PHARMACOLOGY OF CORTICOSTEROID THERAPY IN THE HORSE

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The corticosteroids are divided into two major groups: the mineralocorticosteroids and the glucocorticoids. The glucocorticoids are the anti-inflammatory corticosteroids.

The Glucocorticoids

1. Plasma Levels and Control

Cortisol and corticosterone are the principal glucocorticoids in equine plasma; their rate of secretion is probably about 0.5 mg./kg./day. Their synthesis and secretion are under the direct control of the adrenocorticotrophic hormone (ACTH) (Fig. 1).

The rate of secretion of ACTH and thus the plasma levels of glucocorticoids are directly influenced by factors such as stress, cold, hypoglycemia etc.[7]

2. Mechanism of Action

The glucocorticoids act only after being transported into the cell nucleus (Fig. 1) where they give rise to synthesis of new protein. These proteins re-direct the metabolism of the cell and thereby produce the pharmacologic effects of the glucocorticoids.[6] Most pharmacologic effects of the glucocorticoids will therefore take several hours to develop (Fig. 2).

3. Pharmacologic Actions

(a) In general, the dominant action of the glucocorticoids is anti-anabolic. As a rule, they tend to inhibit cell growth and lead to a breakdown of cells. These effects are seen after local or systemic administration.

4. Systemic Actions

(a) Glucocorticoid administration leads to an increased breakdown of protein and lipid which gives rise to an increase in liver glycogen and blood sugar.

(b) In the blood, glucocorticoids increase the packed cell volume (P.C.V.) and polymorphs, reduce lymphocytes and basophils. The effects on the destruction of lymphatic tissue are marked and lead to their use in the therapy of lymphoma. The hemogram is characteristic and is sometimes called the glucocorticoid hemogram.

(c) Glucocorticoids suppress growth (anti-anabolic effect).

(d) They cause osteoporosis which may lead to compression fractures and

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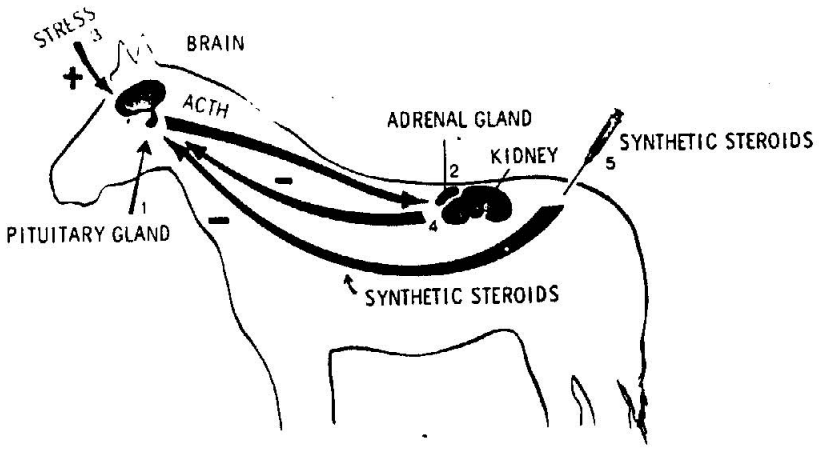

ACTH IS SECRETED BY THE PITUITARY GLAND (1), AND REGULATES THE ACTIVITY OF THE ADRENAL GLAND (2). STRESS (3), CAN INCREASE THE RATE OF RELEASE OF ACTH AND THUS THE ACTIVITY OF THE ADRENAL GLAND. ADRENAL HORMONES, FROM EITHER THE ADRENAL CORTEX (4), OR THE VETERINARIAN'S SYRINGE ACT TO INHIBIT THE RELEASE OF ACTH BY A FEEDBACK INHIBITION MECHANISM.

Fig. 1. Control of Plasma Corticosteroid Levels in the Horse.

Adrenocorticotrophic hormone (ACTH) is secreted by the pituitary gland (1) and travels in the blood to the adrenal, where it regulates the activity of this gland (2). Various forms of stress (3) can increase the rate of release of ACTH and thus the activity of the adrenal gland. The blood levels of corticosteroid from either the adrenal (4) or administered by injection (5) act to inhibit the release of ACTH by a feed-back inhibition mechanism. Administration of prolonged high levels of steroid (5) can lead to atrophy of the adrenal gland by suppressing the release of ACTH. Abrupt cessation of steroid therapy can then lead to a corticosteroid withdrawal crisis and possibly death of the animal.

(e) produce central nervous stimulation.

5. **The Anti-Inflammatory Actions**

(a) The anti-inflammatory actions of the glucocorticoids are inseparable from their actions on protein and carbohydrate metabolism and appear to reflect the same actions of the drug.[4]

(b) The corticosteroids suppress inflammatory responses from **any** cause. They therefore affect only the signs of inflammation and do not in any way neutralize the cause.

(c) Because corticosteroid therapy acts only to suppress the signs of inflammation, a principle of corticosteroid therapy is to neutralize or remove the cause of the problem, if this is at all possible.

