ORIGINAL ARTICLE

High dose methylprednisolone in the immediate management of acute, blunt spinal cord injury: what is the current practice in emergency departments, spinal units, and neurosurgical units in the UK?

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Background: The National Acute Spinal Cord Injuries Studies and the Cochrane Review advocate the administration of high dose methylprednisolone following acute traumatic spinal cord injury. However, controversy surrounds its use and approaches between different units are often inconsistent.

Methods: A questionnaire was sent to all emergency departments receiving major trauma and all specialist neurosurgical and spinal units in the UK to determine the current practice regarding the use of high dose methylprednisolone in the immediate management of acute, blunt spinal cord injuries.

Results: Of 250 emergency departments, 187 replied to the questionnaire. Twelve of the 26 departments with a neurosurgical or spinal service on site stated they received consistent advice from specialist teams. Sixty four departments had a written policy regarding the treatment of spinal injuries, which in 51 departments contained advice about the administration of methylprednisolone. Of the 128 departments who gave methylprednisolone, 88 did so only on the advice of a specialist team, with the remaining 40 giving steroids immediately on identification of the injury. Ten out of 11 spinal units replied, of whom only two advised the use of steroids. Of the 34 neurosurgical units approached, seven out of 17 responders had a policy recommending the use of steroids. Of the 10 units who did not consistently recommend the use of steroids, seven had practise that varied between consultants.

Conclusion: Currently practice varies in the UK regarding the immediate use of methylprednisolone after spinal injury. Clear guidelines need to be established to achieve a more consistent approach.

Injury to the spinal cord causes significant morbidity; most victims are under 30 years of age and many are left permanently disabled and require specialist care for the rest of their lives. In the UK an average of two new patients per day are admitted to spinal units following traumatic spinal cord injury.

Any drug that might mitigate some of the disability associated with these injuries is an attractive prospect. In 1990, Bracken *et al* published the results of the 2nd National Acute Spinal Cord Injury Study (NASCIS II).¹ This study concluded that high dose methylprednisolone, if given within 8 h of injury, could mitigate some of the disability associated with these injuries. NASCIS III² further refined the administration protocol and, following widespread publicity, high dose methylprednisolone was rapidly adopted as the standard of care for acute spinal cord injury.

A report published in the UK in 2001 suggested that "patients presenting within 8 hours of an acute spinal cord injury should be given methylprednisolone 30 mg/kg as soon as possible; further steroid therapy to be discussed with the admitting spinal unit".³ A Cochrane Review⁴ (last substantive update January 2002) concluded "high dose methylprednisolone steroid therapy is the only pharmacological therapy shown to have efficacy in a phase three randomised trial when it can be administered within 8 hours of injury ... there is urgent need for more randomised trials of pharmacological therapy for acute spinal cord injury".

Since the publication of NASCIS II, however, concerns regarding this treatment have been raised and a number of well publicised reviews have cast doubts on the results of the original trials.^{5–9} An audit carried out in 2001 found that only 25% of patients admitted to a specialist unit received

methylprednisolone according to NASCIS protocols.¹⁰ Similarly, O'Conner *et al*¹¹ found that of 196 admissions to their unit in 2001, only 14% received intravenous methylprednisolone.

This survey was undertaken to determine the current UK practice with regard to the use of high dose methylprednisolone in the immediate management of acute, blunt spinal cord injuries, and to determine whether there is a consistent approach to the management of this problem.

METHODS

The clinical directors of emergency departments, spinal units, and neurosurgical units in the UK were sent a questionnaire asking them to detail their use of high dose methylprednisolone in traumatic acute, blunt spinal cord injury. Emergency departments contacted were all those listed in the BAEM directory (2003/4) as units capable of taking major trauma (minor injury units, eye units, and paediatric emergency departments were excluded). Spinal units contacted were those listed on the spinal injuries website (<http://www.spinalnet.co.uk>), and neurosurgical units contacted were identified from the Directory of Critical Care (CMA Medical Data, Loughborough, UK). Separate questionnaires were sent to emergency departments and to specialist units (appendices A and B), and a reply paid envelope was supplied to encourage a response. A reminder and second copy of the questionnaire were sent to all non-responders after 4 weeks.

RESULTS

A total of 187 out of 250 emergency departments responded to the questionnaire (75%). The majority of departments (78%) saw between zero and five spinal cord injuries a year

Figure 1 Number of patients with spinal cord injuries seen per emergency department per year. DK, don't know.

(fig 1). Twenty six of the responding emergency departments had a neurosurgical or spinal service on site, with 12/26 of these stating that they received consistent advice from the specialist teams. Overall, only 43% of emergency departments reported receiving consistent advice (fig 2). Sixty four emergency departments had a written policy regarding the treatment of spinal injuries, of which 51 said it contained advice about the administration of methylprednisolone. Of the 128 departments who gave methylprednisolone, 88 (69%) did so only on the advice of a specialist team, while 40 (31%) gave steroids immediately on identification of the injury.

