Steroids are effective in the treatment of acute spinal cord injury

For years, the role of high-dose corticosteroids in treating neurological trauma has been a controversial component of EMS practice. As paramedics in the 1970s, we routinely administered varying doses of dexamethasone (Decadron) to patients with head injuries. The theory behind its use was that the drug would decrease inflammation and swelling within the brain. The doses varied significantly based upon which medical control physician was on duty. Some physicians would order 4 mg, while others would order massive doses—up to 100 mg on some occasions. Finally, the neurosurgeons said it was not making a difference, and we stopped administering it.

History

High-dose corticosteroid therapy for the treatment of acute spinal cord injury was introduced to prehospital care in the 1980s. The recommended corticosteroid for this purpose was methylprednisolone (MP), and the doses were massive. Prior to the recommendation to use MP for acute spinal cord injury, many EMS services carried standard doses of the drug for use in severe allergic reactions and for difficult cases of asthma and chronic obstructive pulmonary disease. Few carried enough MP to treat acute spinal cord injury as recommended; thus, most systems prepared a special “spinal cord injury kit” that contained adequate quantities of the drug. However, review of pertinent studies has shown that high-dose steroid therapy benefits few, if any, spinal cord injury patients. Furthermore, the side effects and complications of such massive doses of steroids are significant and may outweigh any potential benefits.

The Scientific Evidence

The use of potent anti-inflammatory drugs such as corticosteroids in the management of neurological trauma has always been intriguing. In the 1970s and 1980s, researchers began to look at the use of these drugs for the treatment of acute spinal cord injury. Initially, studies were limited to laboratory animals. The first significant publication of this work was the first National Acute Spinal Cord Injury study (NASCIS 1). In that study, patients received either a 100 or 1,000 mg infusion of MP, followed by a bolus of 250 mg every six hours for 10 days. No significant improvements were noted in either group. Following that study, new data from ongoing animal studies suggested that the MP dose used in NASCIS 1 was too low. Instead, a dose of 30 mg per kilogram of body weight was felt to be the therapeutic threshold. Based upon this finding, researchers embarked on a second study, NASCIS 2.

In NASCIS 2, patients were divided into three treatment groups. One group received high-dose MP (a 30 mg/kg bolus followed by an infusion of 5.4 mg/kg per hour for 24 hours); the second group received a high dose of the narcotic antagonist naloxone (a 5.4 mg/kg bolus followed by an infusion of 4.0 mg/kg per hour for 23 hours); and the third group received a placebo as a control. Naloxone was included in the study because some earlier studies found that it improved systemic hypotension, spinal cord blood flow and neurological recovery in laboratory animals. In NASCIS 2, patients, physicians and researchers were blinded as to which patients were receiving which therapy. They found that patients who received high-dose MP had “significant improvement” compared to those in the other two study groups. When they further analyzed the data, they found that patients who received high-dose MP within eight hours of injury had the best outcomes. The findings were felt to be highly significant, and before peer-reviewed publication, both the media and practitioners were notified of the findings.

In a follow-up study, subsequently termed NASCIS 3, researchers looked at extended dosing regimens of high-dose MP (following the NASCIS 2 schedule) for a period of either 24 or 48 hours. In addition, they compared MP therapy to a drug thought to enhance spinal cord recovery (tiludazam mesylate). They concluded that patients who received high-dose MP within three hours of injury should be maintained on the treatment regimen for 24 hours, while patients who received the first bolus between 3–8 hours post-injury should be maintained on steroid therapy for 48 hours.

As these studies were published, clinicians began to take a critical look at the research. The positive results claimed by researchers in NASCIS 2 and NASCIS 3 could not be reproduced. When the NASCIS 2 study was analyzed in detail, it was found that the reported improvements in neurological function were so small that they could not be considered clinically significant.

In addition, there were numerous reports of significant complications associated with high-dose MP administration. The incidence of respiratory complications (severe pneumonia), infectious complications...
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(severe sepsis), metabolic complications (hyperglycemia) and delayed wound healing was increased in patients who received high-dose MP.94 Others proposed that the high dose of steroids used in the treatment of acute spinal cord injury may have actually damaged the patient's muscles (steroid myopathy). They further postulated that the motor function improvement seen in NASCIS 2 may actually have been a result of the muscles recovering from the effects of the steroids instead of spinal cord healing.95

Numerous analyses of the research studies and available literature indicated that the use of high-dose steroids in spinal cord injury was not nearly as effective as once thought. Some researchers looked at microscopic tissue changes following high-dose MP therapy. They found that while high-dose MP reduced the development of severe edema and preserved spinal cord structure adjacent to the site of injury, it did not alter the development of spinal cord necrosis or astrocytic (nerve cell) response at the area of injury.96 Other researchers went back to animal models and found a lack of benefit.97 Conclusions from scholarly review papers included this: "From an evidence-based approach, MP cannot be recommended for routine use in acute non-penetrating spinal cord injury." Another stated, "The evidence produced by this systematic review does not support the use of high-dose MP in acute spinal cord injury to improve neurological recovery."98 Other experts concurred.99

Based on this, several organizations have published recommendations and position statements related to the use of steroids in acute spinal cord injury. The Congress of Neurological Surgeons issued recommendations that stated there was insufficient evidence to recommend MP in acute cervical spinal cord injury as either a standard of care or a treatment guideline. They further stated, "Treatment with MP for either 24 or 48 hours is recommended as an option in the treatment of patients with acute spinal cord injuries that should be undertaken only with the knowledge that the evidence suggesting harmful side effects is more consistent than any suggestion of clinical benefit." The Canadian Association of Emergency Physicians issued a position paper that concluded there was insufficient evidence to support the use of high-dose MP within eight hours of an acute spinal cord injury as a treatment standard or guideline. Instead, like the neurosurgeons, they listed it as a treatment option supported only by weak scientific evidence.99

Conclusion

The suggested use of corticosteroids in the treatment of acute spinal cord injury is another example of rushing to judgment by members of the medical and EMS communities. As they did with the use of tPA for ischemic stroke, the therapeutic community changed worldwide treatment guidelines for acute spinal cord injury based upon a single study that, in retrospect, was not as strong as initially thought. Furthermore, no quality studies have been able to replicate the results of the NASCIS 2 trial, and based upon this, many organizations and experts have clearly stated that the use of steroids in the management of spinal cord injury is not a standard of care—not even a guideline for care—but only an option based on weak scientific evidence.

So, here is one more useless treatment modality we can remove from our prehospital treatment protocols. We can safely take the large quantities of MP carried in many EMS and rescue units and return them to the pharmacy.

References


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