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High-dose Intravenous Methylprednisolone for Migraines

Clinical Question

P (population/problem)	In children and adolescents admitted for migraine treatment with high-dose intravenous (IV) methylprednisolone pulses,
I (intervention)	does performing vital signs (including TPR and BP) every 15 minutes during infusion,
C (comparison)	as compared to performing vital signs less frequently,
O (outcome)	result in fewer adverse cardiac events?

Target Population

Children and adolescents admitted for migraine treatment with high-dose IV methylprednisolone

Recommendation(s)

1. There is insufficient evidence and a lack of consensus to make a recommendation on the frequency and duration of vital signs to be monitored during and after administration of high-dose IV methylprednisolone to children and adolescents for migraine therapy.
Note: This question arose from A7 Neuroscience management team meetings. Few adverse effects of high dose methylprednisolone infusions have been noted on the unit and the frequent vital signs can be difficult to accomplish when census and acuity are high. The question was raised whether using cardiac monitoring and less frequent vital signs would maintain safety for these patients.
2. There is no specific clinical practice or nursing policy related to monitoring vital signs during and after administering high dose methylprednisolone; a common practice is to take vital signs every 15 minutes during the infusion time (usually approximately 1 hour).
3. Research on this question is needed to identify the risks associated with the treatment in children and adolescents.

Discussion/summary of evidence

Several cases of unexpected death after high dose intravenous methylprednisolone were reported in the 1980s and early 1990s (Bocanegra, et al., 1981; Gardiner & Griffiths, 1990; Moses, et al., 1981) These reports were all about adult patients with a variety of diseases such as allergic angitis, systemic lupus erythematosus (SLE), lupus nephritis, and rheumatoid arthritis. Most had multisystem disease, but several had no evidence of pre-existing cardiac disease.

Pudil & Hrcir (2001) used "minipulse" treatments to limit adverse events, but reported on 2 adults with rheumatoid disease who had severe bradycardia with the lowered doses of methylprednisolone.

Mignna, et al. (2002) reported on a pilot study that evaluated the efficacy of methylprednisolone IV pulse treatment to induce remission in severe oropharyngeal pharyngitis. Adverse events reported were hyperglycemia (most commonly), flushing, metallic taste, pruritis, HEADACHE, palpitations, mood alterations, insomnia and fatigue. Although this study examined a small number of adults with an unrelated diagnosis (to migraine), the presence of headache as an adverse reaction is noted.

Three descriptive studies examined some aspect of this treatment in children. Klein-Gitelman & Pachman (1998) prospectively documented the adverse events of children treated with intermittent IV corticosteroids (IVCS) to

determine their frequency and severity. All doses were administered over 60 minutes or greater at a dose of 30 mg/kg body weight with a maximum dose of 1000 mg/24 hours. Twenty two percent (N=46) of the 213 children treated over 1990-1994 experienced adverse reactions. Ten percent of the total (N=21; 47 % of those experiencing reactions) had behavioral reactions. They report that no children were hospitalized for treatment due to a severe adverse reaction, though some required observation or treatment. One child experienced hypotension, resolved by normal saline bolus. Another child became hypotensive and tachycardic and was treated with normal saline bolus. Five patients experienced transient hypertension which responded to decreased rate of infusion (2 children), diuretics (2 children), or antihypertensive medication (2 children). The only statistically significant association reported was between a history of a drug induced cutaneous reaction and adverse reactions to IVCS (p<0.01).

In 1980, Miller studied the effectiveness of large IV steroid pulses in treating children with rheumatic diseases who were refractory or toxic with other treatments. The patients received one of two treatments. One option was 500 mg of hydrocortisone sodium succinate in 100 ml of 5% dextrose in water over 20-30 minutes every 6 hours for 4 injections; these patients were monitored for pulse and blood pressure every 10 minutes for an hour after each infusion started and hourly for 24 hours after the start of the first infusion. The second option was a single injection of methylprednisolone in 100 ml of 5% dextrose in water in doses of approximately 30 mg/kg body weight; the same pulse and blood pressure monitoring routine was performed on these patients. The sample size was small (19) and the study was not designed to look at adverse events. However, the side effects that were reported with methylprednisolone were transiently blurry vision and transient flushing and tachycardia.

In 2007, Akikusa reported the experience over a 6 month period with five children with rheumatic diseases who developed sinus bradycardia during consecutive daily therapy with IV pulse methylprednisolone. All patients were undergoing continuous cardiac monitoring before, during and after their infusions. Although the author did not report how many patients received this treatment during the same time frame, the patients who experienced bradycardia were noted. All patients were asymptomatic and none were treated for the bradycardia. All continued to have bradycardia for at least 72 hours after it was first noted. Two patients had abnormal electrolytes when the arrhythmia noted, but correction did not have any immediate effect on the heart rate. Four of the 5 were normotensive. Of the 2 patients discussed at length, in one the low heart rate resolved over 5 days and in the second over 8 days.

