

## Corticosteroid and Injuries: A Review of Human and Experimental Studies

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**Abstract:** By the end of forty decade, wondrous evolution occurred in medical science which caused to give a medical novel gift to Hench and colleagues due to characterization of corticosteroids effects on rheumatoid cartilage. Therefore, many researches were done to find out the properties of this fantastic hormone. Therefore, many researches were done to find out the properties of this fantastic hormone. Followed by identifying the side effects, Topical using of corticosteroids showed lower side effects compared with systemic uses. We evaluated the impacts of corticosteroids on different tissues which involved in injuries, focusing on the mechanisms, advantages and disadvantages. The goal of this review study is to guide the orthopedic surgeons and sport physicians to select better approach and to design better future studies without limitations.

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### 1. Introduction

By the end of forty decade, wondrous evolution occurred in medical science which caused to give a medical novel gift to Hench and colleagues due to characterization of corticosteroids effects on rheumatoid cartilage (1). Therefore, many researches were done to find out the properties of this fantastic hormone. Followed by identifying the side effects, Topical using of corticosteroids showed lower side effects compared with systemic uses. Over time, the anti-inflammatory effects of corticosteroids such as inhibiting of edema, fibrin deposition, capillary dilation and migration of leukocytes (2, 3) were known and these effects were not ignored treatment of sport injuries. Although, local injections of corticosteroid decrease inflammation and inhibit the decreasing of physical performance in humans and as follow make the acceleration in returning to exercise and competition, many authors have a contrast opinion and showed the disadvantages of corticosteroid injections in their reports.

Many experimental studies have been designed in assessing the efficacy of corticosteroids but the main point is that the effect of corticosteroid is different in species of animals and also in different cells indifferent tissues. The effect of corticosteroids was showed different on fibroblast cells between animals and humans. This difference has been was also shown between the different cells in different tissues of human body in growth states and other factors (4). For example corticosteroids inhibit the hepatocytes growth and in contrast increase the

growth and proliferation in fibroblasts (5, 6). Whether or not, we shouldn't ignore the information from experimental studies. Because of different effects of corticosteroids on different tissues, evaluation of effects on different tissue separately, will be useful. We evaluated the impacts of corticosteroids on different tissues which involved in injuries, focusing on the mechanisms, advantages and disadvantages. The goal of this review study is to guide the orthopedic surgeons and sport physicians to select better approach and to design better future studies without limitations.

### 2. Review of Human and Animal Studies

The Corticosteroids are the drugs that in addition to therapeutic effects for many injuries may be used for increase the cardio-vascular performance spontaneously. Although this drugs use for increasing cardio-vascular performance, but the studies don't agree with this theory. In a double blind study, Soetens and colleagues injected 1mg ACTH or placebo to 16 professional cyclists 1 hour before cycling and found no increasing in performance (7, 8). Also, a study showed that corticosteroids had no role in the prevention of exercise induced arterial hypoxemia (EIAH) and blood SO<sub>2</sub> did not change (9).

Corticosteroids have therapeutic aspects too. Many studies have been done on the various impacts of this hormone in humans and animals. Advantages and disadvantages of using of corticosteroid in sport injuries are reported but the results of studies are

controversial. Limitations in methodologies, not to mention to chronic tendinopathy and systemic disease in case reports, not enough follow-up time, not to determine tendon rupturing when there is no corticosteroid treatment, inability to generalize the results of experimental studies to humans, errors in diagnosing of some injections and low accuracy of injection without imaging guide are the cause of the controversial results in studies. Corticosteroids can be used as systemic or topical however systemic absorption of local administrations should not be ignored. Harmon and colleagues reported that, despite few evidences exist to prescribe the oral corticosteroids in musculoskeletal injuries, 59% of physicians especially who have fellow ship of sport medicine prescribed it in primary care sport medicine center. They also reported that one third of these physicians prescribed oral corticosteroids for acute cases, one third for the chronic cases and third for both cases.

