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REVIEW ARTICLE

A Review on Post-Traumatic Aggression

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ABSTRACT

Traumatic brain injury is the first cause of death and disability in children and young adults in worldwide. During the acute phase of recovery from moderate to severe brain injury, a period of post-traumatic confusion state (PTCS) will arise that is a combination of cognitive and behavioral dysfunction. Seven key symptoms of PTCS are identified and measured by Confusion Assessment Protocol (CAP). Agitation can be part of PTCS in the acute phase or, part of the recovery of consciousness in chronic phase. There are different hypothesis and classifications of acute and chronic post-traumatic aggressive syndromes. While post-traumatic aggression is common, its mechanism, assessment tool, outcome and treatment plans are not well-defined. Understanding the different aspects of post-traumatic aggression; mechanism, differential diagnosis, and treatment are reviewed in this article.

INTRODUCTION

Neurobehavioral consequences of traumatic brain injury (TBI) such as cognitive impairment, aggression, and emotional instability are the most challenging burdens in the process of recovery with the poorest functional outcome and responsiveness to rehabilitation plans. During the acute phase of recovery from TBI, there is a period of post-traumatic confusion state (PTCS), previously called post-traumatic amnesia (PTA) (1) that is a combination of cognitive and behavioral disorders. It has been classified by Confusion Assessment Protocol (CAP) score with combination of 7 key symptoms as following: 1. disorientation, 2. cognitive impairment, 3. fluctuation of presentation, 4. restlessness, 5. nighttime sleep disturbance, 6. daytime decreased arousal, and 7. psychotic type symptoms (2,3). Restlessness and agitation are part of acute recovery that is defined as over-activity related to PTA (4).

During the later stages of recovery, when the patient is more cognitively aware and is no longer in the phase of PTA or PTCS (5) aggressive behavior can happen. Aggression at this stage is defined as verbal and physical aggression against objects, self, and the others (6). Aggression is also classified as severe irritability, violent behavior and episodic dyscontrol that is defined as goal directed aggression or explosive aggression (7).

PREVALENCE AND PREDICTOR FACTORS

Prevalence of post-traumatic aggression in the acute phase is 35-96% and from 1 year to 15 years post-traumatic it is between 31 to 71% (5). Predictor factors of post-traumatic aggression has been discussed in previous studies that have been defined as pre-injury history of aggression, irritability and impulsivity, new onset of depression, alcohol abuse, infection, epilepsy, metabolic disorders, impaired social interaction, frontal lobe lesion, orbitofrontal syndrome, anterior temporal lesion and increased dependence on activities of daily living (8,9).

Also, there are reports of correlations between the result of the neuropsychological tests and prediction of aggression, e.g., Rancho Los Amigos Scale score (Confused, Agitated) was associated with acute post-traumatic agitation, and lower Function independence measure (FIM) cognitive scores were associated with more severe agitation (10,11).

Some medications can be associated with more severe agitation in the acute phase of recovery, e.g., anticonvulsants with sodium channel blockers activity, high potency second-generation antipsychotics, gamma-aminobutyric acid-A (GABA-A) anxiolytics/hypnotics, alcohol, benzodiazepines, barbiturates, anticholinergic, and steroids (12).

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Some studies have found that patients with impulsive aggression may have more severe cognitive dysfunction with deficits in executive functioning and impulse regulation (13). This finding can be explained by the study that has shown executive attention deficit as part of post-traumatic impaired attention may be the most common and debilitating cognitive deficit causing rehabilitation barriers and long-term disability (13,14). Another study have found a significant association between low satisfaction with life and aggression 6 and 24 months post-TBI that can be due to the patient's feeling of invasion to their personal space by their caregiver's assistance. Therefore, their resistance to any type of assistance can lead to some type of aggression and conflict or be as a result of post-traumatic depression and lack of motivation (15,16).

STRUCTURAL CHANGES, NEUROTRANSMITTER DYSREGULATION, AND ENVIRONMENTAL FACTORS

Post-traumatic cognitive and behavioral complexity are a cause for the existence of different hypotheses to find the main reason for aggression in some patients. Several structural lesions are considered as reasons for post-traumatic aggression such as orbitofrontal cortex, hippocampus, parahippocampal gyrus, insula, temporal pole, olfactory cortex, cingulate cortex, amygdala, septal nuclei, hypothalamus, and select thalamic nuclei (17).