Departments that never gave methylprednisolone ($n = 59$) were asked to give reasons for their decision (fig 3). Forty seven of 59 replied that this was a result of a decision by their regional centre. Other reasons given included review of the evidence by the emergency department and a joint discussion between the emergency department and regional centre. Two departments stated that they had other reasons, although these reasons were not specified.

Ten out of 11 spinal units replied, of whom only two advised the use of steroids. There was no recorded inconsistency of approach between consultants in the same unit. Of the eight units who did not recommend the use of steroids, the most common reasons given were that the improvement seen with methylprednisolone was not clinically significant and that the risk of side effects outweighed any clinical improvement. Two units also felt that the methodology of the NASCIS studies was flawed. One unit did not give a reason.

Response from the 31 neurosurgical units approached was more variable with seven out of 17 responders having a policy that recommended steroid use. Of the 10 units who did not consistently recommend the use of steroids, seven units had practice that varied between consultants. Those who did not recommend steroids gave reasons similar to those given by spinal units.

DISCUSSION

The evidence for the use of methylprednisolone after acute, blunt spinal cord injury comes from subgroup analysis of one trial, NASCIS II. However, closer analysis of the trial's results

Figure 2 Percentage of departments receiving consistent advice. DK, don't know.

Figure 3 Reasons given by emergency departments for not prescribing steroids.

casts doubt on their robustness. NASCIS II was designed to assess the effects of methylprednisolone (or naloxone) on acute spinal cord injury when given within 12 h of injury; overall no treatment benefit was demonstrated when comparing the treated groups to those given placebo. The authors of the trial concentrated instead on evidence of benefit coming from a subgroup analysis of those patients treated within 8 h of injury. In this group it was claimed that patients treated within 8 h with methylprednisolone had significant improvement in motor function ($p = 0.03$), sensation to pinprick ($p = 0.02$), and touch ($p = 0.03$). The authors claimed that the 8 h subgroup had in fact been defined a priori, although the design of the trial fails to make this clear and the reliance on subgroup analysis undoubtedly detracts from the quality of the paper. It has also been argued that the placebo group treated before 8 h did poorly, not only compared to the methylprednisolone group treated before 8 h, but also in comparison to the placebo group treated after 8 h, suggesting that the positive result was caused by a weakness in the control group.⁸

Other criticisms levelled at the study include the charge that as no functional measurement of patient recovery was undertaken, it was therefore impossible to assess whether the improvement of motor and sensory scores demonstrated had any clinical significance,⁹ and that there was no consistency of approach in other treatment aspects between centres.⁶⁻¹² A 1 year follow up found no significant difference between the patient groups in all neurological modalities studied.¹³

As with NASCIS II, the subsequent NASCIS III (which did not include a control group) has also been criticised for its reliance on post hoc subgroup analysis. The authors claimed the trial demonstrated a benefit in giving methylprednisolone even earlier, within 3 h of injury. As with NASCIS II, all primary outcomes defined before patient enrolments were negative, and the only interesting findings were encountered when post hoc analyses were performed.⁸ As a consequence of subgroup analysis, almost 70% of the patient population was excluded from further analysis and it has also been suggested that the small changes in neurologic function described were not clinically significant.¹⁴⁻¹⁵ Although the improvement was greatest in those with incomplete injuries

at 6 weeks, as with NASCIS II, the benefits seen were not sustained at 1 year.

Despite the incorporation of recommendations for the use of methylprednisolone into ATLS guidelines, and the widespread publicity surrounding the publication of NASCIS II, including dissemination of results to clinicians before the release of the scientific paper,¹⁶ implementation of those guidelines has not been universal. Even in the USA, where it has been suggested that any physician who does not administer methylprednisolone will place themselves in "severe legal jeopardy",¹⁷ Gerhart *et al* reported clear documentation of implementation of the protocol in only 46% of eligible patients in 1990–91, rising to a maximum of 61% in 1993.¹⁸

In 2001, Hurlbert and Moulton¹⁹ undertook a survey of Canadian neurological and orthopaedic spine surgeons; 60 surgeons representing about two thirds of those treating acute spinal cord injuries in Canada replied. Thirteen did not recommend the use of methylprednisolone at all, while 17 followed NASCIS II guidelines and 21 NASCIS III. Of those prescribing steroids, the two most common reasons given were "because everyone else does", or out of fear of litigation. Only 10 prescribed steroids primarily because they believed there was benefit to their patients. In 2003, following a review of the evidence, the Canadian Neurosurgical Society, the Canadian Spine Society, and the Canadian Association of Emergency Physicians^{14–15} adopted the recommendation that a 24 h infusion of methylprednisolone started within 8 h of an acute spinal cord injury is neither a standard of care nor a guideline for treatment but rather a treatment option for which there is weak evidence.²⁰ They concluded that there was insufficient evidence to support extending the infusion of methylprednisolone beyond 24 h.