Although in some studies have been reported the advantages of the use of systemic corticosteroids in treatment of sports injuries, Nichols in review article in 2005 showed that no study recommended of using oral corticosteroids in the treatment of sports injuries (10). Vergas and Ross (11) compared the effects of intravenous injection and oral administration of corticosteroids in patients who have done the ACL repair with the group were undergoing ACL repair, but were received different drugs. In the group which had used corticosteroids, 50% decreasing in using analgesic drugs, 59% reduction in hospitalization time and 38% faster to start walking were found than the control group. The prevalence of complications did not differ between groups 1 year after surgery.

Systemic corticosteroids effects in animals have also been investigated. Wrenn and colleagues (12) in an experimental study showed that intramuscular administration of 10mg/kg cortisone in dogs inhibited the formation of fibrous tissue around the tendon, but decreased breaking point of sutured tendons and tendon tensile strength compared to control group. Unlike the results of this study, other studies showed use of systemic corticosteroids in Aschille tendons in Rats have not role in tension to failure.

The evidence-based advantages of using systemic corticosteroids in Acute Spinal cord injury have been reported. Patients who have spinal cord injury frequently have permanent and often devastating neurologic deficits and disability. This injury mostly occurs in men and sports such as football, horseback riding, wrestling and jumping on a trampoline. the second US national acute spinal cord injury study (NASCIS2) compared 24-hour

treatment with methylprednisolone or placebo in acute spinal cord injury in 333 patients, and reported patients who received corticosteroid within 8 hours after injury had better motor function and sensation 6 months after injury (13). Similar results with the same treatment regimen in a study on 151 patients in Japan were reported. Also the using of methylprednisolone in acute spinal cord injury for 48 hours was showed to have better outcomes than 24 hours (121).According to these results, currently high dose (30mg/kg) of methylprednisolone is used for treatment of acute spinal cord injury.

About the use of systemic corticosteroids, in addition to advantages, disadvantages also has been reported in previous studies. Although complications such as fractures, osteonecrosis, osteoporosis, especially in the high dose and permanent use were reported in the studies (6, 10) but the prevalence of short-term systemic corticosteroids side effects in athletes is not well specified (3). Madanagopal and colleagues showed 6 % short-term side effects of oral corticosteroids in high school and university athletes (14). This study has many limitations respectively. First, Athletes didn't follow for a long time. Second, the athletes did not call all the complications to physicians when they recall. Third, the study measured the effects on immature skeletal bodies which may vary with the mature types. The local treatments of corticosteroids are used more in injuries. Intra-articular injection, pretendinous injection, inhalation, intrabursal injections are the samples. Inflammation of soft tissues that may be caused by overuse or trauma can recover by corticosteroids injections.

Rotator cuff injuries are common in sports that are leading to shoulder pain. These injuries are seen more in sports which have overhead activities like serving in tennis, spiking in volleyball, throwing a football or baseball. Shoulder pain causes discomfort in the patient rehabilitations, reduced daily activities and sleep disturbances. So pain control is very important. One systemic review study has shown that the drug of choice for pain management is corticosteroids (15). In a study about the impact of corticosteroids on the outcome of rotator cuff tendinitis, improvement / remission introduced as a more important outcome than improving in range of motion and reducing pain, which can help in calculating the number of patients needed to treat (16). This recommendation also has supporters in other studies.

Price and colleagues (17) reported that corticosteroid injections were much better than lidocaine injections in the treatment of lateral epycondylitis and the rate of relapse was similar in both groups However, the Newcomer and colleagues

showed that patients who have lateral epicondylitis for a period of less than four weeks, had no benefit from corticosteroid injections and rehabilitation should be the first line of treatment. Labelle and colleagues in a systemic review in 1992 evaluated the impact of different treatments on lateral epicondylitis. The study included 5 randomized clinical studies and they noted that because of poor quality in methodologies and controversial results, there were no evidences for distinction of any treatments (18).

