

Effect of ESI on Blood Glucose & Cortisol levels

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- In 1948, Lindblom and Rexed first proposed that pressure on the spinal nerve, caused by a disc fragment or bone spur, is the primary cause of sciatic pain in patients with lumbar disc herniation.

Lindblom K, Rexed B. Spinal nerve injury in dorsolateral protrusions of lumbar disks. *J Neurosurg* 1948; 5:413–432.

- In 1960, Brown , reported complete transient relief in four patients with sciatica lasting 6 to 24 months treated with methylprednisolone.

Brown JH. *Northwest Med (Seattle)* 1960; 59:905–909.

- Mechanical compression may be the initial event leading to numbness and weakness, but **inflammation** often is the cause of radicular pain.
- Since that, ESI is gaining popularity and offers some advantages over traditional radicular & some of low back pain management.

- Up to **40%** of symptom-free people have disc herniation .

McRae DL. Asymptomatic intervertebral disc protrusions. Acta Radiol 1956; 46:9–27.

- Once **inflammation** is present, the nerve becomes sensitive to pressure, producing prolonged, pain-generating discharges spontaneously or with either gentle manipulation or pressure .

Howe JF, Loeser JD, Calvin WH. Pain 1977; 3:25–41.

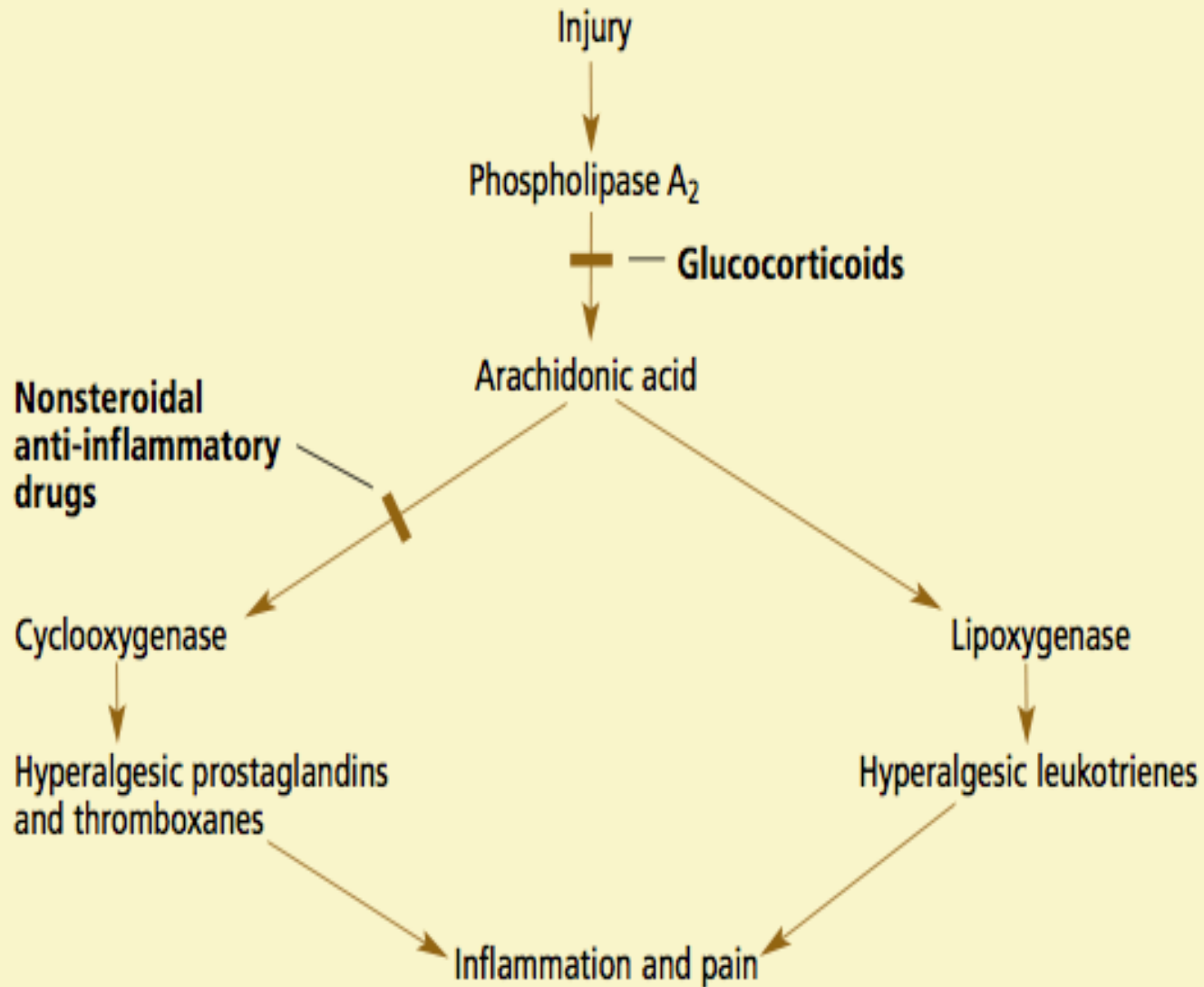
Murphy RW. Clin Orthop 1977; 129:46–60.

Pharmacology

In pharmacologic doses, glucocorticoids

- Decrease inflammation by stabilizing leukocyte lysosomal membranes.
- Preventing release of destructive acid hydrolases from leukocytes.
- Inhibiting macrophage accumulation in inflamed areas; reducing leukocyte adhesion to the capillary endothelium;
- Reducing capillary wall permeability and edema formation;
- Decreasing complement components;
- Antagonizing histamine activity, and release of kinin from substrates;
- Reducing fibroblast proliferation, collagen deposition, and subsequent scar tissue formation; and possibly by other mechanisms as yet unknown (70).

