CHAPTER 33

SYSTEMIC STEROIDS

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Systemic steroids are synthetic derivatives of cortisol which is secreted from the adrenal glands. They act like natural cortisol in body. These drugs are used in a wide and serious group of diseases. They are widely used in dermatology practice; including bullous diseases, dermatitis and autoimmune diseases since 1950s.[1] The main effects of natural cortisol are regulation of protein, carbohydrate, lipid and nucleic acid metabolism, increasing plasma glucose in acute stress, inflammation and immune response, distribution and excretion of water and solutes, secretion of adrenocorticotrophic hormone from the pituitary gland. The effect of exogenously produced steroids is more anti-inflammatory and less mineralocorticoid. Glucocorticoids have bilateral dynamic and complex effects on many organs and the immune system. There is a significant effect on blood cells and immune system cells. While increasing the number of red blood cells, neutrophils and platelets; the number of lymphocytes, eosinophils, basophils and monocytes reduce. Steroids allow the migration of peripheral blood T and B lymphocytes to the lymphoid system. They supress proinflammatory cytokines (IL-1β, IFN-α), induce antiinflammatory cytokines (TGF-β, IL-10) and anti-inflammatory cytokines receptors. Antigen activated monocytes and lymphocytes release IL-1, IL-2, PAF, IFN-gamma, TNF-alfa. By blocking these cytokines, T cytotoxic lymphocytes can not turn into T cells and monocytes can not turn into macrophages.[2]

Steroids can affect the inflammatory process by cytosolic phospholipase A2 and arachidonic acid mechanism by suppressing the production of COX-2, an important element of the inflammatory response. Besides, phospholipase A2 activity is reduced by nongenomic mechanisms.[3] In consequence, arachidonic acid and its metabolites are reduced. Nitric oxide (NO) which is responsible for the synthesis of inducible nitric acid synthase (iNOS) is also responsible for the occurrence of vasodilation in inflammation. It has been proved that glucocorticoids suppress the iNOS production by transcriptional and posttranscriptional mechanisms.[4,5] In particular, the role of fibroblasts in chronic inflammation is suppressed by high-dose use of steroids. In such case, collagen, elastin and glucosamine formation is inhibited.[6] Over 50% of administered corticosteroids are absorbed in the upper jejunum.[7] Peak plasma levels are achieved within 30-100 minutes. Steroids become water soluble by conjugation in the liver. Metabolites are excreted by kidney and liver. Approximately 90%-95% of endogenous steroids are bound to cortisol-binding protein (transcortin) or to albumin in the circulation. The other 5% is unbound cortisol; this is the active moiety. Many factors influence circulating quantities of cortisol-binding protein (CBP). Transcortin is produced by liver and is increased by estrogens. It is increased in pregnancy, estrogen therapy, and hyperthyroidism. However, conditions such as hepatic failure, renal failure, and hypothyroidism decrease CBP levels and, therefore, increase drug toxicity. Synthetic glucocorticoids have less affinity for CBP (estimated at 70%).[8] Cortisol levels are regulated by a feedback mechanism between the hypothalamic pituitary adrenal system. The highest levels of cortisol are synthesized in the early morning hours. Daily synthesized cortisol level is 10-20 mg,[9] but can be up to 10-fold in situations of stress.[10]

The most commonly used steroids are prednisone, prednisolone, methylprednisolone, beclomethasone,

Table 1

	Glucocortikoid Potency (mg)	Mineralocorticoid Potency	Plasma Half Life (minute)	Duration of action (hour)
Cortisone	25	1	30	8-12
Prednisone	5	0.25	60	24-36
Methylprednisolone	4	0	180	24-36
Triamcinolone	4	0	300	24-36
Dexamethasone	0.75	0	200	36-54

Nonsteroidal anti-inflammatory drugs (acetylsalicylic acid, indomethacin): Clearance of salicylates is increased by corticosteroids, and this may cause salicylate toxicity.

Cyclosporine: Steroids may increase cyclosporine levels.

Skin tests: Reaction to the skin test can be suppressed.

Vaccines: Corticosteroids may enhance the replication of some organisms contained in live vaccines. In particular, while application of high doses of steroids, *live* attenuated *vaccines* should be delayed until the end of treatment.

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