Intra-Articular Steroid Injection
A Risk-Benefit Assessment

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Summary

Intra-articular injections with steroids may offer additional help in the treatment of inflammatory joint diseases. The major side effects are the systemic effects of steroids, infectious arthritis and cartilage damage. These are infrequent, however, and to a great extent preventable.

Steroids are of little effect in radiological progression and function, and this is the most important limitation on liberal use. On the other hand, they powerfully suppress inflammation and pain, for a varying length of time which depends on the preparation used.

The systemic treatment of inflammatory joint diseases is not always satisfactory. Gold, penicillamine, azathioprine, methotrexate, etc., are all slow to take effect and occasionally fail to do so. The advent of steroids, with their quick and powerful action, brought new hope; their side effects, however, preclude widespread use in rheumatology.

A definite place is reserved for local therapy.
Steroids are the most frequently used intra-articular drugs, and by this route of application their effect is rapid and intense. Systemic side effects may occur and local side effects are added to the list of risk factors.

A careful assessment of risks and benefit must guide the intra-articular application of steroids.

1. Benefits

1.1 History

Cortisone was first used in the treatment of rheumatoid arthritis in the late 1940s (Hench et al. 1949). Its major side effects became clear in the next few years (Sprague et al. 1950).

In 1950, Thorn was the first to inject steroids into the knee of a patient with rheumatoid arthritis (Hollander 1953). In the beginning, the results were somewhat disappointing; it later became clear that cortisone is dependent for its action on hydroxylation to hydrocortisone in the liver. Direct injection of hydrocortisone gave better results, but the effect was only transient. The development of less soluble esters provided steroids with longer half-lives and long term effectiveness (Hollander et al. 1961). Triamcinolone hexacetonide provided results comparable with the intra-articular injection of osmic acid (Anttinen & Oka 1975).

1.2 Mechanisms of Action on Inflammation

The pathways that induce inflammation are complex, and there is no single mechanism that can explain all the effects of steroids on inflammation or immune responses (Owen 1985). On the cellular level, steroids influence protein synthesis. Other mechanisms of action may be involved. The final action results in expressed inflammation and, to a lesser extent, suppression of immunology.

Steroids penetrate freely through the cell wall and bind to a specific protein receptor in the cytoplasm or in the nucleus. The steroid-protein complex enters the nucleus, where it binds to the DNA template and alters its transcription. In this way, the synthesis of protein is modified (Gustafsson 1987).

Unlike NSAIDs, steroids do not interfere with the cyclo-oxygenase enzyme. They inhibit the formation of arachidonic acid from phospholipids; thus, not only prostaglandin synthesis but also leucotriene production is impaired. This factor may explain the superior anti-inflammatory effect of steroids compared with NSAIDs.

It is not clear to what extent these basic mechanisms explain the measurable effects of steroids in synovial cells and the composition of the synovial fluid.

Systemic steroids induce leucocytosis due to accumulation of neutrophils in the intravascular space. Mature neutrophils are stimulated to leave the bone marrow; at the same time, migration to the site of inflammation is inhibited. Steroids reduce the vasodilatation and increased permeability of the capillary vessels. Synovial membrane permeability is reduced and the neutrophil count of the synovial fluid is diminished (Duff et al. 1955). Neither neutrophil phagocytosis nor killing potency appears to be hampered. A stabilising effect on lysosomal membranes of liver cells noted by Weissman and Thomas (1963) was not confirmed by others (Persellin & Ku 1974).

Monocytopenia parallels the decreased migration of monocytes and macrophages to sites of inflammation. Monocytes and macrophages produce a peptide hormone that inhibits microtubular assembly in polymorphonuclear cells, and this may cause decreased migration and phagocytosis (Stevenson 1977).

Steroids induce lymphopenia; in particular, T cells are depressed, with a marked effect on cellular immunity. As T cells are the predominant cells in the rheumatoid synovium, suppression of cellular immunity may explain a great deal of the effect of intra-articular steroids. γ-Globulins and rheumatoid factor decrease, but the alteration in humoral immunity is not clinically important (Fauci et al. 1976).

The viscosity of the synovial fluid increases after intra-articular steroid injection, an effect which may be entirely due to enhancement of hyaluronate concentration and polymerisation (Jessar et al. 1953). Total haemolytic complement and C4 levels