

Frequency of Epidural Steroid Injections

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Myth #1: Epidural steroid injections (ESI) can be repeated without concern regarding the duration of time between injections.

Myth #2: A "series" of ESIs is sometimes required regardless of the clinical response to a single ESI.

Fact: After an ESI, a period of up to 14 days may be needed to assess the clinical response. Systemic effects on the hypothalamic-pituitary-adrenal (HPA) axis may last three weeks or longer. These factors must be considered when determining if or when another ESI is indicated. There is no evidence to support routine performance of a "series" of repeat injections without regard to the clinical response to an initial injection.

The frequency of ESIs is dependent on both the number of injections performed within a given time period (e.g. one year), as well as the amount of time that has passed between repeat injections (e.g. one month, two months). While there are numerous online references and society guidelines promoting a time period of at least two weeks to one month between injections [1-3], this is stated generally and without direct evidence to provide supportive reasoning. The general rationale stated is that the treating provider should wait until the peak effect of the injection has occurred before making the decision to provide an additional dose, in order to potentially spare the patient an unnecessary procedure and the potential side effects of additional corticosteroid. Early studies often noted that at one- to two-week follow-up after ESI, many patients experienced relief [4-5]. However, these follow-up assessments were arbitrary and the studies were designed mainly to identify the "peak" response to an ESI. A more recent study by El-Yahouchi *et al.* suggests that a two-week assessment is superior to immediate assessment and will more reliably predict long-term outcomes from a single ESI [6]. The investigators observed immediate relief post-transforaminal ESI to be weakly associated with longer term pain relief or functional recovery; however, the clinical response at two weeks was much more strongly associated with longer-term outcomes. Similar to earlier research, this study was not specifically designed to assess the time of "peak" response to an ESI or a time at which long-term outcomes can be optimally assessed following ESI.

In conjunction with the time course of clinical benefit, the preferred interval between injections is also influenced by the ability to minimize unwanted systemic sequelae of ESI. These include hyperglycemia, blood pressure elevation, and hypothalamic pituitary adrenal (HPA) axis suppression. Hyperglycemia and blood pressure elevation, which if present, are usually limited to 48-72 hours [7-9]; however, additional delay of normal HPA axis function may occur [10]. Limited evidence has shown that methylprednisolone (a particulate steroid) remains in the epidural space for more than two weeks, though this is of unclear clinical significance [11]. Some studies have demonstrated that if HPA axis suppression occurs, it can last for over three weeks [12,13]. It is important to note that the duration of systemic effects from an ESI are likely influenced by the type of steroid used, as both betamethasone and dexamethasone demonstrate a reduced average time of endogenous cortisol reduction after ESI compared with triamcinolone and methylprednisolone [12].

A final consideration pertinent to decision making regarding the frequency of ESI is the likelihood that a second injection will provide additional relief or restore prior relief. Two separate studies suggest that repeat injections may improve outcomes in patients with a partial response to a first (index) ESI [14,15]. Repeat ESI at greater than two weeks and less than one year from the index injection has also been shown to result in a statistically and clinically significant decrease in pain,

and patients with acute to subacute symptoms recover all prior benefit with a statistically significant cumulative benefit [15]. Additionally, a study by Kennedy *et al.* found that the type of steroid used in the injection may influence the need for repeat injections [16]. Patients treated with dexamethasone (a non-particulate steroid) were more likely to require three injections over the course of six months than patients treated with triamcinolone (a particulate steroid), in order to maintain a treatment benefit.

Conclusions & Recommendations

When patients have a positive but incomplete response to an initial ESI, the published evidence suggests that a repeat ESI is reasonable [15]. ESIs may also be repeated to reinstate previous treatment benefit that subsequently diminished [3]. While a two-week interval between injections may be a reasonable balance of risk versus benefit, there is no direct evidence that distinguishes this exact time point as optimal. There is no evidence to support administering a series of ESIs irrespective of the clinical response to an initial injection.

The decision to repeat an ESI is dependent on:

1. Providing sufficient time to assess the response to a first ESI
2. Allowing for recovery from adverse systemic effects of steroid administration
 - a. Hypertension and hyperglycemia effects are generally limited to two to three days
 - b. HPA axis suppression, if present, may occur for three weeks or longer
 - c. These effects may be dependent on steroid type and dose
3. Variable risk/benefit ratios for each individual patient, as the presence of co-morbid diabetes mellitus, osteopenia/osteoporosis, endocrinopathies, high surgical risk, and a range of other factors may influence the threshold to provide versus withhold additional injections.

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