Mediators and blockers of inflammatory pain



- **The evidence of interlaminar epidural steroid injections in managing lumbar radiculopathy is strong for short-term relief and limited for long-term relief.**

Table 12. Results of published reports of lumbar interlaminar epidural steroid injections

Study	Study Characteristics	Methodological Quality Score(s)		No. of Patients	Initial Relief	Long-term Relief		Results	
		AHRQ Score(s)	Cochrane Score(s)		< 6 weeks	3 mos	6 mos	Short-term relief <6 weeks	Long-term relief >6 weeks
Arden et al (910)	RA, DB, PC	10/10	9/10	228	75%	NSD	NSD	<i>P</i>	<i>N</i>
Carette et al (913)	RA, DB, PC	10/10	10/10	C=80 T=78	SIT	NSD	NSD	<i>P</i>	<i>N</i>
Cuckler et al (915)	RA, DB	9/10	9/10	C=31 T=42	NSD	NSD	NSD	<i>N</i>	<i>N</i>
Rogers et al (921)	RA, SB	6/10	5/10	C=15 T=15	SI	NSD	NSD	<i>P</i>	<i>N</i>

RA = randomized; SB = single blind; DB = double blind; PC = placebo controlled; NA = not available; SI = significant improvement; SIT = significant improvement in treatment group; AM = amitriptyline; NSD = no significant difference; vs = versus, C = control, T = treatment; P = positive; N = negative

● **In managing cervical radiculopathy,
the evidence is moderate for short-term and long-term
relief.**

Table 13. Results of published reports of cervical interlaminar epidural steroid injections

Study	Study Characteristics	Methodological Quality Score(s)		No. of Patients	Initial Relief	Long-term Relief		Results	
		AHRQ Score(s)	Cochrane Score(s)		< 6 weeks	3 mos.	6 mos	Short-term relief <6 weeks	Long-term relief ≥6 weeks
Castagnera et al (922)	RA	7/10	6/10	Local anesthetic ± steroids =14 Local anesthetic ± steroids ± Morphine =10	75% vs 96%	79%	79%	P	P
Stav et al (926)	RA	6/10	5/10	C=17 T=25	36% vs 76%	12% vs 68%	12% vs 68%	P	P

RA = randomized; vs = versus, C = control, T = treatment; P = positive

The evidence for lumbar transforaminal ESI in managing lumbar nerve root pain **is strong for short-term and moderate for long-term improvement.**

The evidence for cervical transforaminal ESI in managing cervical nerve root pain **is moderate for short-term and long-term improvement.**

Table 14. *Results of published reports on lumbar transforaminal epidural injections*

Study	Study Characteristics	Methodological Quality Score(s)		No. of Patients	Initial Relief	Long-term Relief		Results	
		AHRQ Score(s)	Cochrane Score(s)		< 6 weeks	3 months	6 months	Short-term <6 weeks	Long-term ≥6 weeks
Karppinen et al (951, 952)	RA, DB, PC	9/10	8/10	C=80 T=80	NA	NA	NA	N	N
Riew et al (961)	P, RA, DB	8/10	7/10	55	33% vs 77%	33% vs 77%	33% vs 77%	P	P
Riew et al (950)	RA, DB	8/10	7/10	LA = 27 LA±S =28	33% vs 77%	33% vs 77%	33% vs 77%	P	P
Ng et al (958)	RA, DB	8/10	8/10	LA=43 LA±S=43	42% vs 48%	42% vs 48%	NSI	N	N

The evidence for caudal epidural steroid injections is **strong for short-term relief and moderate for long-term relief**, in managing chronic low back and radicular pain. The evidence in **post-lumbar laminectomy syndrome and spinal stenosis is limited**.

Table 11. Results of published reports on caudal epidural steroid injections

Study	Study Characteristics	Methodological Quality Score(s)		No. of Patients	Initial Relief	Long-term Relief		Results	
		AHRQ Score(s)	Cochrane Score(s)		< 6 weeks	3 mos	6 mos	Short-term relief <6 weeks	Long-term relief ≥6 weeks
Dashfield et al (889)	RA, DB	9/10	8/10	Caudal=30 Endoscopy=30	SI	SI	SI	P	P
Breivik et al (894)	RA, DB	8/10	7/10	C=19T=16	25% vs. 63%	20% vs 50%	20% vs. 50%	P	P
Bush and Hillier (895)	RA, DB	8/10	8/10	C=11T=12	100%	NA	64% vs 83%	P	N
Matthews et al (896)	RA, DB	8/10	7/10	C=34T=23	56% vs 67%	SI	NA	N	P
Helsa and Breivik (899)	RA, DB	7/10	7/10	69crossover	NA	NA	59% vs 25%	P	P

Table 3. Potential side effects or complications of epidural steroid administration

i. Endocrine	vi. Ocular
Adrenal suppression	Retinal hemorrhage
Hypercorticism	Posterior subcapsular cataracts
Cushingoid syndrome	Increased intraocular pressure
Hyperglycemia	Exophthalmos
Precipitation of diabetes mellitus	Glaucoma
Immunosuppression	Damage to optic nerve
Hypokalemia	Secondary fungal and viral infection
Amenorrhea	
Menstrual disturbances	vii. Dermatologic
Retardation of growth	Facial flushing
	Impaired wound healing
ii. Cardiovascular	Hirsutism
Hypertension	Petechiae
Fluid retention	Ecchymosis
Congestive heart failure	Hives
Deep vein thrombosis	Dermatitis
	Hyperpigmentation
iii. Musculoskeletal	Hypopigmentation
Osteopenia/osteoporosis	Cutaneous atrophy
Avascular necrosis of bone	Sterile abscess
Pathologic fracture	
Muscle wasting and atrophy	viii. Metabolic
Muscle pain	Hyperglycemia
Joint pain	Glycosuria
	Redistribution of fat
iv. Psychological	Negative nitrogen balance
Mood swings	Sodium and water retention
Insomnia	
Psychosis	ix. Nervous system effects
Anxiety	Headache
Euphoria	Vertigo
Depression	Insomnia
	Restlessness
v. Gastrointestinal	Increased motor activity
Ulcerative esophagitis	Ischemic neuropathy
Hyperacidity	Seizures
Peptic ulceration	
Gastric hemorrhage	x. Other adverse effects
Diarrhea	Epidural lipomatosis
Constipation	Fever

SIDE Effects OF ESs

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Society of Interventional Pain

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COMMON SIDE ACTION OF ESs

• Hyperglycemia & Adrenal suppression....

- **Exogenous glucocorticoids(GC)** —
mimic the bodies own stress response. Increased gluconeogenesis, glycogenolysis, the catabolism of proteins and lipids, and inhibition of glucose uptake in peripheral tissues all contribute to the rise in blood glucose affected by GC.

Rheumatology (Oxford). 2002 Jan;41(1):68-71.

Glucocorticoid epidural for sciatica: metabolic and endocrine sequelae.

