

[Primary Care]

Pharmacologic Therapies for Pediatric Concussions

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Context: Pediatric concussions are common, and emphasis on correct diagnosis and management is stressed in consensus guidelines. Medications may have a role in management of concussion, but no consensus exists regarding appropriate pharmacologic therapy.

Evidence Acquisition: Nonsystematic review.

Study Design: Clinical review.

Level of Evidence: Level 4.

Results: There is limited evidence for hypertonic saline to improve posttraumatic headache in the emergency department setting. There is essentially no evidence for the use of any other medication in management of pediatric sport-related concussion.

Conclusion: Further research is necessary to determine whether there is benefit to the use of any pharmacotherapy in the management of pediatric-aged athletes with concussions.

Keywords: concussion; medication; pharmacology; pediatric

Concussions are commonplace in youth sports. Estimates have ranged from 300,000 to 3.8 million occurring annually.^{10,13} The recommended mainstay of concussion management is initially resting from physical activity and modifications to cognitive activity to help with recovery.⁵ With the majority of concussions improving within 3 weeks from the injury without medication, there has not been a great emphasis on research for pharmacotherapy for the sport-related concussion.

There are several reasons to give consideration to pharmacotherapy for concussion. These include the potential to shorten the course of the injury, lessening symptoms in the athlete, possibilities for prevention or reduction in likelihood of future injury or severity of future injuries, and potential for improving long-term outcomes after concussion. Currently, there are no medications that have conclusive evidence to accomplish any of the proposed benefits of treatment with medication.

CURRENT PRACTICES

Many medications have been proposed for the management of concussions but all are intended to address specific symptoms the athlete may be experiencing. Medications are used to reduce headaches, improve sleep, improve cognitive function,

and address psychological comorbidities. Currently, there are no medications approved by the Food and Drug Administration for the treatment of a sport-related concussion.

In a survey of pediatricians, 62% reported using acetaminophen and 54% used nonsteroidal anti-inflammatory drugs (NSAIDs) in the management of sport-related concussions.⁸ Other commonly used medications were melatonin (20%), tricyclic antidepressants (20%), amantadine (10%), and stimulants (8%). Pediatricians who managed more than 16 concussions per year were more likely to use prescription medication and less likely to use NSAIDs than pediatricians who managed less than 16 concussions per year.

In a similar survey of pediatric emergency medicine physicians, acetaminophen was utilized by 78% and NSAIDs by 77%.⁷ Ondansetron was also used frequently (54%), with narcotic use to a much lesser extent (7%).

MEDICATIONS

Headache

Acetaminophen and NSAIDs

No studies were identified that evaluated the use of acetaminophen or NSAIDs for treatment of symptoms in

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sport-related concussion or traumatic brain injury. Also, no studies were identified suggesting a harmful effect of NSAID use, such as increased risk for subdural hematomas, in the management of sport-related concussion. This is despite widespread recommendations to avoid NSAID use after a mild traumatic brain injury. A retrospective chart review of adolescent patients treated in a headache clinic with chronic posttraumatic headaches found that 70% met criteria for medication overuse headaches.⁶ After discontinuation of the over-the-counter medications that were being overused (naproxen, ibuprofen, acetaminophen, and oxaprozin), 68.5% of patients had resolution or improvement of their headaches, suggesting caution in chronic administration of over-the-counter analgesics in concussion headache management.

Amitriptyline and Nortriptyline

Amitriptyline and nortriptyline are tricyclic antidepressants that also have been used as an off-label indication for treatment of headaches, specifically migraines. Pediatricians report using amitriptyline to treat concussion-related symptoms.⁸ A retrospective chart review of adolescent patients treated at a regional concussion center found 17% had been prescribed amitriptyline.² Of those patients, 82% reported improvement of their headache symptoms. Side effects such as oversedation, irritability, heart palpitations, and vivid dreams were reported in 23%. No controlled trials have been published on the use of tricyclic antidepressants for pediatric concussions.

Stimulants

Amantadine

Amantadine is a dopaminergic agent that helps increase the release of dopamine in the brain. Since dopamine is a neurotransmitter, increasing the release of dopamine after a concussion theoretically has the potential to improve brain function. A small, retrospective, case-controlled study compared 25 athletes with concussion who were still symptomatic after 3 weeks of rest treated with 100 mg of amantadine twice daily for 3 to 4 weeks with 25 controls.¹² Those treated with the amantadine demonstrated statistically significant improvement in symptoms ($P < 0.005$) as well as performance on ImpACT test reaction time ($P < 0.05$) and verbal memory ($P < 0.009$) components. However, prior to treatment, the amantadine group had statistically greater symptoms and worse performance on ImpACT verbal memory and visual memory components. Ultimately, the treatment and control groups finished the study with essentially identical symptom reporting and performance on all 4 ImpACT components, which questions the conclusions of the potential benefits of amantadine suggested by the study's authors.

Methylphenidate

Methylphenidate acts as a stimulant to help improve cognitive function. Several studies exist in the literature evaluating the use of methylphenidate for improving cognition and mental fatigue after traumatic brain injury. These studies tend to focus on adults, and those that evaluate pediatric-aged patients are often

small in number or focus on patients with moderate to severe traumatic brain injuries. To date, no research trials have been published regarding the use of methylphenidate or other similar stimulants in the use of a pediatric sports concussion.

Sleep Aids

Melatonin

Melatonin is often used as an over-the-counter sleep aid. Sleep disturbances can be common after concussion. Currently, no published research exists regarding melatonin use for concussions, although a double-blind, placebo-controlled study protocol for melatonin use at various doses for postconcussion syndrome in young athletes has been published.¹

Trazodone

Trazodone is a serotonin antagonist and is often used for insomnia. Currently, no research studies have been published on the use of trazodone for sleep disturbances after pediatric concussion.

Acute Management

Hypertonic Saline

Hypertonic saline has been used for the treatment of severe traumatic brain injury to help reduce intracranial pressure.^{4,9} A randomized controlled trial was conducted on 44 patients (23 treatment, 21 controls) that consisted of treatment with 3% hypertonic saline (treatment group) or normal saline (control group) of 10 mL/kg over 60 minutes.¹¹ Total fluid did not exceed 1000 mL. Outcomes were assessed based on a pain score using the Wong-Baker FACES Pain Rating Scale. Statistically significant improvements in pain scale scores were seen in the hypertonic saline group compared with the control group at 1 hour after the treatment and at 2 to 3 days after discharge. The 2 groups did not have a statistically significant difference in final pain score, however.

Intravenous Migraine Therapy

A retrospective chart review was conducted on patients presenting with posttraumatic headache from a mild traumatic brain injury to an emergency department within 14 days of their injury treated with intravenous therapies such as ketorolac, prochlorperazine, metoclopramide, or ondansetron.³ Treatment success was defined as equal to or greater than a 50% reduction in pain. Ketorolac alone was successful in 80%, metoclopramide or prochlorperazine alone was successful in 93%, ketorolac plus metoclopramide or prochlorperazine was successful in 89%, and ondansetron was only helpful in 78% of patients. No follow-up was conducted in this study to determine whether the pain relief of the headache persisted beyond the immediate treatment in the emergency department.

CONCLUSION

Unfortunately, at this time, there is very limited research on the pharmacologic management of pediatric sport-related

concussions. Future research should be directed toward the efficacy of the medications commonly used on an off-label basis in concussion management.

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