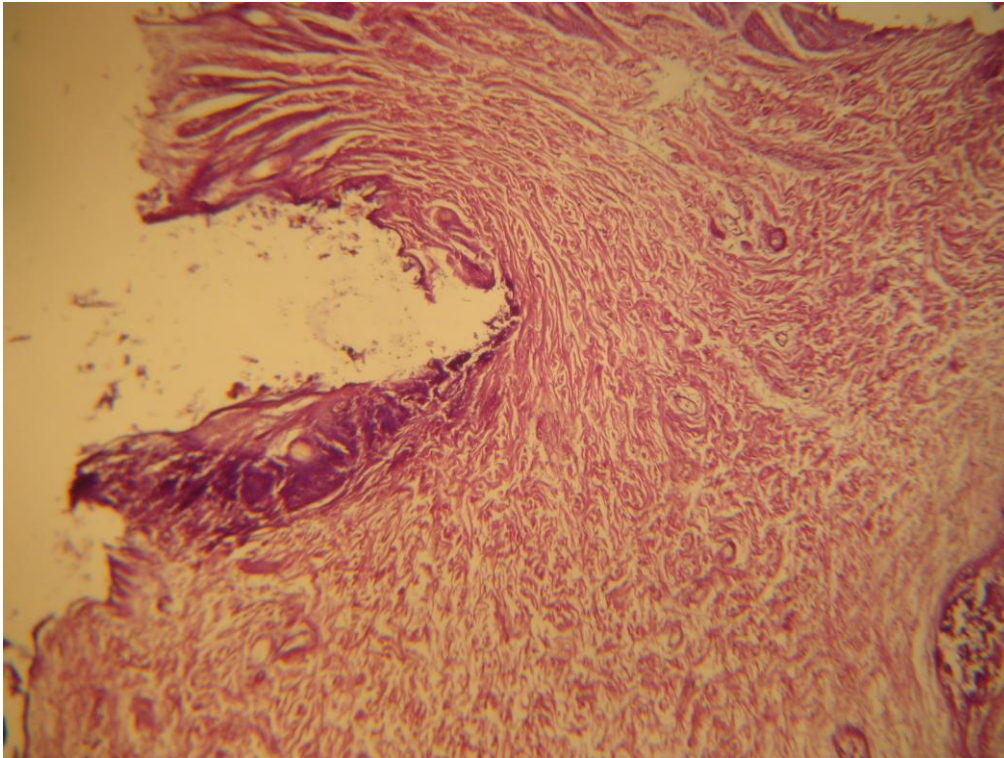


Fig. 3: section of skin rabbit in dexamethason group after 3days, note ulceration area and thickening of dermis. 10X (H&E)

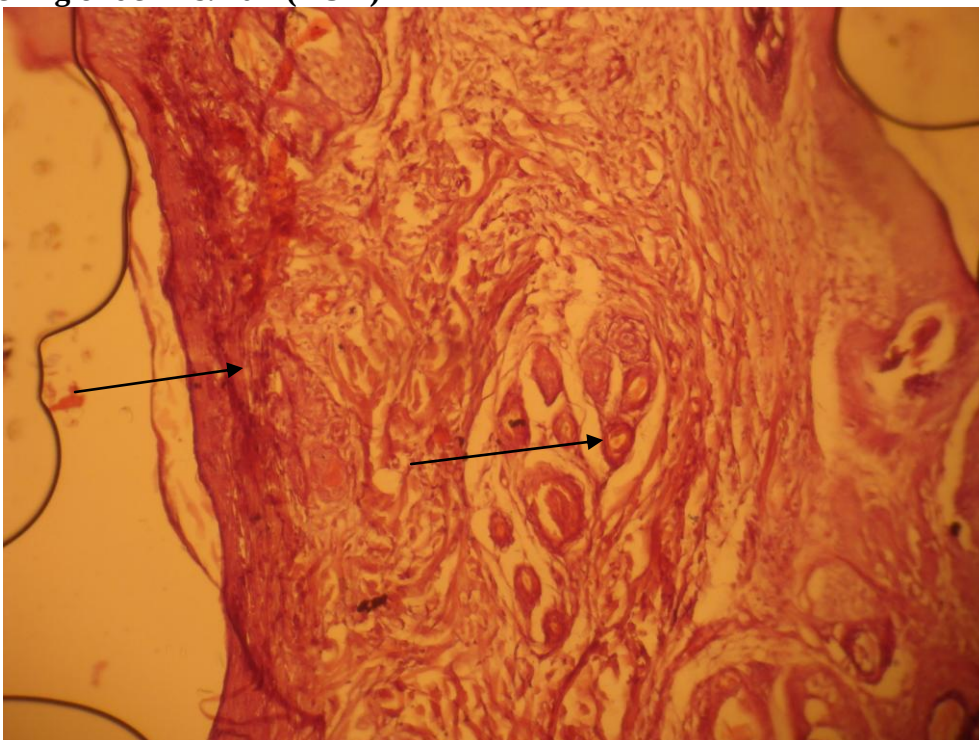


Fig.4 : section of skin rabbit in dexamethason group after 7days, note thickening of epidermis and marked fibrinous deposit between skeletal muscles . 10X (H&E).