6. **Systemic Corticosteroid Therapy**

(a) Generally, single large doses of corticosteroid can be given without serious adverse effects.

(b) Prolonged treatment with corticosteroids can be dangerous because they increase the body's susceptibility to inflammation and suppress the adrenal cortex.

(c) The ability of the corticosteroids to suppress the signs of disease have led to the comment that corticosteroid therapy enables the patient to "walk all the way to the postmortem room."

(d) For these reasons, short-term or local therapy is easier to justify than long-term therapy.

7. **Local Corticosteroid Therapy**

(a) If possible, the cause of the problem should be removed.

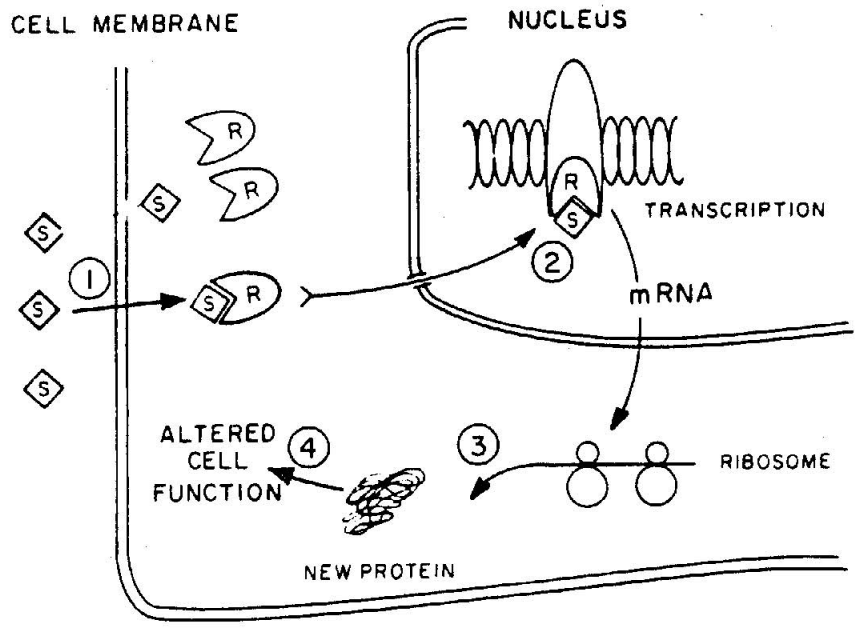

Fig. 2. Mechanism of Action of the Corticosteroids.

Corticosteroid drugs (S) enter the target cells and bind to specific receptors (R) in the cell cytoplasm (1). In binding, they change the shape of these receptors and the altered drug-receptor complex diffuses into the nucleus of the cell. In the nucleus this complex binds to receptors on the genes and initiates transcription (2). The newly formed mRNA diffuses out of the nucleus, binds to the ribosomes and gives rise to new proteins which re-direct the function of the cell (4). Although the primary action of the corticosteroids is therefore to cause the synthesis of new proteins, their ultimate effects usually lead to tissue breakdown. (Reproduced with permission from Tobin, J. eq. Med. Surg., 3, (1979):10.)

(b) When treating, ensure that the joint is non-infected and use full aseptic technique.

(c) It is important to remember that the corticosteroids are anti-anabolic. Although the clinical signs of inflammation are suppressed, so is the resistance of the joint cartilage to wear and tear. Adequate rest is therefore important.[1]

8. **Adverse Reactions to Intra-Articular Corticosteroids**

(a) Post-injection flare-up: This is short and acute and begins a few hours after the injection; the cause is unclear and the condition is usually mild and transient.

(b) Steroid arthropathy[2]

(1) narrow joint space

(2) loss of articular cartilage

(3) crepitation

(4) new bone growth around the joint.

(c) Septic Arthritis: This may be due to Gram-positive or Gram-negative organisms, with Gram-negative organisms appearing more slowly.

(d) Osseous metaplasia. This implies new bone formation.

(e) Surgery should (in general) not be performed on corticosteroid-injected joints for at least six weeks.

(f) When handled judiciously and in combination with rest, corticosteroids can be used to prolong the racing career of certain horses. They should, however, be used in minimum doses as infrequently as possible.

(g) With repeated joint injections and work, severe destruction of the joint will occur.

9. **Adverse Responses to Systemic Corticosteroids**

(a) The corticosteroids are anti-anabolic and suppress the immune response. Most of their adverse reactions are linked to these characteristics of their actions.[1,8]

(b) If animals are maintained on large doses of corticosteroids for two weeks or more they (1) leave the animal open to systemic infection and (2) lead to feedback atrophy of the adrenal cortex. If the steroids are suddenly withdrawn, the animal goes into an acute Addisonian crisis. One way to handle this problem is to administer the steroids intermittently. Another way is to administer exogenous ACTH to maintain the adrenal cortex.

(c) They may reactivate bacterial or viral diseases,

(d) may delay wound and fracture healing,

(e) may cause cleft palate in the newborn, and

(f) may cause laminitis.

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