Health Benefits, Side Effects and Risks

	Some (be explicit)	Minimal (comment?)	None (comment?)
Health Benefits	Potential to quickly detect adverse cardiovascular adverse reaction to the treatment.		
Side Effects	.	Taking frequent VS increases the nursing time needed per patient, could be a factor in high census/high acuity periods	

References/citations

Akikusa, J. D., Feldman, B. M., Gross, G. J., Silverman, E. D., & Schneider, R. (2007). Sinus bradycardia after intravenous pulse methylprednisolone. *Pediatrics*, 119(3), e778-782. (Level VI)

Bocanegra, T. S., Castaneda, M. O., Espinoza, L. R., Vasey, F. B., & Germain, B. F. (1981). Sudden death after methylprednisolone pulse therapy (letter). *Annals of Internal Medicine*, 95(0003), 122. (Level VII)

Gardiner, P. V., & Griffiths, I. D. (1990). Sudden death after treatment with pulsed methylprednisolone (letter). *British Medical Journal*, 300(6717), 125. (Level VII)

Klein-Gitelman, M. S., & Pachman, L. M. (1998). Intravenous corticosteroids: Adverse reactions are more variable than expected in children. *The Journal of Rheumatology*, 25(10), 1995-2002. (Level VI)

Mignogna, M. D., Lo Muzio, L., Ruoppo, E., Fedele, S., Lo Russo, L., & Bucci, E. (2002). High-dose intravenous 'pulse' methylprednisolone in the treatment of severe oropharyngeal pemphigus: A pilot study. *Journal of Oral Pathology & Medicine*, 31(6), 339-344. (Level VI)

Miller III, J. J. (1980). Prolonged use of large intravenous steroid pulses in the rheumatic diseases of children. *Pediatrics*, 65(5), 989-994. (Level VI)

Moses, R. E., McCormick, A., & Nickey, W. (1981). Fatal arrhythmia after pulse methylprednisolone therapy (letter). *Annals of Internal Medicine*, 95(6), 781-782. (Level VII)

Pudil, R., & Hrcir, Z. (2001). Severe bradycardia after a methylprednisolone "minipulse" treatment (letter). *Archives of Internal Medicine*, 161, 1778-1779. (Level VII)

Quality Ratings for an individual study

- Level I:** Systematic review or meta-analysis of RCTs or evidence-based practice guidelines based on RCTs
- Level II:** At least one well-designed RCT
- Level III:** Well-designed controlled trials without randomization (quasi-experimental)
- Level IV:** Well-designed case-control and cohort studies
- Level V:** Systematic reviews of descriptive and qualitative studies
- Level VI:** One descriptive or qualitative study
- Level VII:** Expert opinion or reports of expert committees

*Adapted from: Melnyk BM & Fineout-Overholt E, Evidence-Based Practice in Nursing & Healthcare: A Guide to Best Practice. 2005, Lippincott, Philadelphia,PA

Strength and Consistency for a body of evidence

- A:** Level I Evidence
- B:** Consistent findings from Levels II, III, IV, or V
- C:** Inconsistent findings from Levels II, III, IV, or V
- D:** Little or no evidence or Level VI only
- E:** Level VII

*Adapted from: Schiffer CA et.al., ASCO Special Article - Platelet Transfusion for Patients with Cancer: Clinical Practice Guidelines of the American Society of Clinical Oncology, Journal of Clinical Oncology,19(5),March 2001, 1519-1538.

Supporting information

Group/team members

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Search strategy

1. DATABASES
 - OID Medline
 - OID CINAHL
 - OID EBM Reviews (Cochrane)
 - Scopus

Reviewed reference lists of articles found for other pertinent references

2. SEARCH TERMS

Methylprednisolone, migraine, children, pulse dosing, adverse effects or events, vital signs.

Additional search terms were used with methylprednisolone, children, pulse dosing, and adverse effects and searched through the above databases: (other possible indications for high dose IV methylprednisolone) acute disseminated encephalomyelitis, acute spinal cord injury, asthma and optic neuritis

3. LIMITS AND FILTERS

English

Humans

Age Range: 0-21 years

Publication date not limited due to few references found

Note

This Best Evidence Statement addresses only key points of care for the target population; it is not intended to be a comprehensive practice guideline. These recommendations result from review of literature and practices current at the time of their formulation. This Best Evidence Statement does not preclude using care modalities proven efficacious in studies published subsequent to the current revision of this document. This document is not intended to impose standards of care preventing selective variances from the recommendations to meet the specific and unique requirements of individual patients. Adherence to this Statement is voluntary. The clinician in light of the individual circumstances presented by the patient must make the ultimate judgment regarding the priority of any specific procedure.

Reviewed by Center for Professional Excellence/Research and Evidence-Based Practice and Clinical Effectiveness