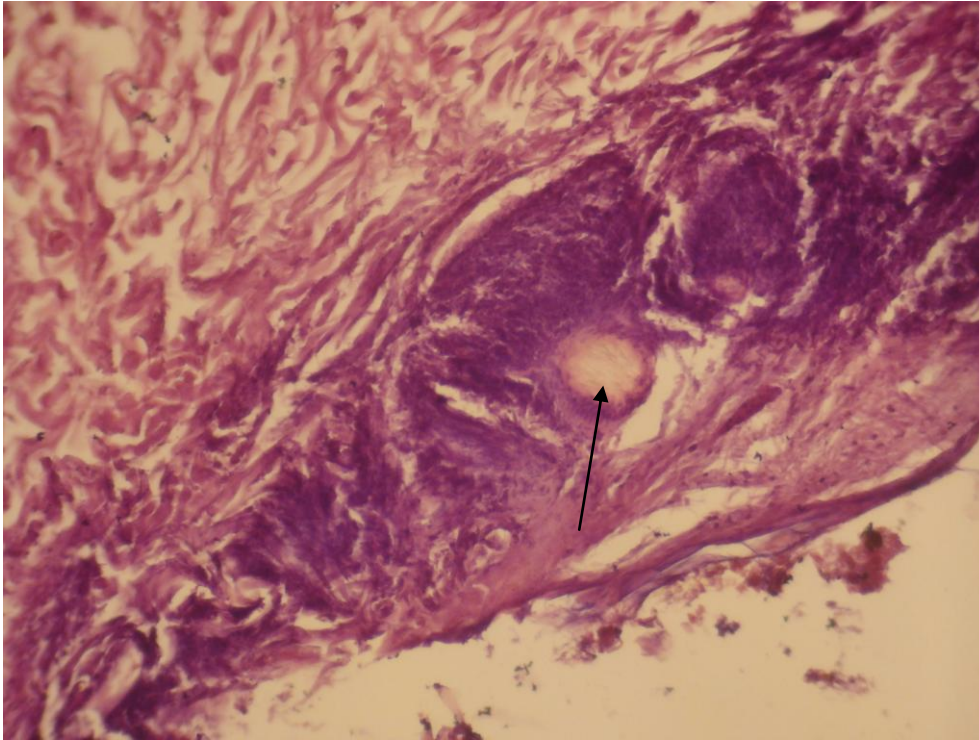


Fig.5 : section of skin rabbit in dexamethason group after 3days, note scar tissue. 10X (H&E).

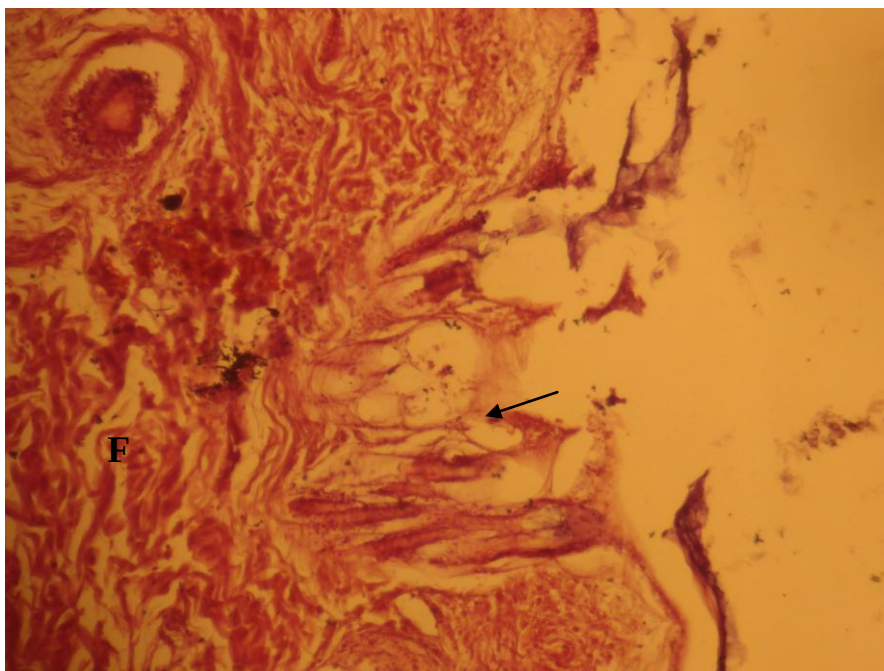


Fig.6 : section of skin rabbit in dexamethason group after 7days, note fibrinous material in derms (F) and purulent inflammation (arrow) . 10X (H&E).