Molloy *et al* undertook a questionnaire survey of the delegates at the European Cervical Spine Research Society to determine their views on the use of methylprednisolone.²¹ They found that although 75% of the delegates recommended the use of methylprednisolone, they had a number of reservations about it, the most common being that they did not think that the benefit of administering methylprednisolone had been clinically or functionally proven. Although some delegates stated that they prescribed methylprednisolone because of concern over the medico-legal consequences of not doing so (unlike the USA and Canada at that time), many delegates also felt that it was defensible to withhold steroids. The current guidelines published by the British Association of Spinal Cord Injury Specialists (BASCIS) state: "In common with clinicians in other countries BASCIS has carefully evaluated the information now available. The published evidence does not support the use of high dose Methylprednisolone as a standard treatment in acute spinal cord injury" (<http://www.bascis.pwp.blueyonder.co.uk/philosophy.htm>).

CONCLUSIONS

Neither the Canadian nor the British spinal injuries associations currently recommend the use of steroids in acute, blunt spinal cord injury, yet a consistent approach is practised in neither emergency departments nor specialised units in the UK. There is currently no good quality evidence for the use of methylprednisolone in this context and its use in the emergency department should be discontinued until such evidence is available. Clear guidelines should be established to ensure a consistent and evidence based approach to acute spinal cord injury.

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APPENDIX A

Methylprednisolone for acute traumatic spinal cord injury (A&E)

Hospital

1. How many new acute traumatic spinal cord injuries have been seen in your department in the last 12 months? a. 0–5; b. 6–10; c. >10

2. Do you have a spinal or neurosurgical service on site? Yes/No

3. Do you have a written policy regarding the management of acute traumatic spinal cord injury? Yes/No

If YES, does this policy include advice regarding the administration of high dose methylprednisolone? Yes/No

Table 1A

Spinal units		Neurosurgical units	
1	Belfast	1	Aberdeen Royal Infirmary
2	Glasgow	2	Addenbrooke's Hospital, Cambridge
3	Middlesbrough	3	Atkinson Morely's Hospital, London
4	Oswestry	4	Charing Cross Hospital, London
5	Rockwood	5	Derriford Hospital, Plymouth
6	Salisbury	6	Frenchay Hospital, Bristol
7	Sheffield	7	Hope Hospital, Salford
8	Southport	8	Hull Royal Infirmary
9	Stanmore	9	Kings College Hospital, London
10	Stoke Mandeville	10	Leeds General Infirmary
11	Wakefield	11	Liverpool (Walton centre)
12	Other	12	Middlesbrough General Hospital
		13	Morriston Hospital, Swansea
		14	Newcastle General Hospital
		15	Ninewells Hospital, Dundee
		16	North Staffordshire Hospital Trust, Stoke
		17	Oldchurch Hospital, Romford, Essex
		18	Princess Royal Hospital, Haywards Heath
		19	Queen Elizabeth Hospital, Birmingham
		20	Queens Medical Centre, Nottingham
		21	Radcliffe Infirmary, Oxford
		22	Royal Free Hospital, London
		23	Royal London Hospital
		24	Royal Hallamshire Hospital, Sheffield
		25	Royal Preston Hospital
		26	Southampton General Hospital
		27	Southern General Hospital, Glasgow
		28	The National Hospital for Neurology and Neurosurgery, Queen Square, London
		29	University Hospital of Wales, Cardiff
		30	Walsgrave Hospital, Coventry
		31	Western General Hospital, Edinburgh
		32	Other

4. Do you give high dose methylprednisolone to acute traumatic spinal cord injuries? Yes/No

If **YES**, do you give it

a. Immediately on identification of acute traumatic spinal cord injury?

b. Only if advised to by the regional spinal/neurosurgical service?

If **NO**, is this

a. The result of a decision made by the A&E staff based on a review of the evidence?

b. The result of discussion held with the regional spinal/neurosurgical service?

5. Which spinal/neurosurgical units do you refer patients with acute traumatic spinal cord injury to? (please circle unit in Table 1A)

6. Do you receive consistent advice from your regional service regarding the use of high dose methylprednisolone in acute traumatic spinal cord injury? Yes/No

7. Any other comments regarding the acute management of spinal cord injuries?

APPENDIX B

Methylprednisolone for acute traumatic spinal cord injury (specialist units)

Unit _____

1. How many new acute traumatic spinal cord injuries have been referred to your department in the last 12 months?

a. 0–5; b. 6–10; c. >10

2. Do you have a written policy regarding the management of acute traumatic spinal cord injury? Yes/No

If **YES**, does this policy include advice regarding the administration of high dose methylprednisolone? Yes/No

3. Does your unit routinely advise high dose methylprednisolone to acute traumatic spinal cord injuries? Yes/No

If **NO**, is there individual variation between consultants in their use of methylprednisolone? Yes/No

4. If you do **NOT** routinely use methylprednisolone, is this because: (please circle any or all that apply)

a. The improvement following methylprednisolone is not significant?

b. The methodology of the NASCIS studies is flawed?

c. The risk of side effects (infection, GI bleeding, etc) outweighs any benefits?

d. Other please specify _____

5. Any other comments regarding the acute management of spinal cord injuries?