Ward A, Watson J, Wood P, Dunne C, Kerr D.

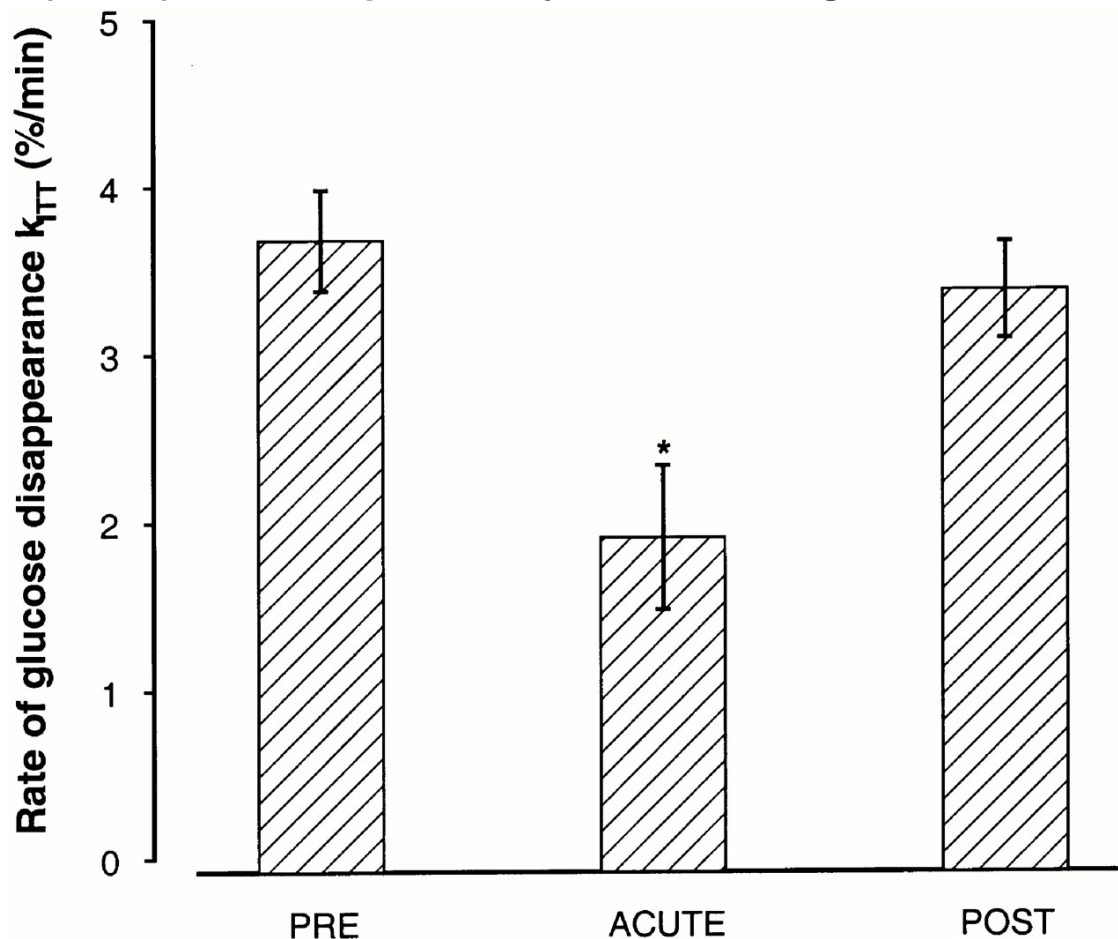
Bournemouth Diabetes and Endocrine Centre, Royal Bournemouth Hospital, Castle Lane East, Bournemouth BH7 7DW, UK.

Abstract

OBJECTIVE: The study was designed to investigate the effect of epidural administration of glucocorticoid on insulin sensitivity.

METHODS: Ten healthy individuals with sciatica underwent a short insulin tolerance test before and twice following (at 24 h and 1 week) a caudal epidural containing 80 mg triamcinolone. Fasting glucose, insulin and cortisol concentrations were also measured.

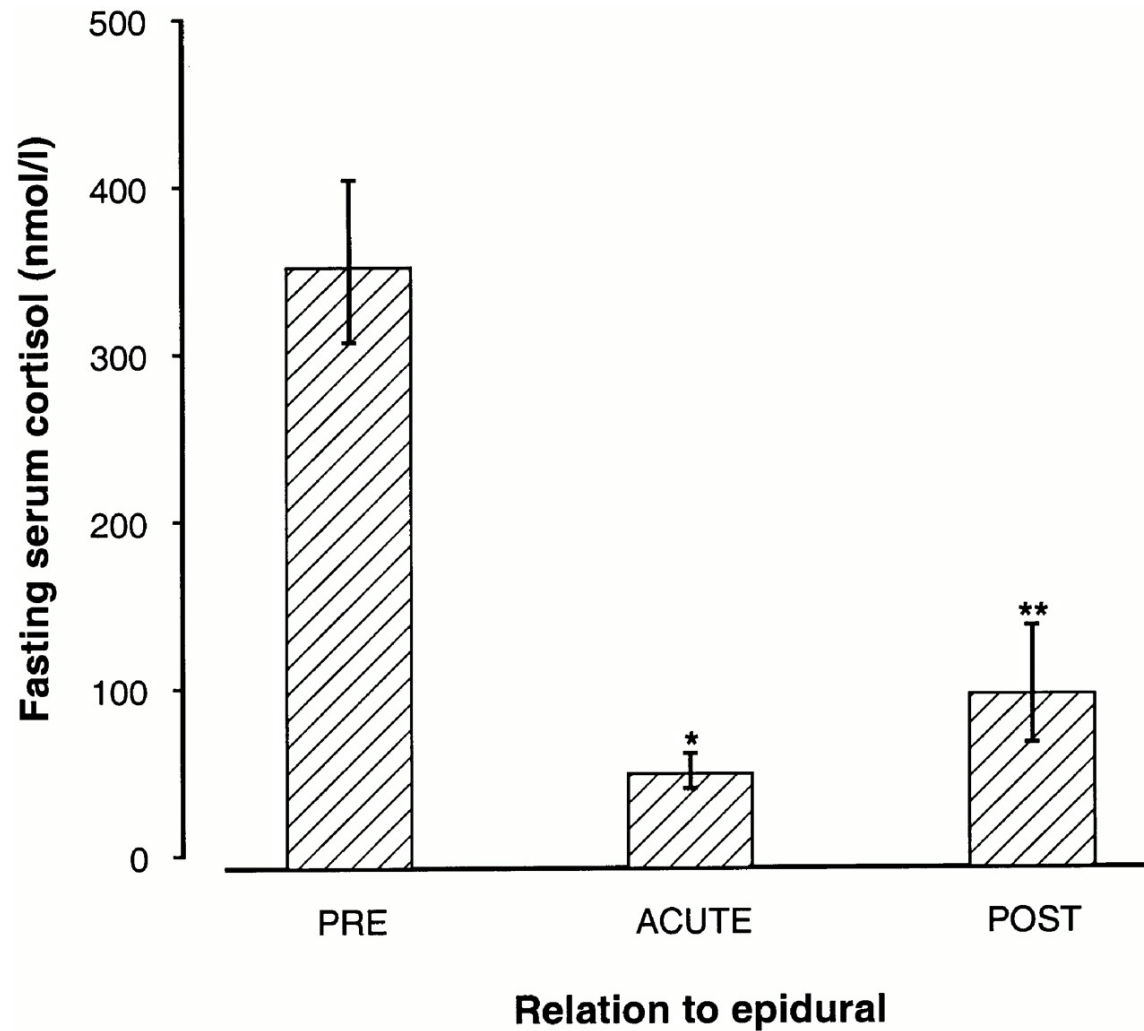
Insulin sensitivity in 10 healthy patients with sciatica expressed as the rate of glucose disappearance (k_{ITT}) during a short insulin tolerance test at baseline (PRE) and 24 h (ACUTE) and 1 week (POST) after an epidural injection of 80 mg triamcinolone acetonide.



