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Assiut University

Faculty of medicine

Rheumatology and Rehabilitation Dept

LOCAL INJECTION IN TREATMENT OF RHEUMATIC DISEASES

BY

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AN ESSAY

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CONTENTS

Contents

Historical

The first intra-articular injection used in treatment of rheumatic diseases was steroid. The insight that initiated the course of events leading to corticosteroid therapy for rheumatic diseases especially rheumatoid arthritis occurred in 1929, when a patient of Phillip Hench related the disappearance of rheumatoid arthritis to an attack of jaundice. Hench had observed previously that pregnancy occasionally ameliorates rheumatoid disease, and he suspected that an unidentified - "Substance x" - compound increased both in hepatitis and pregnancy was the agent responsible for this effect.

He eventually concluded that it was an increased secretion of a hormone from the adrenal cortex that accounted for the temporary remission of rheumatoid activity. By 1948, a process for synthesizing significant amount of compound E (now known as cortisone), was successfully developed.

On September 1948, the first rheumatoid patient received cortisone.

By September 1948, there was dramatic response. Corticosteroids quickly became widely prescribed for the treatment of rheumatoid arthritis, (Wiss M.M., 1989).

Shortly after systemic cortisone and hydrocortisone were first used in the management of rheumatoid arthritis, Thorn in the late 1940s injected 10 mg. hydrocortisone into the knee joint of a patient with rheumatoid arthritis (Hollander JL, 1979), the knee was improved locally, but the patient also improved generally; it was concluded that the improvement resulted from systemic absorption of the intra-articular injected material.

No further studies of intra-articular corticosteroid injection were done untill the early 1950s.

At 1951, Hollander et al., used hydrocortisone. Then prednisolone followed (Rothermich and Phillip, 1957).

More recently both methyl prednisolone and triamcinolone have became available.

Baine et al., 1967 found significantly greater improvement with methyl prednisolone than with prednisolone, then Dixon et al., 1972, found that triamcinolone produced marginally greater benefit with fewer local side effects than prednisolone acetate.

*Intra-articular non-steroidal anti-inflammatory drugs have been evaluated but their use lacks relevance.

*A lot of studies were made lately with other injectable drugs, in treating both articular and non-articular rheumatism.

At 1995, in Eva Bagge Department of Rheumatology in Sweden, there was a study about intra-articular injection of polyclonal Immuno-globulin G, in rheumatoid arthritis and the effect of treatment was evaluated clinically by magnetic resonance imaging (E. Bagge & A. Tarkowski, 1995).

At 1997, in Gartnavel General Hospital, Glasgow, there was a study about the addition of intra-articular methotrexate or rifampicin to relieve pain of a joint injected with triamcinolone hexacetonide (J.A. Hunter and A. Stirling, 1997).

Also there were other studies about intra-articular injection of osmium tetroxide, superoxide dismutase, osmic acid, radio-isotopes and others.

But until now the most drug which is locally injected in treating rheumatic diseases is steroid which is now well established in the inflammatory arthrorpathies as an effective adjunct to other modes of treatment, but this treatment needs to be supplemented with rest, physical therapy and other analgesic or anti-inflammatory medication, as the effects of intra-articular injections tend to be short-lived (Caldwell, JR. 1996).

Role of Local injection in treatment of rheumatic diseases:

Action of steroids:

Steroid is the most drug used as intra-articular injection in treatment of rheumatic diseases. It has several roles in treating arthritis either if it was administrated orally or as a pulse therapy or if it was locally injected.

–Generally, inflammatory cytokines i.e. interleukin [IL-6, IL-1, tumour necrosis factor alpha (TNF-α)] as soluble products of synovial arthritis, stimulate the production of corticotrophin-releasing hormone (CRH) in the hypothalamus, CRH release leads to pitutary production of adrenocorticotrophic hormone (ACTH), followed by glucocorticoid secretion by the adrenal cortex and indirect perturbations of gonadal function (Chrousos G.P., 1995), (Cutolo M., 1998).

–Conversely, hormonal products of hypothalamus-pitutary-adrenal (HPA) and gonadal (HPG) axis modulate cytokine production. (Bellido T., Jilka R., Boyce B et al., 1995), (Masi AT, 1994).

–Notably, glucocorticoids are the most potent endogenous inhibitors of immune and inflammatory processes, including pro-inflammatory cytokine

production. (Lee SW, Tsou AP, Chan H. et al., 1988).

–Periphral levels of IL-6 and to a lesser extent those of TNF-α and IL-1β, are tonically inhibited by basal levels of glucocorticoids. (Parpanicolau DA, Tsigos C, Oldfield EH et ali., 1996)

–On the other hand in systemic arthritic conditions such as rheumatoid arthritis (RA), the increased IL-6 levels stimulate secretion of CRH, ACTH and cortisol, however the overall HPA activity seems normal and insufficient to inhibit ongoing inflammation.

In particular a relative deficiency of adrenal glucocorticoid production with compensatory ACTH hypersecretion is frequently observed in RA, and chronically elevated cytokines might directly cause the observed decrease in adrenal production. (Crofford LJ, Kalogerus KT, Mastorakos G et al., 1997).

–However, immune-mediated synovial inflammation may also arise from glucocorticoid resistance in the target tissue. In RA, the concentration of glucocorticoid receptors in circulating leucocytes has been found to be reduced by 50%. (Chrousos GP, et al., 1993).