Managing Patients with Prolonged Recovery Following Concussion

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KEYWORDS

• Concussion • Postconcussion syndrome • Pharmacologic interventions
• Non-pharmacologic management

KEY POINTS

- Persistent symptoms following concussion can be challenging for clinicians, given variable presentations among patients.
- A thorough history and physical examination are key to developing a treatment approach.
- Pharmacologic treatments can be considered when symptoms are negatively affecting quality of life.

INTRODUCTION

Concussion awareness, particularly in sports, has significantly increased over the past decade, and the body of literature regarding diagnostic criteria, evaluation, management, risk factors, prognosis, and long-term effects has grown exponentially. Recommendations for acute concussion management emphasize physical and cognitive rest balanced with supervised graded exertion until symptoms resolve before return to play.[1–3] Although this approach is effective in most patients with concussion, it is estimated that the incidence of postconcussion syndrome (PCS) can range from 1.4% to 29.3% among different populations evaluated using inconsistent diagnostic criteria.[4–7]

Persistent symptoms following concussion can be debilitating for patients and challenging for clinicians, given the limited data available on the management of prolonged recovery from concussion. PCS refers to the collection of symptoms across several clinical domains that occur after concussion. Symptoms may include headache, nausea, dizziness, impaired balance, blurred vision, confusion, memory impairment, mental "fogginess," and fatigue, in varying combinations.[8–13] Although evidence-based approaches are emerging, issues related to the diagnostic criteria continue

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to complicate the literature and clinical identification. The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, and *International Classification of Diseases, 10th Revision*, both provide criteria for the diagnosis of PCS; however, Rose and colleagues[14] were able to demonstrate ongoing variability among practitioners by using an electronic survey. Another challenge to developing strict diagnostic criteria is that symptoms seen following PCS also have been reported in a variety of other diagnoses, such as uninjured controls, patients with general trauma, personal injury claimants, soldiers with combat stress, patients suffering from depression/anxiety, and patients with chronic pain.[15–19]

PATHOPHYSIOLOGY

Concussion is a complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces.[1–3] Following impact, the brain experiences a complex cascade of ionic, metabolic, and physiologic events, well described by Giza and Hovda.[20] Indiscriminate release of excitatory amino acids, coupled with a massive efflux of potassium, induces a brief period of hyperglycolysis. This is in response to ATP-powered sodium-potassium pumps operating at maximum capacity in attempts to restore neuronal membrane potential. The hypermetabolic state occurs in the setting of diminished cerebral blood flow causing a cellular "energy crisis," as the supply of glucose cannot meet the demand. What follows is a period of depressed metabolism secondary to persistent calcium influx causing mitochondrial dysfunction and impaired oxidative metabolism. ATP consumption and production become unbalanced, thus worsening the energy crisis. In the later stages of the cascade, the balance between glucose metabolism and cerebral blood flow is restored, but delayed cell death, chronic alterations in neurotransmission, and axonal disconnection occur.[20] The metabolic derangement and the postconcussion "energy crisis" are considered chiefly responsible for the compromised synaptic plasticity and subsequent cognitive deficits.[21] Clinical signs and symptoms of concussion, such as impaired coordination, attention, memory, and cognition are manifestations of underlying neuronal dysfunction, likely due to the processes described.[20]

Using animal models, Rathbone and colleagues[22] described the potential role systemic inflammation may have regarding symptoms of PCS. These models have demonstrated activation of immune and nonimmune cells and increases in inflammatory mediators (ie, cytokines) following brain injury. Microglia, which become activated after injury, appear to be an important component of the long-term inflammatory response. Once activated, they release immune factors, such as reactive oxygen species, prostaglandins, and excitotoxins.[22–24] The role of inflammation in headache, irritability, anxiety and depression, personality changes, apathy, sleep disturbance, fatigue, and reduced tolerance to stress has been described via literature review in animal and human subjects with no history of head injury.[22] These symptoms are commonly reported in PCS and it may be postulated that PCS following concussion represents a "persistent, low-grade, chronically smoldering neuroinflammatory response."[22,24]

RISK FACTORS FOR PROLONGED RECOVERY

It has been stated that recovery from concussion occurs within a relatively short time frame, with more than 90% of injured athletes returning to play within 7 to 14 days after injury.[4,25] However, recent work by Henry and colleagues[26] evaluated 66 subjects (64% male, ages 14–23 years) and found that although the greatest rate of symptom improvement occurred in the first 2 weeks after injury, recovery time across all