Relation to epidural

Ward A et al. Rheumatology 2002;41:68-71

Fasting 9 a.m. serum cortisol levels in 10 healthy patients with sciatica before and after glucocorticoid epidural (time course as in Fig. 1).



Ward A et al. Rheumatology 2002;41:68-71

Rheumatology Oxford journal 2002;41:68–71

TABLE 1.

Mean (S.D.) insulin sensitivity (k_{ITT}) and fasting glucose, insulin and cortisol levels in 10 healthy individuals with sciatica measured before (Pre), 24 h after (Acute) and 1 week after (Post) a caudal epidural containing 80 mg triamcinolone acetonide

	Pre	Acute	Post
k_{ITT} (%/min)	3.7 (1.4)	1.9 (1.0)	3.4 (0.9)
Blood glucose (mmol/l)*	4.7 (1.1)	5.3 (1.2)	4.6 (1.1)
Plasma insulin (mU/l)*	11.6 (1.9)	16.2 (1.7)	11.8 (1.5)
Serum cortisol (nmol/l)*	352 (1.5)	49 (2.0)	96 (2.9)

Result :

- The rate of glucose disappearance after insulin administration ($k(\text{ITT})$) fell from 3.6%/min before the epidural to 1.9%/min 24 h afterwards ($P=0.001$) and returned to pretreatment values by 1 week. Significantly raised fasting insulin and glucose levels also reflected impaired insulin sensitivity immediately after the epidural. Morning cortisol levels were suppressed after the epidural (49 nmol/l at 24 h and 95 nmol/l at 1 week vs 352 nmol/l at baseline; $P<0.01$).

CONCLUSIONS:

- Epidural administration of glucocorticoid results in potent suppression of insulin action and this should be taken into account when patients with diabetes require treatment for sciatica.

The Effects of Epidural Betamethasone on Blood Glucose in Patients with Diabetes Mellitus

Peter Gonzalez, MD, Scott R. Laker, MD, William Sullivan, MD,
Jeri E. F. Harwood, PhD, Venu Akuthota, MD

Objective: To determine the effects of lumbosacral transforaminal and caudal epidural betamethasone injections on blood glucose levels in diabetic subjects. The hypothesis is that epidural steroid injections result in transient elevation of blood glucose levels in diabetic subjects.

Design: This is a prospective, observational cohort. Twelve diabetic subjects (6 non-insulin-dependent and 6 insulin-dependent) receiving lumbosacral or caudal epidural betamethasone injections for neurogenic claudication or radicular pain were studied. Spinal level and approach were decided based on symptoms, pathology, and magnetic resonance imaging findings. Subjects recorded their finger stick blood glucose levels twice daily for 3 days before the injection, the day of the injection, and 3 days after the injection.

Setting: A tertiary, university-based, spine center.

Participants: Inclusion criteria included diabetic subjects (age 18 years) with the ability and willingness to monitor and report their blood glucose. Exclusion criteria included epidural steroid injections (ESIs) within the previous 2 months or peripheral corticosteroid injections within the previous 2 weeks. Nineteen subjects initially enrolled, and 12 successfully completed the study.

Interventions: After informed consent was obtained, subjects underwent fluoroscopically guided lumbosacral transforaminal ESIs (TFESIs) or caudal ESIs, using contrast to confirm targeted needle placement and to rule out vascular uptake.

Main Outcome Measures: Subjects recorded morning and evening blood glucose (mg/dL) via glucometer.

Results

- There was a **106 mg/dL** average elevation in blood glucose level on the evening of the injection day. The blood glucose elevation remained statistically significant for **3 days** after the injection ($P < .002$). .

Conclusions

- Lumbosacral transforaminal and caudal epidural betamethasone injections are associated with statistically significant elevations in blood glucose levels in diabetic subjects. This effect peaked on the day of the injection and lasted approximately 2 days.

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[Spine \(Phila Pa 1976\)](#). 2012 Jan 1;37(1):E46-50.

Effects of epidural steroid injections on blood glucose levels in patients with diabetes mellitus.

[Even JL](#), [Crosby CG](#), [Song Y](#), [McGirt MJ](#), [Devin CJ](#).

Vanderbilt University Medical Center, Nashville, TN 37232, USA.

Abstract

STUDY DESIGN: A prospective cohort study.

OBJECTIVE: To evaluate the effects of epidural steroid injections (ESIs) on blood glucose levels in patients with diabetes mellitus.

SUMMARY OF BACKGROUND DATA: ESIs are commonly used in the treatment of multiple spinal disorders. Corticosteroid injections have been evaluated in the total joints and hand literature showing systemic effects to diabetics.