Assendelft and colleagues in a comprehensive systemic review in 1996, survey 11 studies and they reported also there is lack of evidence for corticosteroid injections. However, they pointed out that corticosteroid injection is safe and had beneficial effects on Short term (2-6 weeks) (19). Golfer's elbow or medial epicondylitis is an inflammation of the flexor muscle tendon in medial side of elbow. Although these injuries like tennis elbow more to be seen in the racquet sport in other sports such as bowlers, archers, and weight lifters are also seen (20).

Studies showed that short term effects of corticosteroid injection was helpful in the treatment of this injury but the patients outcomes is not different in long term follow-up (19). In patients with recalcitrant medial epicondylitis corticosteroids injection has been recommended too. Trigger Finger affects the tendons in the finger or thumb and can cause it to lock in a bent or flexed position. The repetitive nature of the golf swing puts a lot of pressure on the fingers, especially if the grip is too tight. Female players and players over 40 tend to be more prone to Trigger Finger. Ignoring the early warning signs and continuing to play will probably make the condition much worse. It is also more likely to occur if the athlete already has a hand injury. In the treatment of trigger finger, Lambert and colleagues found 60% success of the treatment with corticosteroid injections compared to 16% success in local injection of anesthetic.

As like as upper extremities in the lower extremities, corticosteroids are used especially in the knee. Bursitis around the hip and knee, surrounding knee tendinopathy, intra-articular injections, Achillettendinopathy, ankle impingement syndrome and plantar fasciitis are the samples. Trochanteric bursitis is one of the common causes of hip pain in athletes. This bursitis is more in runners and in sports that are related to running such as soccer and football. A retrospective cohort study comparing treatments for trochanteric bursitis showed a 2.7-fold increase in the number of patients who were pain free five years after a single corticosteroid injection compared with those who did not receive an injection (21). The most common indications for corticosteroid

injection in knee injuries include patellar tendon injuries, damaged hamstring, pes anserine bursitis and IlioTibial Band Friction Syndrome (ITBFS). Blazina et al first used the term jumper's knee (patellar tendinopathy, patellar tendinosis, and patellar tendinitis) in 1973 to describe an insertional tendinopathy seen in skeletally mature athletes (22). Jumper's knee usually affects the attachment of the patellar tendon to the inferior patellar pole. The definition was subsequently widened to include tendinopathy of the attachment of the quadriceps tendon to the superior patellar pole or tendinopathy of the attachment of the patellar tendon to the anterior tuberosity of the tibia. Although studies showed the effectiveness of corticosteroid injection, but many studies indicated that corticosteroid injections were the cause of worsening (changed the stage III to stage IV) (23).

Many studies also have been performed on animals. In a study, biomechanical properties of tendons after bilateral corticosteroid injections in retrocalcaneal bursitis were far less than reported in unilateral injection. Ferland and Uthoff showed 100 % of intra-tendinous corticosteroid injection in the albino rat in Achilles tendons had necrosis at the injection site. The Rats with pretendinous injection had 95% healthy structure in tendons. In this study, no necrosis was found in rat tendon by injected saline (24). Noys and Nussbaum demonstrated that direct injection of corticosteroids in Rhesus Monkey ACL reduced tensile strength one year after injection. However, no changes were found in tensile strength or histology in monkeys who had intra-articular injections (25).

Kepetanous showed that repeated injection of corticosteroids into the tendon in a group of rabbits, reduce the formation of adhesion, but tendon weight, load to failure and energy to failure also decreased (26). In experimental studies the effect of corticosteroids on the muscle was evaluated. Guttu and colleagues evaluated the changes in the intramuscular injection of corticosteroids and analgesics in the Rat. Rats injected by corticosteroid injections with bupivacaine had been suffered extensive necrosis of muscle fibers for more than four weeks. However, the corticosteroid injection alone had no such symptoms (2). Although studies on animals teach us much information, but generalizing of these results to humans is ambiguity.

### 3. Conclusion

Although there are many reports in corticosteroids and their effects on injuries but limitations in studies cause to not to receive to exact decision in use of corticosteroids in sport injuries. We

recommended future studies should be design in mentioned to described biases and limitations.

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