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Mild traumatic brain injury (TBI) - Mini review

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Introduction

In America, more than two million annual emergency department visits and 289,000 annual hospitalizations present with traumatic brain injury (TBI) [1]. Whereas in New Zealand (NZ), it is estimated that 35,000 head injuries occur per year of which 21% of head injuries are sustained from sports such as rugby, cycling and equestrian [2]. Ethnic disparities and rural populations have also been reported to present with higher TBI incidences. For example, NZ Maori had a 1.23 greater relative risk of mild TBI compared to European [3]. Rural population have a 2·5 times greater risk than urban population for developing TBI (73 versus 31 per 100 000 person-years) [3]. Peak ages for TBI are between 0-4 and 15-24 years of age, with males at greater risk of injury than females [4].

Mortality rates after brain injury are highest in people with a severe TBI. In the first year after a severe TBI, people who survive are more likely to die from seizures, septicemia, pneumonia, digestive conditions, and external injuries compared to people of similar age, sex, and race [5]. The Glasgow Coma Scale (GCS) which evaluates the coma criteria based on the best eye, verbal and motor responses has been described as a predictor of survivorship following a brain injury [6,7]. Following TBI, a total GCS score of between 3-8 for the three sections indicates severe TBI, a score of 9-12 indicates moderate TBI, whereas a score of 13-15 indicates mild TBI. Greenwald et al have also described that the duration of loss of consciousness or mental status change to be useful in determining the severity of TBI [8]. This review focuses on mild TBI while acknowledging the huge overlap between concussion and mild brain injury. The pathophysiology, clinical evaluation, brief management are also outlined below [Table 1].

Pathophysiology

Intrinsic and extrinsic mechanisms play a vital role in the manifestation of post-concussion symptoms. Intrinsically, the brain has several neurotransmitters such as Acetylcholine and Glutamine. Pharmacologic pathways serve to either stimulate or inhibit these pathways to assist with rehabilitation following a brain injury. Physiologically, cerebral blood flow is tightly coupled to neuronal activity and cerebral glucose metabolism [9]. However, cerebral blood flow may be reduced by up to fifty percent following TBI, producing an energy crisis due to a mismatch of supply and demand in the setting of increased glucose uptake [10]. This process may explain why patients who are asymptomatic at rest may become symptomatic during physical or higher functioning tasks. Other notable findings post-concussion includes dynamic heart rate variability, circadian rhythm disturbance, and altered cytochrome P450 mechanisms [11-13]. These complex interactions may have implications for treatment of post-concussion syndrome via pharmacological and non-pharmacologic means.

Table 1. Evaluation of the Severity of Traumatic Brain Injury (TBI) based on Loss of Consciousness (LOC) and Glasgow Coma Scale (GCS). (Adapted from Greenwald et al, 2003 and Nancy *et al.*, 2014 [7,8]

Severity of TBI	Findings	GCS
Mild	Mental status change or LOC < 30 min.	13-15
Moderate	Mental status change or LOC 30 min to 6 h.	9-12
Severe	Mental status change or LOC > 6 h.	3-8

Concussion is a complex pathophysiological process induced by biomechanical forces within the brain. TBI affects the axons following acceleration and deceleration forces [14]. These rapid movement results in fibers which undergo shearing; also described as axonal shearing. Depending on the actual location of these dynamic forces, focal areas of the brain with specific functionalities are impaired. For example, the cerebral cortex processes the incoming stimulation that is processed and perceived by the senses. Whereas the Limbic system controls the intrapersonal aspects of a being at an emotional and mood level. These faculties often get affected in mild TBI and clinical signs may go unnoticed by inexperienced clinicians. Other faculties such as the frontal lobe; which is involved in goal directed behavior, and executive functioning (dopaminergic) may also be impaired and so do motivation and reward systems which are governed by the orbital frontal system. These notable dysfunctions may serve as potential precursors for developing chronic disorders such as anxiety and depression. Hence, early recognition and assessment of concussions followed by symptoms directed treatment in preferably a specialized brain rehabilitation facility is encouraged.

Clinical evaluation of concussion

Following a concussion or mild TBI, many patients are often discharged to the community and expected to continue employment following a brief period of medical leave i.e. varying between days to months. For the medical personnel evaluating post-concussion symptoms, the exact mechanism of injury and appreciating risk factors such as female, older age, lower socioeconomic status, prior history of headaches and insomnia are important. An open, neutral and non-judgmental space and allowing adequate time for the patient to voice out their symptoms is crucial. Often, the exact mechanism may not be obtained from the history and often substance abuse history is not volunteered and often inaccurate. The post-acute phase of mild TBI may clinically manifest as sexual dysfunction, dissatisfaction, loss of desire or feeling less important and not uncommonly reported by

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spouses or partners of TBI patients [6,15]. Thus, collateral history, a thorough drug (to exclude potential drug-drug interactions) and social history along with careful evaluation of other source documentation and investigations serve to be valuable.