METHODS: Diabetic patients who were scheduled for an ESI were given an opportunity to enroll in our IRB-approved study. We collected the patient's most recent hemoglobin A(1c) (hA(1c)) and then asked them to track their blood glucose numbers at least twice per day for 2 weeks prior to and after their ESIs.

result

- We noted a statistically significant increase in blood glucose levels in diabetic patients (n = 30) after ESI. **The mean blood glucose level prior to ESI was 160.18 ± 47.46 , and, after ESI, it was 286.13 ± 111.11 . This represents an average 125.96 ± 100.97 increase in blood glucose levels after injection.** Using a nonlinear mixed effect model, **the estimated half-life of this increase was 1.06 days** (95% CI 0.80, 1.58), meaning that the patients were back within their normal standard deviation mean glucose levels within 2 days of injection. **There was no association between observed glucose level change and preinjection hA(1c) levels or age** (Spearman = 0.0326 and -0.1091 separately), indicating that **there is no correlation between preinjection hA(1c) levels and systemic response to ESI.**

CONCLUSION:

- ESIs were noted to cause a significant increase in the blood glucose levels in diabetics. There was no correlation between preinjection diabetic control, represented by hA(1c) levels, and postinjection response. Diabetics who are candidates for ESI should be counseled that a blood glucose increase may be apparent post intervention, but effects should not last longer than approximately 2 days.

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Joint Bone Spine. 2007 Oct;74(5):472-6. Epub 2007 Jul 6.

Systemic effects of epidural and intra-articular glucocorticoid injections in diabetic and non-diabetic patients.

Younes M, Neffati F, Touzi M, Hassen-Zrou S, Fendri Y, Béjia I, Ben Amor A, Bergaoui N, Najjar MF.

Rheumatology Department, Monastir Public Health Facility, Monastir, Tunisia. mohamed.younes@rns.tn

Abstract

INTRODUCTION: Whereas the systemic effects of glucocorticoid therapy have been extensively reported, little is known about those of local glucocorticoid injections. The objective of this study was to look for systemic effects of local glucocorticoid injections at two sites in diabetic and non-diabetic patients.

METHODS: We studied 29 patients (18 women and 11 men with an age range of 18-86 years). The injection site was the epidural space in 18 patients (4 with and 14 without diabetes) with disk-related sciatica and the shoulder in 11 patients (8 with and 3 without diabetes) with frozen shoulder. Each patient was given three injections of 1.5 ml cortivazol (5.625 mg of

Results

- Mean systolic blood pressure increased significantly between baseline (123+/-10 mmHg) and the first two post-treatment visits (day 1, 127+/-9 mmHg; and day 7, 128+/-10 mmHg) but returned to baseline values by the third post-treatment visit (day 21). **Mean postprandial blood glucose was significantly higher at the day 1 post-treatment visit (10.1+/-5.4 mmol/l) than at baseline (7.5+/-2.9 mmol/l). At the day 7 post-treatment visit, blood glucose remained significantly elevated compared to baseline in the 12 diabetic patients (13.9+/-4.8 mmol/l versus 9.4+/-3.3 mmol/l at baseline).** In both the overall population and the various subgroups, plasma cortisol and ACTH and urinary free cortisol were markedly reduced at the day 1 and day 7 post-treatment visits, compared to baseline. At the day 21 visit, these variables were diminished in the group given epidural injections, whereas plasma cortisol and ACTH were normal in the group treated intra-articularly. **No significant variations were noted for fasting blood glucose** or for serum levels of cholesterol, triglycerides, sodium, and potassium.

CONCLUSION:

- The administration of three local cortivazol injections was followed by suppression of the corticotropic axis that persisted beyond 21 days after epidural injection and recovered more rapidly after intra-articular injection. Systolic blood pressure increased transiently. **Elevations in postprandial glucose levels lasted longer in diabetic than non-diabetic patients.**

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[Rev Rhum Engl Ed.](#) 1995 Jun;62(6):429-32.

Systemic effects of epidural dexamethasone injections.

[Maillefert JF](#), [Aho S](#), [Huguenin MC](#), [Chatard C](#), [Peere T](#), [Marquignon MF](#), [Lucas B](#), [Tavernier C](#).

Department of Rheumatology, General Hospital, Dijon, France.

Abstract

OBJECTIVES: to evaluate potential systemic effects of a single epidural injection of dexamethasone.

PATIENTS AND METHODS: each of nine patients (five males and four females, mean age 47 +/- 11.8 years) admitted for sciatica was given a single epidural injection of 15 mg dexamethasone acetate. Before the injection (D0) and two (D2), seven (D7) and 21 (D21) days after the injection, the following laboratory tests were performed: serum cortisol and ACTH in the morning after an overnight fast, free cortisol in a 24-hour urine collection, fasting serum levels of glucose, triglycerides and cholesterol, serum levels of sodium and potassium. Blood pressure was measured on D0, D2, and D7.

Results

- Serum cortisol, ACTH and urinary cortisol were profoundly decreased on D2 and D7 but normal on D21. **There were no changes in fasting serum glucose,** triglycerides, cholesterol, sodium or potassium levels.

CONCLUSION:

- a single epidural injection of 15 mg dexamethasone acetate is associated with transient adrenal suppression, denoting passage of the steroid into the systemic bloodstream.

Glucocorticoids

- Glucocorticoids are life-sustaining cholesterol derivatives produced in the zona fasciculata of the adrenal cortex under the negative feedback control of both the hypothalamus and pituitary gland, maintained by the hypothalamic-pituitary-adrenal (HPA) axis.
- The hypothalamus produces corticotropin-releasing hormone (CRH), which stimulates the pituitary gland to synthesize adrenocorticotrophic hormone (ACTH) to signal production of cortisol, the main endogenous glucocorticoid (1, 3, 64)

Glucocorticoids

- Glucocorticoids play a crucial role in maintaining cell homeostasis and viability of the organism.
- Glucocorticoids are required to maintain normal carbohydrate, lipid, and protein metabolism (64).
- Glucocorticoids are postulated to enhance normal immune activity and wound healing, maintenance of cardiovascular integrity and cardiac contractility, and various other functions (64).

