

# The Role of Corticosteroids in the Treatment of Metastatic Epidural Spinal Cord Compression

Lisa M Ruppert\*

Rehabilitation Medicine Service, Memorial Sloan Kettering Cancer Center-Sillerman Center for Rehabilitation, New York, USA

Metastatic epidural spinal cord compression is the third most common cause of adult compressive myelopathy, after acute trauma and degenerative etiologies. In individuals with systemic cancer it is one of the most common neurologic complications, following the brain parenchymal metastases [1]. Epidural spinal cord compression can be caused by metastases from most primary malignancies. Solid tumors of the lung, breast, prostate and kidney, lymphoma and sarcoma, however, have a higher predisposition for spinal metastases [2].

Metastases most commonly reach the epidural space from the vertebral body (85% of cases) or the intervertebral foramen (15% of cases). Hematogenous spread to the epidural space is extremely rare. Injury to the spinal cord results from mechanical injury to axons and myelin as well as from secondary vascular compromise of the spinal arteries and epidural venous plexus with resulting cord infarction and venous congestion [1]. Left untreated, epidural spinal cord compression ultimately results in paralysis and sphincter incontinence [2]. Corticosteroids are considered the first line of treatment for most individuals with epidural spinal cord compression [1]. They have been shown to reduce tumor and spinal cord edema and can potentially have tumoricidal effects [3]. It is recommended that corticosteroids be administered as soon as the diagnosis of epidural cord compression is made to improve or stabilize neurological deficits until other more definitive therapies are initiated [1,3].

Anecdotal reports of the effectiveness of corticosteroids in reducing mass effect of epidural cord compression from metastatic disease date back to the 1960s [3]. Cantu described two cases of spinal metastases associated with paraparesis in which significant neurological improvement occurred within 24 hours of starting methylprednisolone [4]. Ushio et al. [5] developed an animal model using Walker 256 carcinoma to evaluate spinal cord edema in epidural cord compression from spinal metastases. They concluded that epidural compression results in vasogenic spinal cord edema which is responsive to steroids. In 1977, Posner et al. suggested that corticosteroids may lead to clinical improvement in individuals with epidural cord compression not only by decreasing spinal cord edema, but through oncolytic effects they have on a variety of tumors, particularly lymphomas [6].

There is no consensus on the best loading dose and maintenance regimen for corticosteroids in epidural spinal cord compression. Doses tend to fall into moderate dose (10 mg IV loading dose followed by 16 mg orally with 2 week taper) and high dose (100 mg IV loading dose followed 96 mg orally with 2 week taper) regimens [3]. Moderate doses were derived from clinical experience with dexamethasone in treating brain metastases. The high dose regimen was proposed based on animal studies [7]. Ushio et al. [8] suggested treatment with high dose dexamethasone (100 mg to 150 mg/70 kg man) based on their animal model of epidural spinal cord compression in rats injected with Walker 256 carcinoma. Delattre et al. [9] later compared low dose (0.1 mg/kg), intermediate dose (1 mg/kg) and high dose (10 mg/kg) dexamethasone in T8-T10 epidural cord compression in 50 rats implanted with Walker 256 tumor. Based on this study, the authors suggested use of high dose dexamethasone for the shortest time consistent with maintaining spinal cord function and rapid taper after initiation of more definitive therapy.

Inspired by animal studies, Greenberg et al. designed a protocol for the treatment of metastatic spinal cord compression with high dose dexamethasone (96 mg/day) as adjunct to radiation therapy [10]. At the completion of their protocol they were unable to assess the effects of steroids alone on preserving neurological function since radiation therapy was begun immediately after steroid therapy. They did however report substantial improvements in pain in the majority of patients treated with dexamethasone even before the initiation of radiation therapy [10,11]. In an attempt to obtain consensus on the role of glucocorticoid administration as an adjuvant to definitive therapy, a randomized control trial of high dose dexamethasone versus no steroid treatment was performed in patients with metastatic spinal cord compression from solid tumors. The authors of this study suggested a beneficial effect of high dose dexamethasone as an adjunct therapy to definitive treatment for individuals with metastatic epidural spinal cord compression [11]. They also noted that lower doses may prove equally effective; sighting a comparison of conventional (10 mg IV bolus followed by oral taper) versus high dose dexamethasone (100 mg IV bolus followed by oral taper), in which no advantage of high dose over conventional dose was found [11,12].

These studies provide good evidence that dexamethasone is an effective adjuvant to definitive therapies such as surgical resection and radiation therapy using ambulatory status, bladder function, or pain as functional outcome measures. All studies of the treatment of spinal cord compression agree on the importance of early diagnosis and treatment. They suggest that pretreatment motor function is the most important prognostic indicator of ambulatory outcomes [3]. In individuals with metastatic epidural spinal cord compression, ambulation can be preserved in 75-85% of individuals who are ambulatory at the time of treatment but only restored in 10-20% of individuals who are non-ambulatory at the onset of treatment [11].

The authors of these studies acknowledge that the use of steroid treatment is not without risk of serious side effects. They report that the risk of serious side effects is related to total dose received and duration of treatment [13]. Hyperglycemia, infections, gastrointestinal ulceration, proximal myopathy, peripheral edema, weight gain, psychosis, hiccups, intense tingling and burning of the perineum and death have been reported [1,11].

Although these studies have established the efficacy and side effect

\*Corresponding author: Lisa M. Ruppert, Rehabilitation Medicine Service, Memorial Sloan Kettering Cancer Center-Sillerman Center for Rehabilitation, New York, USA, E-mail: [rupperl1@mskcc.org](mailto:rupperl1@mskcc.org)

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profile of corticosteroids in the treatment of malignant epidural spinal cord compression, they have not determined the optimum loading and maintenance doses [3]. Currently one approach has been to administer moderate doses to ambulatory individuals with minimum or non-progressive motor findings, reserving high doses for individuals with severe neurologic dysfunction [1,3,14]. There is however consensus that corticosteroids should be tapered rapidly once definitive treatment is underway [14]. Further studies comparing moderate dose to high dose dexamethasone in treatment of metastatic epidural spinal cord compression are recommended. The primary outcome of these studies should be post treatment ambulatory status, and the secondary outcome overall complication rate. These studies would serve to answer the question of optimum steroid dosing, and satisfy the validity of many of the clinical decisions that are made with regard to the management of metastatic epidural spinal cord compression [15].

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