Post-concussion or mild TBI may present with a wide range of signs and symptoms. The most prevalent and consistent indicators of concussion are observed and documented disorientation or confusion immediately after the event, impaired balance within one day after injury, slower reaction time within two days after injury, and impaired verbal learning and memory within two days after injury [6]. Patients or their caregivers may report fatigue, personality change, hyper or hypo arousal, agitation, inattention, slow processing speed, memory impairment, dizziness, sleep disturbances, depression, and headache. Symptoms are not necessarily associated with loss of consciousness and only seen in 10-20 % of cases [16]. A formal physical examination with particular focus on cardiovascular (including lying and standing blood pressure) and neurological examination (including memory assessment) is vital. Many patients also report poor attention or have experienced the difficulty to spell back words. It is important that signs of physical abuse are also excluded especially in children, women and the elderly. Laboratory investigations for e.g. exclusion of anemia, infection, thyroid and electrolyte abnormalities may be required and in some cases formal brain imaging via CT or MRI is warranted to exclude intracerebral hemorrhage or chronic subdural hematoma.

It is important that medical personnel, patients and caregivers appreciate that post-concussion may temporarily have consequences with employability, and restriction to functional capabilities such as driving and managing high functional tasks such as banking. Differential diagnoses of mild TBI include but not limited to depression, somatization, chronic fatigue and pain, cervical injury, vestibular dysfunction, visual dysfunction, fibromyalgia, post-traumatic stress disorder, vertebral artery dissection, alcohol abuse, and infection. It is hence vital that other reversible conditions masquerading mild TBI are corrected and excluded. To further evaluate concussion, various specialized tools have also been developed. For example, balance Error Scoring System (BESS) for maintaining balance after brain injury [17]. Memory and executive function require formal assessment by allied health e.g. neuropsychologist, physiotherapist, and speech therapy via a multidisciplinary approach, which reiterates the need for managing these patients in a specialized unit.

Interventions

Both non-pharmacological and pharmacological interventions have been recommended in the management of mild TBI which consists of 85% of all brain injuries. Among these, post-concussion syndrome affects up to a quarter of patients one year following their injury. Non-pharmacological treatments include but not limited to providing early education intervention, staying well hydrated, aerobic exercises, cognitive therapy and bed rest [2]. However, limited evidence has been described behind the utility of non-pharmacologic interventions. Four randomized controlled trials and one controlled clinical trial evaluated three interventions; educational information sheets, telephone or person follow up and bed rest. One study offered pharmacological treatment. However, these comprise of poor quality studies. Only two out of five studies showed improvement with early educational intervention. Bed rest has not been shown to reduce the incidence of post-concussion syndrome. Neurocognitive rehabilitation which improves cognition, assists the individual in developing compensatory strategies helps alleviate depression and anxiety [17]. Preparing the individual to prevent further head injuries is not to be undermined such as fastening seat belts, emphasizing the use of helmets and ensuring falls prevention programs are in place. As for athletes, sport coaches should sight medical clearance before permitting a player to return to training which averages approximately three weeks with the exception of players involved in international competitions who may receive a clearance from a neurologist with a recognized skillset in this area [2].

Pharmacological interventions include medications, botox, peripheral nerve blocks and hyperbaric oxygen which are prescribed as symptom directed. Antidepressants are the most common prescribed medication for post-concussion syndrome. These include but not limited to selective serotonin reuptake inhibitors which aid in cognitive deficits and depression, low dose amitriptyline often used to aid sleep and headaches, non steroidal analgesics, prochlorperazine and metoclopramide for nausea and vomiting, melatonin for sleep and sodium valproate for migraine. However, these medications are not without side effects, dose dependent and many not backed by randomized controlled trials for the indication of concussion. In a meta-analysis by Wang et al, hyperbaric oxygen was statistically shown to improve Glasgow coma scores. However, access to such facilities prove to be a limiting factor [18]. On the other hand, botox and peripheral nerve blocks have been associated with improved quality of life with decreased post-concussion scores, however this is limited by specialists with the relevant skill set [19].

Potential future directions

Pre-clinical studies are evaluating the role of toll like receptor 4 antagonist (Resatorvid) in providing a neuroprotective effect [20]. Mice studies as demonstrated by Feng et al showed that administration of the drug ten minutes prior to injury attenuated neuronal loss, brain edema and neurobehavioral impairment. In a separate study by Zhu et al, large doses of curcumin (100mg/kg) was also found to reduce inflammation by inhibiting TLR4 signaling pathway in experimental traumatic brain injury in microglia and macrophages [21]. However, how relevant and practical these interventions are in the clinical setting remains to be known. At a practical level, dedicated concussion clinics by physician who are specially trained in this field with particularly special interest in this field are required. Training and exposure to such clinics are equally important to heighten the awareness of clinicians in recognizing mild TBI.

Conclusion

In summary, concussion or mild traumatic brain injury is relatively common. Its pathophysiology is complex and requires recognition, careful evaluation and management by clinicians. Broad range of both non-pharmacological and pharmacological interventions have been reported in the literature, however with limited number of randomized control trials. This mini review heightens the awareness of TBI and calls for future prospective randomized controlled trials to improve future outcomes of this important condition.

Competing interests

Nil

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