Table 4. Characteristics of adrenal insufficiency

Type	Etiologies	Features
Tertiary Most common form	Usually from iatrogenic corticosteroid therapy and suppression of the hypothalamic-pituitary-adrenal axis	Hypothalamic/pituitary suppression or absence
Secondary Uncommon	Decreased or absent ACTH (may be panhypopituitary or anterior pituitary dysfunction) Pituitary depression, dysfunction/damage Tumor, postpartum	ACTH dependent Signs and symptoms usually due to loss of glucocorticoid function Usually have intact mineralocorticoid function Renal hypovolemic, more commonly hypoglycemic
Primary Rare	Autoimmune (70% -90% of cases in United States), frequently associated with a polyglandular deficiency syndrome Prevalence: 40-110 cases/million Infection HIV is the most common infectious cause in the United States. AI develops in 30% of patients with advanced AIDS. Tuberculosis is the most common infectious cause worldwide Inflammation Cancer (breast, lung, melanoma most common) Acute addisonian crisis Incidence: 6 cases/million per year	ACTH independent Adrenal gland dysfunction, destruction, or replacement; requires >90% loss of adrenal tissue Loss of mineralocorticoid and glucocorticoid production Increased ACTH production May be hyperpigmented Requires lifetime therapy

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**Does it causes adrenal
suppression**

- Recently it has been estimated that glucocorticoid secretions are approximately 5 mg/m² per day to 10 mg/m² per day of cortisol, which is apparently much less than previously reported (67, 68).
- These estimates of glucocorticoid secretion are equivalent to about 20 to 30 mg/day of hydrocortisone or 5 to 7 mg/day of oral prednisone.
- However, the synthesis of cortisol can increase 5- to 10-fold under conditions of severe stress, to a maximal level of approximately 100 mg/m²/day (3, 69).

- Recent literature suggests that patients who receive 5mg/day or less of prednisone continue to have an intact HPA axis (78). However, the recovery of the HPA axis after the discontinuation of exogenous glucocorticoids may take up to a year (69).
- Measure of plasma cortisol levels when patients are not receiving exogenous glucocorticoids and judicious application of adrenal stimulation with a lower high-dose cosyntropin stimulation test are recommended on an individual basis to determine HPA axis reserve in persons with adrenal suppression secondary to glucocorticoid therapy (2, 79).

Review Article

Role of Neuraxial Steroids in Interventional Pain Management

Laxmaiah Manchikanti, MD

The clinical introduction of cortisone in 1949 revolutionized medical care of patients with a host of diseases. Soon after that, the first use of steroids in epidural injections was described in 1952 and 1953. A variety of corticosteroid agents (hydrocortisone, methylprednisolone, triamcinolone, betamethasone) have been applied neuraxially to treat spinal pain and other types of painful conditions. The utilization of neuraxial steroids had its empirical beginning in the 1950s and '60s. When steroid administration seemingly was effective for management of low back pain and sciatica, the concept was adapted for other types of neural blockade, including facet joint injections. It is postulated that corticosteroids reduce inflammation by inhibiting either the synthesis or release of a number of pro-inflammatory substances and by causing a reversible local anesthetic effect.

Multiple complications of corticosteroid administration are

two-fold: those resulting from withdrawal of steroids and those resulting from continued use of large doses. These include neural toxicity, separation of pituitary-adrenal axis, weight gain, osteoporosis, as well as many other complications. However, a review of the literature on epidural steroids or other types of neuraxial blockade mentions very few complications that can be directly attributed either to the chemistry or the pharmacology of the steroids, except for reports of adrenal suppression.

This review describes various aspects of neuraxial steroids including historical concepts, mechanism of action, pharmacological aspects, side effects, complications and their role in treatment.

Keywords: Neuraxial steroids, epidural steroid injections, corticosteroids, hypothalamic-pituitary-adrenal suppression, neurotoxicity, osteoporosis, deposteroids

The clinical introduction of cortisone a purified glucocorticoid preparation, in 1949, revolutionized the medical care of patients with a host of diseases (1-3). Soon after this, the first use of steroids in epidural injections dating back to 1952 and 1953 was reported (4, 5). Simultaneous with the introduction of steroids in management of low back pain neuraxially, case reports also started appearing with the introduction of chronic glucocorticoid therapy despite

controversy with regards to their pharmacology mechanism of action, neural toxicity and other side effects and complications.

HISTORY

The first descriptions of the use of neural blockade in managing low back and lower extremity pain date back to an

Janicki et al (73) reported pharmacokinetic analysis of methylprednisolone after epidural administration in rabbits, with only traces of methylprednisolone being detected at 6 and 12 hours after the administration of highest epidural dose of the drug, ie, 5 mg/kg, whereas plasma methylprednisolone levels were undetectable at 24 to 72 hours after 5 mg/kg dose and at all sampling times for the epidural doses of 2.5 and 1.25 mg/kg.

Jacobs et al (71) studied 12 patients following administration of a single lumbar epidural steroid injection of methylprednisolone acetate, 80 mg, and found no absorption of the corticosteroid into the systemic circulation

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A-955
2004

Prevalence of Impaired Adrenal Function after Epidural Steroid Application for Low Back Pain

Tobias Huebner
Ph.D.
Department of

Gerber, M.D.,

Background: The prevalence of adrenal insufficiency in patients with low back pain.

Results; 22 patients. Plasma cortisol values on day 0 (immediately before epidural steroid injection) and on day 14. Baseline and stimulated plasma cortisol values differed significantly between day 0 and 14 ($p < 0.001$).

mortality. Few patients with low back pain.

Materials and Methods: All patients gave informed consent. We performed a retrospective analysis of 22 patients with low back pain who had undergone epidural steroid injection. All patients had a baseline cortisol level and a stimulated cortisol level on day 0 and day 14. The patients were divided into two groups: those who had a cortisol level < 550 nmol/L on day 0 and those who had a cortisol level > 550 nmol/L on day 0. The patients who had a cortisol level < 550 nmol/L on day 0 were included in the analysis.

and informed consent. All patients had a baseline cortisol level and a stimulated cortisol level on day 0 and day 14. The patients were divided into two groups: those who had a cortisol level < 550 nmol/L on day 0 and those who had a cortisol level > 550 nmol/L on day 0. The patients who had a cortisol level < 550 nmol/L on day 0 were included in the analysis.

Results: 22 patients had adrenal insufficiency shown in the ACTH test ($p < 0.001$). Cortisol values were < 550 nmol/L on day 0 in 19 patients and > 550 nmol/L on day 0 in 3 patients.

