

# The effect of intra-articular glucocorticoid injections on HPA axis function

Philip C Johnston, Laurence Kennedy  
Department of Endocrinology and Diabetes, Cleveland Clinic, Ohio, USA

## BACKGROUND

After injection into the intra-articular space, glucocorticoids may be systemically absorbed; the degree of absorption can depend on the size of the joint injected, the injectable glucocorticoid preparation used, the dosage and the frequency of the injection.

Intra-articular glucocorticoid injections (IAGC) have the potential to have deleterious effects on HPA axis function which can result in adrenal suppression and/or iatrogenic Cushing syndrome.

## INTRODUCTION

A recommendation of up to three glucocorticoid injections per year with a minimum of thirty days between injections has been advocated due to the concern regarding hypothalamic-pituitary-adrenal (HPA) axis suppression; however, guidelines on the frequency and interval between injections are currently lacking.

The majority of studies examining the effects of glucocorticoid joint injections on HPA-axis function have been in adult patients with osteoarthritis and rheumatoid arthritis, in addition these studies have particularly focused on the knee joint which has a large synovial resorption area, therefore the influence of IAGC and their subsequent effects on HPA-axis are not always seen with other joint/s injected.

Exogenous glucocorticoids can suppress the release of ACTH from the pituitary leading to adrenal suppression and cessation of endogenous cortisol production. The extent to which adrenal suppression occurs, can depend on the site of the joint injected, frequency and dose of injection.

Cushing syndrome can also result from IAGC, although this is not as commonly reported as adrenal suppression in this context.

A single dose of intra-articular triamcinolone hexacetonide (TH) can suppress the HPA-axis for as long as seven weeks.

## IAGC AND HPA AXIS FUNCTION

Intra-articular glucocorticoid injections can result in a sharp decline in cortisol to low or undetectable levels within the first days after administration. The potential for glucocorticoid injections to cause adrenal suppression and/or iatrogenic Cushing syndrome appears to be under-recognized and if both occur together confusion can arise.

The dose of ACTH used in the 250 µg ACTH stimulation test is supra-physiologic and therefore a potential drawback to this test in assessing secondary adrenal suppression is that it is less sensitive in detecting subtle changes in HPA axis-function that could otherwise only be observed using the 1 µg ACTH stimulation test.

Normalization of serum cortisol levels usually occurs at 1-2 weeks following the usual doses of MPA, betamethasone, TH usually takes 2-4 weeks and TA is normally beyond 28 days.

After the administration of intra-articular glucocorticoid it is important to note however, that hypercortisolemia is generally not observed, as even though the patient can appear cushingoid, HPA-axis suppression will result in low cortisol levels.

This can cause confusion and result in the patient being erroneously diagnosed as having adrenal insufficiency or labeled as having 'Addison's' based on these findings. Although their use is widespread, the true incidence of iatrogenic Cushing syndrome occurring in the context of intra-articular glucocorticoid injection is unknown.

CRH produced by the hypothalamus, stimulates the pituitary to produce ACTH. ACTH signals production of cortisol from the adrenal cortex. Cortisol exhibits negative feedback on the hypothalamus and pituitary. Exogenous glucocorticoids can suppress release of ACTH and subsequent cortisol production from the adrenal cortex, leading to adrenal suppression and/or iatrogenic Cushing syndrome

## CONCLUSION

HPA-axis suppression can last up to four weeks after a single injection, although recovery of HPA axis to baseline can take longer depending on the dose and frequency of injections. Considering the widespread use of intra-articular steroid injections and their clinical effectiveness, physicians who administer these need to be aware of the potential risks of HPA-axis suppression and/or iatrogenic Cushing syndrome. Guidelines for the frequency of dosing in addition to defined time intervals between each injection should be clear. Johnston PC, Kennedy L, et al Endocrine 2015