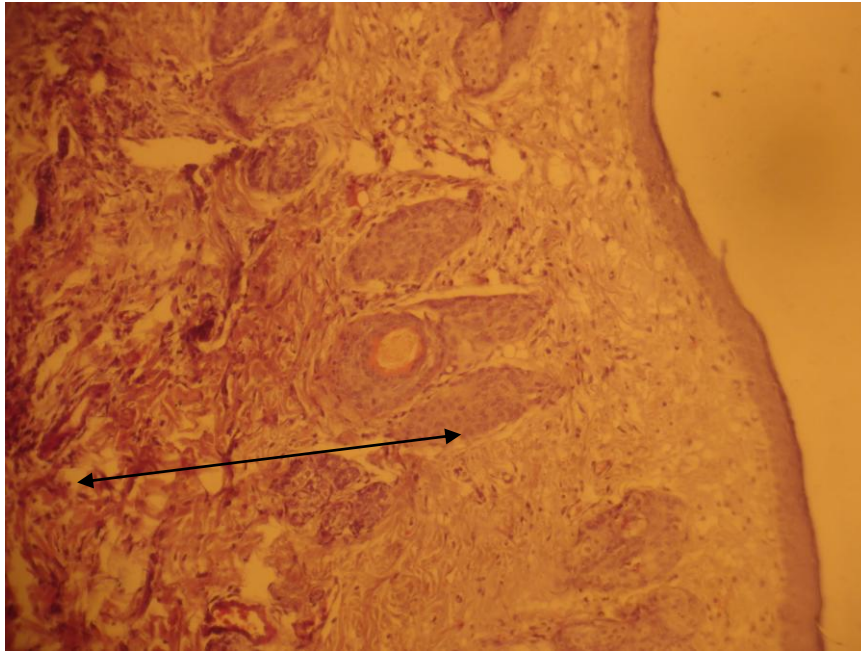


Fig.7 : section of skin rabbit in dexamethason group after 14days, note marked dermal thickening (arrow) . 10X (H&E).

DISCUSSION

In the present study there was sever purulent inflammation in the control group on third day because the essential phase of wound healing is the inflammatory phase characterized by increased vascular permeability ,chemotaxis of the cells from circulation into the wound area [6, 10 ,11, 12] .

The dexamethasone corticosteroid inhibit the inflammatory phase which causes delayed wound healing also it inhibited collagen synthesis in wounded tissues [13,14,15] .

Collagenization epithelization and fibroblast content were significantly less in the dexamethasone group and the vasocularity and the degree of inflammation cells were more intense in the dexamethasone group compare with control [6] .

Like all glucocorticoids ,dexamethasoneacts on the glucocorticoid receptor glucocorticoid including direct DNA binding which results in changes to gene transcription this results in changes to carbohydrate , protein and fat metabolism and it's decreased release of bradykinin ,tumor necrosis factor ,interleukin -6 , interleukin -2 ,and interleukin -6 as well as decreased production of prostaglandins [16 , 17] .

The presence of inflammatory cells and vascularity in the dexamethasone groups compared with the control group might be related to delayed inflammatory and proliferation

phases [5 , 17 , 18]. Dexamethasone decreases inflammation or swelling by stopping white blood cells, which normally fight infection, from traveling to area of the body where there is swelling . It's anti-inflammatory actions ,can actually stop the swelling around a tumors (especially on the spin, brain, and bone) , and the resulting pain and other symptom caused by tumors pressing on nerve ending [7]. Dexamethasone and other steroids suppress certain action of the immune system and also inhibit cytokines ,which are chemicals in the body that control inflammation . Increase collagenization and epithelization with fewer inflammatory cells and less vascularity provided evidence of repletion of granulation tissue to collagenous scar in the control group due to mice wound healing was rapid , and the gluco-corticoids exert their biologic action by binding to specific intracellular receptors [9 , 19] .

دراسة نسيجية لالتئام الجروح في الأرانب المعاملة بعقار الديكساميثازون

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الخلاصة

تضمنت هذه الدراسة على 15 أرنب تم تقسيمها عشوائيا الى ثلاث مجاميع كل مجموعة تتضمن خمسة ارانب خضعت للقطع الجراحي في طبقة الجلد وكان طول الجرح (3 - 5) سم بعدما تم تخدير الحيوان وتنظيف المنطقة من الفرو . تم قطع الجلد بواسطة المشروط المعقم بعدها تم خياطة الجرح بواسطة خيوط سلك قياس 2.5 سم وتم حقن عقار ديكساميثازون بجرعة 1 مغم / كغم من وزن الحيوان . اخذت عينات من الجلد إلى التقطيع النسيجي حيث اعتبرت المجموعة الاولى مجموعة السيطرة اما المجموعة الثانية حقنت حيواناتها بمادة الديكساميثازون واخذت المقاطع النسيجية بعد مرور 7 ايام و المجموعة الثالثة اخذت المقاطع النسيجية بعد مرور 14 يوم .

اظهر الفحص النسيجي ان العقار ليس له تاثير ايجابي على التئام الجروح سواء كانت بعد 7- 14 يوم ووجد ان محتوى مكونات الالتئام يكون من الكولاجين والخلايا الطلائية والخلايا الليفية وكثافة الخلايا الالتهابية تكون اقل في المجموعة التي حقنت بالعقار منه في مجموعة السيطرة .

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