Conclusions: 14 Days after epidural lumbar steroid therapy, a high incidence of deficient ACTH stimulation tests with depressed baseline plasma cortisol values were found, and therefore, by means of the low-dose ACTH test, adrenal insufficiency can be diagnosed in high proportion of these patients. These patients not only have diminished stimulated plasma cortisol levels, but also significantly reduced cortisol increase to ACTH.

Results: 22 patients were included. One patient had adrenal insufficiency shown in the ACTH test ($p < 0.001$). Cortisol values were < 550 nmol/L on day 0 in 19 patients and > 550 nmol/L on day 0 in 3 patients.

Conclusion: The prevalence of adrenal insufficiency in patients with low back pain is high. The prevalence of adrenal insufficiency in patients with low back pain is high. The prevalence of adrenal insufficiency in patients with low back pain is high.

Conclusion: The prevalence of adrenal insufficiency in patients with low back pain is high. The prevalence of adrenal insufficiency in patients with low back pain is high. The prevalence of adrenal insufficiency in patients with low back pain is high.

Anesthesiology

Plasma

Day 0
Day 14
Mean plasma

ACTH stimulation
0
D

Epidural Triamcinolone Suppresses the Pituitary-Adrenal Axis in Human Subjects

At 48 days after the first ESI (34 days after the third ESI), plasma ACTH and Cortisol were significantly suppressed only in the group that had received midazolam before each ESI. At 48 days, the plasma Cortisol response to cosyntropin was blunted (<500 nmol/L) in 5 of 14 patients. **All patients had a normal Cortisol response to cosyntropin by 3 mo after the last ESI. Weekly ESI over 3 wk caused a dramatic acute and chronic suppression of the HPA axis.** Median suppression was less than 1 mo, and **all patients had recovered by 3 mo. Sedation with midazolam accentuated the suppression of the HPA axis.** Exogenous steroid coverage during this potentially vulnerable period should be considered in patients undergoing major stress especially if the adrenocortical response to ACTH is subnormal.

suppressed in the group receiving midazolam and plasma Cortisol was markedly suppressed in both groups.

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Adrenal suppression following extradural steroids

Summary

Adrenocortical function was tested in 12 patients following a single lumbar extradural injection of methyl-prednisolone acetate ('Depo-Medrol') 80 mg as treatment for chronic sciatica. There was no absorption of the corticosteroid into the systemic circulation, but ***marked suppression of plasma Cortisol levels was documented for up to 3 weeks following the injection and the capacity of the adrenal cortex to secrete Cortisol in response to synthetic adrenocorticotrophin (ACTH) was diminished.*** These results suggest that the dose and frequency of extradural steroid administration should be kept to a minimum to prevent suppression of the hypothalamic-pituitary-adrenocortical axis and that ***patients thus treated should be considered candidates for steroid cover during surgery and other stressful procedures***

FRACR, Senior Lecturer in Pharmacology, St Charles Hospital, Queen Elizabeth II Medical Centre, Nedlands, Western Australia 6009, Australia.

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Epidural Steroid Injections

- Author: Boqing Chen, MD, PhD; Chief Editor: Rene Cailliet, MD [more...](#)

Updated: Nov 8, 2011

Overview

Epidural steroid injections (ESIs) have been endorsed by the North American Spine Society and the Agency for Healthcare Research and Quality (formerly, the Agency for Health Care Policy and Research) of the Department of Health and Human Services as an integral part of nonsurgical management of radicular pain from lumbar spine disorders.

Radicular pain is frequently described as a sharp, lancinating, radiating pain, often shooting from the low back down into the lower limb(s) in a radicular distribution. Radicular pain is the result of a nerve root lesion and/or inflammation. Clinical manifestations of nerve root inflammation include some or all of the following: radicular pain, dermatomal hypesthesia, weakness of muscle groups innervated by the involved nerve root(s), diminished deep tendon reflexes, and positive straight or reverse leg-raising tests. In contrast to oral steroids, ESIs offer the advantage of a more localized medication delivery to the area of affected nerve roots, thereby decreasing the likelihood of potential systemic side effects. Studies have indicated that ESIs are most effective in the presence of acute nerve root inflammation.

The first documented epidural medication injection, which was performed using the caudal approach (see Approaches for Epidural Injections), was performed in 1901, when cocaine was injected to treat lumbago and sciatica (presumably pain referred from lumbar nerve roots).^[1] According to reports, epidurals from the 1920s-1940s involved using high volumes of normal saline and local anesthetics. Injection of corticosteroids into the epidural space for the management of lumbar radicular pain was first recorded in 1952.

ESIs can provide diagnostic and therapeutic benefits. Diagnostically, ESIs may help to identify the epidural space as the potential pain generator, through pain relief after local anesthetic injection to the site of presumed anatomic pathology. In addition, if the patient receives several weeks or more of pain relief, then it may be reasonable to assume that an element of inflammation was involved in his or her pathophysiology. Since prolonged pain relief is presumed to result from a reduction in an inflammatory process, it is also reasonable to assume that during the period of this analgesia, the afflicted nerve roots were relatively protected from the deleterious effects of inflammation. Chronic inflammation can result in edema, wallerian degeneration, and fibrotic changes to the neural tissues.

In these authors' opinion, ESIs are best performed in combination with a well-designed spinal rehabilitation

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Epidural Steroid Injections, Medscape reference

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Medscape Reference



Epidural Steroid Injections

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Timing, Frequency, Dose, and Volume of Epidural Injections

The optimal timing of epidural injection is unknown. Patients with radicular symptoms often undergo a few weeks of treatment, including relative rest or activity modification, medication, physical therapy, and/or manual therapy, prior to undergoing epidural injections. If the patient does not have success with such a program, or if the therapy cannot progress because the patient's pain is too severe (as long as there are no signs of progressive neurologic deficits), epidural injection is indicated for pain control.

In contrast, early use of epidural steroid injections (ESIs) can be considered in patients with severe radicular pain that does not respond even to opioid medication or in whom the pain is severely interfering with sleep habits and daily functioning. Early ESIs also carry the theoretical benefit of controlling inflammation at the early stage and of preventing permanent neural damage, such as nerve fibrosis from the prolonged inflammatory process. Under these circumstances, early administration of ESIs may have a more beneficial effect than would later/delayed use.

