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CHAPTER 2: CORTICOSTEROIDS AND LOCAL ANAESTHETICS

CORTICOSTEROIDS

Corticosteroids were first administered systemically in 1948 by Philip Hench in the United States[1] and were hailed as the new universal panacea, but it soon became apparent that there were major side effects greatly limiting their systemic use.[2,3] In 1951, Hollander, in the United States, reported the first use of local hydrocortisone injections for arthritic joints.[4]

The commonly used injectable corticosteroids are synthetic analogues of the adrenal glucocorticoid hormone cortisol (hydrocortisone), which is secreted by the middle layer (zona fasciculata) of the adrenal cortex. Cortisol has many important actions, including antiinflammatory activity. Corticosteroids influence the cells involved in the immune and inflammatory responses primarily by modulating the transcription of a large number of genes. They act directly on nuclear steroid receptors to control the rate of synthesis of mRNA.[5] However, they also reduce the production of a wide range of proinflammatory mediators, including cytokines and other important enzymes.[2,3,6-8]

RATIONALE FOR USING CORTICOSTEROIDS

We know surprisingly little about the precise pharmacological effects of corticosteroids when they are injected directly into joints and soft tissues.[9-11] There are few injection-therapy studies comparing different doses of the same corticosteroid for the same condition, but those that have been performed suggest that lower doses may be as effective as higher ones.[12,13]

Local corticosteroid injections are thought to work by a number of mechanisms.

Suppressing inflammation

They suppress inflammation in inflammatory systemic diseases such as rheumatoid or psoriatic arthritis and gout.[3,6,14-17] Synovial cell infiltration and proinflammatory cytokine expression are reduced in a multifaceted manner by intraarticular corticosteroid injection.[6] The role of inflammation in tendinopathy is controversial and in recent years, mainstream opinion has asserted that the condition is purely degenerative. However, this view is being challenged because it has been found that increased numbers of specific inflammatory cells are present in pathological tendons, consistent with a chronic inflammatory process.[18-23]

Suppressing inflammatory flares

They appear to suppress inflammatory flares in degenerative joint disease.[5,16,24,25] However, the pathophysiology of osteoarthritis is poorly understood,[26] and there are no reliable clinical features that predict which osteoarthritic joints will respond to injection. Often, the only way to find out is with an empirical trial of injection therapy.[16,24]

Breaking up the inflammatory damage-repair-damage cycle

This is postulated to set up a continuous, low-grade, inflammatory response, inhibiting tissue repair and sound scar formation while forming adverse adhesions.[27,28] However, there is little direct evidence to support this.[10]

Protecting cartilage

There may be a direct chondroprotective effect on cartilage metabolism or other effects not related to the antiinflammatory activity of the steroids, such as promotion of articular surfactant production.[5,8,29-37]

Direct analgesic effect:

Inflammation is a complex cascade of molecular and cellular events.[38,39] The precise role of inflammation in tendinitis is the subject of considerable debate, and many authors prefer the terms *tendinosis* or *tendinopathy* to describe the pathological changes.[38,39] Tendon pain may not be caused by inflammation (tendinitis) or structural disruption of the tendon fibres (tendinosis), but might instead be caused by the stimulation of nociceptors by chemicals such as glutamate, substance P and chondroitin sulphate released from the damaged tendon.[40,41] Corticosteroids (and possibly local anaesthetics) may inhibit the release of noxious chemicals and/or the long-term behaviour of local nociceptors. In vitro, corticosteroids have also been shown to inhibit the transmission of pain along unmyelinated C fibres by a direct membrane action.[42]

Other effects

Intraarticular corticosteroid given over 3 months protects against periarticular bone loss in inflamed finger joints in rheumatoid arthritis.[43]

Note: The authors strongly advise that all clinicians thoroughly study the most up to date manufacturers' data sheets for the drugs that they propose to use for injection therapy and stay abreast of any subsequent modifications.

COMMONLY USED CORTICOSTEROIDS

The following are commonly used corticosteroids. The dosages and concentrations are shown in parentheses.

- **Triamcinolone acetonide**

  Adcortyl (10 mg/ml, dilute)
  Kenalog (40 mg/ml, concentrated)

Throughout this text, Kenalog is our reference drug, but we appreciate that other clinicians, for various reasons (e.g., being licensed to mix with local anaesthetics), prefer to use different corticosteroids. Dosage conversions may be made using the antiinflammatory equivalence (Box 1.1).

Box 1.1 Equivalent antiinflammatory doses of corticosteroids

Triamcinolone acetonide – 40 mg is equivalent to the following:

- Triamcinolone hexacetonide, 20 mg
- Methylprednisolone, 40 mg
- Hydrocortisone, 200 mg
- Betamethasone, 7.5 mg
- Dexamethasone, 7.5 mg
- Prednisolone, 50 mg

Kenalog can be used in very small quantities, so it is ideal for small joints and tendon entheses, in which distension may increase pain. Adcortyl, however, is useful when a larger volume is required, as in larger joints and bursae. The duration of action of the drug is approximately 2 to 3 weeks.[44,45]

- **Triamcinolone hexacetonide**
  Lederspan (20 mg/ml, concentrated)

The least soluble and longest lasting injectable corticosteroid, Lederspan was unavailable in the United Kingdom from 2001 to 2013. It is licensed to be mixed with 1% or 2% lidocaine or other similar local anaesthetics. Pharmacokinetic studies have shown that the biological effect of triamcinolone acetonide is equivalent to that of triamcinolone hexacetonide if used at double the dosage, but even when triamcinolone acetonide is given at higher doses, triamcinolone hexacetonide has proven to be more effective, with a greater duration of action in head-to-head studies.[46-48] It is available in the United States as Aristospa

- **Methylprednisolone acetate**
  Depo-Medrone (40 mg/ml, concentrated)

This drug may cause more postinjection pain than triamcinalone acetonide.[49] It is also available premixed with local anaesthetic as Depo-Medrone (40 mg/ml) with lidocaine (10 mg/ml) in 1- and 2 ml vials, which we do not use because it is a fixed-dose combination and therefore difficult to adjust.

- **Betamethasone**
  Celestone Soluspan (United States; betamethasone sodium phosphate, 3 mg, and betamethasone acetate, 3 mg = 6 mg/ml, concentrated)

The dose of Celestone Chronodose in Australia is slightly different. Celestone is licensed to be mixed (in the syringe, not the ampoule) with 1% or 2% lidocaine.

- **Hydrocortisone**
  Hydrocortistab (25 mg/ml, very dilute)

This is very soluble and has the shortest duration of action of the corticosteroids mentioned here, perhaps as little as 6 days.[11] It may be particularly useful for superficial injections in thin, dark-skinned patients, in whom depigmentation or local fat atrophy may be more noticeable.