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The systemic effects of local infiltrations with corticosteroids. Implications for palliative care?

Abstract

Corticosteroids are used in approximately 50% of palliative care patients. Increasingly corticosteroids are used as local infiltrations together with local anaesthetics. This treatment may be adjuvant to other measures to control pain. Depo preparations, although their main activity is topical, may also exercise systemic toxicity. This may include transient suppression of adrenal activity which may be exacerbated by the use of morphine. Some women in reproductive age may experience vaginal blood loss between the periods. Other toxicities are rare.

Key words: corticosteroids, methylprednisolone acetate, triamcinolone acetonide, triamcinolone hexacetonide, depo preparations, adrenal suppression

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Introduction

Corticosteroids are used frequently in Palliative Care. Approximately 30-50% of patients cared for their terminal disease are prescribed corticosteroids [1]. There are many indications to use steroids in palliative care [2]. Whereas most of the steroids are used systemically, topical steroid infiltrations are used increasingly as an adjuvant in pain control [3–8]. We reported successful treatment with corticosteroid infiltrations in terminally ill patients several times in this journal [9, 10]. The idea to use topical, rather than systemic corticosteroids is to deliver high concentration of the drug locally with a minimum of systemic toxicity. This approach is usually successful; however, clinicians should be aware of systemic toxicity as it may contribute to patient's morbidity. In this article we analyse the literature and comment on systemic effects of topical corticosteroid use.

How do they work?

General idea is that topical corticosteroids work topically where there is an irritation or inflammation. However, newer data suggest that topical corticosteroids acts through inhibition of local discharges by the damaged nerve, independent of the anti-inflammatory effect [11]. Drugs absorbed from the site of infiltration are detectable in plasma during first until second weeks [12]. The pain controlling effect may be much longer than that and may be sustained for many months after infiltration. On the other hand preparations for topical infiltrations when injected intramuscularly in higher doses, far from the painful site, may also have some systemic effect on pain [13]. On the other hand the effect of topical corticosteroid infiltration can be additive to the effect of systemic steroids. When identified a local painful spot in a patient on systemic corticosteroids, it is still worth to try infiltration. (Z. Zylicz, unpublished).

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Pharmacokinetics and pharmacodynamics of topical steroids

Insoluble preparations absorb slower than the more soluble. Triamcinolone acetonide is absorbed much more rapidly than triamcinolone hexacetonide [12, 14]. Plasma levels of the injected drugs peak within 24 hours and significant plasma levels are maintained for 1–2 weeks [12]. Suppression of hypophysis-adrenal axis is observed also in the same time period.

Toxicity of the topical steroids

Triamcinolone hexacetonide may in comparison to triamcinolon acetonide cause more prolonged adrenal suppression and hence be more dangerous in long term. Adrenals of most of the patients recover spontaneously after couple of weeks [15, 16]. Depression may be more permanent when the injections are repeated couple of times. Not the dose, but long time exposure to the drug warrants adrenal suppression [17]. Most of the adrenal depression is never diagnosed. However, patients with subclinical adrenal insufficiency may suffer symptoms of relative adrenal insufficiency during infections. In the context of Palliative Care it is possible that this effect may contribute to patients' earlier death.

Adrenal suppression may be more pronounced or even less reversible in patients using opioids and suffering of opioid induced hypogonadism [18]. Special care should be taken, when local infiltrations with corticosteroids are offered to the patients with pre-existing adrenal failure, like in patients who previously used glucocorticoids for long time and discontinued them, but also those with adrenal carcinomas or adrenal metastases of (for example) lung cancer.

Glucocorticoid effect of topical steroids may occasionally result in a Cushing syndrome. Couple of these patients were described in the past [19].

Other relevant toxicity is the (usually mild) increase of plasma glucose levels in patients with known diabetes mellitus, or occasionally in an apparently healthy person. The effect is usually limited to the first two weeks after infiltration.

Woman in a reproductive age may suffer of vaginal blood loss between the periods after local infiltration with Depo steroids; and they should be warned about this before treatment. Although this toxicity is mentioned in drugs licence I was unable to trace the appropriate literature about this. Personally, I recall one female patient, aged 45, with an advanced metastatic carcinoma of unknown primary who did not menstruate for 9 months, but experienced severe vaginal blood loss after successful treatment of her localised pain with 80 mg of methylprednisolone acetate. Blood loss was successfully treated with tranexamic acid [20]. The gynaecologist excluded any intrauterine pathology. Next time she came for infiltration, vaginal blood loss could be anticipated and blood loss was limited.

Injecting depo steroids (as in Depo Medrol®) into the soft tissues other than peritoneal, pleural or joint cavities, may be painful. Most probably benzyl alcohol, used as preservative, is responsible for pain on injection. Therefore it is a good practice to dilute the drug with for example local anaesthetic like bupivacaine. Local pain after injection could also be due to local sensitisation and allergic reaction [21]. This is probably rare.

Polymorphism of the glucocorticoids receptor gene may result in abnormal sensitivity to corticosteroids [22]. Patients with this abnormality tend to have increased BMI and decreased bone mineralisation with normal plasma cortisol levels. In these patients effects of topical steroids, as well as their toxicity may be increased.

Finally, although extremely rare, locally injected corticosteroids are able to produce psychosis, which may be difficult to be recognised and treated [23]. Local atrophy of the subcutaneous tissues had been described in several patients after infiltration with depo steroids [24].

Conclusions

Depo corticosteroids like triamcinolone acetonide or methylprednisolone acetate may be useful in the treatment of some conditions in palliative care. Although the drugs are injected locally and exercise their effect locally, their toxicity may be systemic. Especially the first two weeks after injection patients are prone to adrenal suppression which may blunt hormonal stress response during infection. Other toxicities may be rare, but significant in Palliative Care population.

Some patients may be more susceptible for steroid toxicity and they either should be warned about this or the treatment should be postponed. To the first category belong female patients in a reproductive age, to the second patients with adrenal primary tumours or metastases.

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