The interval between injections varies with the steroid preparation used. Because injected methylprednisolone has been reported to remain in situ for approximately 2 weeks, the clinician should consider waiting approximately 2 weeks after the injection to assess the patient's response and to determine if it would likely be beneficial to administer a repeat injection. However, this 2-week interval may be reduced if a different (short-acting) steroid is used or if the clinical scenario warrants an earlier performance of the repeat epidural. In general, however, routine performance of a predetermined fixed number of epidural injections without a clinical reevaluation in between injection procedures should be discouraged.

The ideal number of epidural injections to be administered for a given clinical scenario is often unclear, because there are no clear data in the current literature on the exact number ESIs to be administered and the timing that should be employed. Clinical practice patterns, however, suggest that up to 3-4 injections may be used for acute radicular pain syndromes. Reevaluation by a physician after each injection seems to be indicated to determine the need for additional procedures prior to pursuing a "series" of 3 epidural injections, regardless of clinical response, since there are no medical outcome studies to clearly support such a regimen.

Studies have suggested that, depending on the particular clinical scenario, the total dose of methylprednisolone should probably not exceed approximately 3 mg/kg of body weight, in order to prevent excessive salt and water retention. A study of methylprednisolone dosage in patients with chronic lower back pain found that a 40-mg dose is just as effective as an 80-mg dose in improving disability. The lower dose should be considered for patients who receive repeat injections.^[17] For interlaminar ESIs, the typical corticosteroid doses are 12-18 mg for betamethasone and 80-120 mg for methylprednisolone. Half of these steroid doses are generally used when performing transforaminal ESIs. The epidural steroid is injected in a diluent, such as lidocaine (1-2%) and/or normal saline.

The volume of the injectate is dictated mainly by the approach used. In cervical and thoracic epidural injections, a total of 3-5 mL may be used for ESIs employing the interlaminar approach. However, in cervical and thoracic transforaminal ESIs, clinicians generally use a total volume of only about 1.5-2 mL. The volume used for lumbar ESIs is slightly greater, generally being 6-10 mL for interlaminar ESIs, up to 20 mL for caudal ESIs, and 3-4 mL for transforaminal ESIs.

Contributor Information and Disclosures

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- **Timing;**

unknown, but as long as there are no signs of progressive neurologic deficits), epidural injection is indicated for pain control.

Frequencies:

- The interval between injections varies with the steroid preparation used. Because injected methylprednisolone has been reported to remain in situ for approximately 2 weeks, the clinician should consider waiting approximately 2 weeks after the injection to assess the patient's response.
- The ideal number of epidural injections to be administered for a given clinical scenario is often unclear, because there are no clear data in the current literature on the exact number ESIs to be administered and the timing that should be employed. Clinical practice patterns, however, suggest that up to 3-4 injections may be used for acute radicular pain syndromes

Frequencies:

- Some authors recommend one injection for diagnostic as well as therapeutic purposes; others preach three injections in a series irrespective of patient's progress or lack thereof;
- still others suggest three injections followed by a repeat course of three injections after 3; 6; or 12-month intervals; whereas others propose an unlimited number of injections with no established goals or parameters.
- A limitation of 3 mg/kg of body weight of steroid or 210 mg/year in an average person and a lifetime dose of 420 mg of steroid also has been advocated

Doses:

Studies have suggested that, depending on the particular clinical scenario, the total dose of methylprednisolone should probably not exceed approximately 3 mg/kg of body weight, in order to prevent excessive salt and water retention.

A study of methylprednisolone dosage in patients with chronic lower back pain found that a 40-mg dose is just as effective as an 80-mg dose in improving disability. The lower dose should be considered for patients who receive repeat injections.^[17]

For interlaminar ESIs, the typical corticosteroid doses are 12-18 mg for betamethasone and 80-120 mg for methylprednisolone. Half of these steroid doses are generally used when performing transforaminal ESIs. The epidural steroid is injected in a diluent, such as lidocaine (1-2%) and/or normal saline.

The volume of the injection is directed mainly by the approach used:

In cervical and thoracic epidural injections, a total of 3-5 mL may be used for ESIs employing the interlaminar approach.

However, in cervical and thoracic transforaminal ESIs, clinicians generally use a total volume of only about 1.5-2 mL.

The volume used for lumbar ESIs is slightly greater, generally being 6-10 mL for interlaminar ESIs, up to 20 mL for caudal ESIs, and 3-4 mL for transforaminal ESIs.

- However, patients with adrenal suppression secondary to corticosteroid drug therapy usually have intact mineralocorticoid function via the renin-angiotensin aldosterone system (1).

Table 1. Profile of commonly used epidural steroids

Drug	Equivalent Dose	Epidural Dose	Anti-inflammatory Potency	Sodium Retention Capacity	Duration of Adrenal Suppression		
					IM	Single Epidural	Three Epidurals
Hydrocortisone	20 mg	N/A	1	1	N/A	N/A	N/A
Depo-Methyl Prednisolone (Depo-Medrol)	4 mg	40-80 mg	5	0.5	1-6 weeks	1-3 weeks	N/A
Triamcinolone diacetate (Aristocort)	4 mg	25-50 mg	5	0	1-2 weeks	1-5 weeks	N/A
Triamcinolone acetonide (Kenalog)	4 mg	40-80 mg	5	0	2-6 weeks	N/A	2-3 months
Betamethasone (Celestone Soluspan)	0.6 mg	6-12 mg	25	0	1-2 weeks	N/A	N/A

N/A = Not applicable Data adapted and modified from McEvoy et al (70), Jacobs et al (71), Kay et al (72), Hsu et al (74), Mikhail et al (75, 76), and Schimmer and Parker (77).

In summary

Epidural steroids results in elevation of blood glucose for limited period of time (2 days) by:-

- 1- Decrease sensitivity to insulin.
- 2- Modulation of pancreatic insulin secretion.
- 3- Modulation of hepatic and extra-hepatic responses to insulin.
- 4- Glucocorticoids are important stress hormones whose hyperglycemic effects are enhanced in disease states such as DM where insulin secretion is limited .

In summary

The patients with diabetes should be given specific advice on the management of their condition after glucocorticoid epidural in the form of a protocol jointly agreed by the interventionist , rheumatology and diabetes teams.

In addition, the possibility of impaired stress responses due to adrenal suppression should be borne in mind in any patient who has received a glucocorticoid epidural within the last month. Finally, when investigating a patient with insulin resistance or impaired glucose tolerance, a history of recent glucocorticoid exposure should include epidural administration.