The prefrontal cortex is the center of executive cognitive functioning such as planning, initiative, and evaluation, and also regulation of behaviors and impulses (18). Studies have shown an association between decreased metabolism in the orbitofrontal cortex with increased aggression in patients with personality disorders (19). Disruption of orbitofrontal efferent projections to limbic structures may lead to denervation hypersensitivity and limbic neural excitability which induces aggression (20,21). Lesions in this area could cause depression, withdrawal, general personality change, impulsivity, and persistent impulsive aggression, as well as perseveration, disinhibition, apathy, inattention, loss of memory, planning impairment, and problem-solving deficiency (22).

Also, some researchers hypothesize since the nature of most brain injuries is diffuse; lesions in frontotemporal, subcortical and brainstem areas may predispose patients to post-traumatic agitation (23). Frontotemporal, subcortical and brainstem coordinate arousal, attention, memory and limbic behavioral functions. Also, lesions in the frontotemporal area can cause seizure or subclinical epileptic focus that may manifest as dyscontrol syndrome with aggressive behaviors (24).

Another hypothesis for aggression is the lack of emotional awareness as a requirement for conscious regulation of emotions (25). Without awareness, the patient will not be able to learn copying skills (26). While anger and emotional dysregulation have been characterized as aggression, it can be referred to as alexithymia which is a combination of poor emotional awareness, difficulty processing physical sensations and self-reporting of their own emotion and a preference for discussing superficial facts rather than emotion (27,43).

Hypothalamus controls flight or fight reaction by regulating autonomic and neuroendocrine responses,(8) and amygdala in limbic system mediates impulses from the prefrontal cortex and hypothalamus and can regulate the emotional content of cognition so that any damage can lead to emotional liability and impairment of impulse control (28,29).

Neuroimaging studies suggest that the cognitive process of labeling emotions helps down-regulate the emotional limbic reaction. (18-21) Therefore, people who have trouble describing their emotions may have difficulty regulating unpleasant feelings. (40)

Several neurotransmitters such as serotonin, 5-hydroxytryptamine (5Ht2), GABA, acetylcholine, norepinephrine, dopamine and monoamine oxidase inhibitor (MOI) are involved with aggression (30-33). Cholinergic transmitters are more concentrated in the nucleus basalis of Meynert in the basal forebrain. Increased cholinergic activity may cause more neurotoxicity and aggression (34,35). An increase in their activity of serotonergic and catecholaminergic can reduce cerebral metabolism and affect as a neuroprotective that decrease in their activity is associated with impulsivity and aggression (35). Also, a reduction in the level of 5-hydroxy indoleacetic acid (5-HIAA) is associated with aggression (36). Dopaminergic transmitters are located at ventral tegmentum or substantia nigra and increased activity in dopamine and norepinephrine may be associated with aggression (37).

Environmental factors such as well-designed neuro-psychotherapy and family relationship play an important role in functional and psychosocial outcomes of TBI, especially in the case of aggression and cognitive impairment (38).

TREATMENT PLANS

There are several recommendation plans to prevent and treat aggression that their effectiveness has not been studied in a large study population or clinical trials.

1. Anger management training and insight-oriented psychotherapy will focus on increasing awareness of the cause of anger and symptom reduction (39).
2. Training caregivers to reduce environmental and interpersonal factors that may trigger any misbehaviors such as aggression by using structured daily program, in-home cognitive and behavioral rehabilitation (41,42).
3. Medications that can decrease aggression have been reviewed, and there has been different results and recommendations either in the acute or chronic phase of post-traumatic aggression. Several various medications exist to achieve the following desired goals:
    a. To inhibit the excessive activity of limbic: Anticonvulsant, noradrenergic blockade (propranolol), dopaminergic (haloperidol).
    b. Augmentation of orbitofrontal, dorsolateral prefrontal: Monoaminergic agonist (amantadine, methylphenidate, buspirone).
    c. To increase serotonergic input: Selective serotonin reuptake inhibitor (SSRI)

Several studies have recommended using SSRIs as the first line of therapy along with adding an atypical antipsy-

chotic. Some of the medications can lead to increased akathisia or restlessness, cognitive impairment, longer PTA, memory dysfunction, the problem with coordination and balance and, therefore, should be avoided, e.g. benzodiazepines and haloperidol. (44-46)

List of the medications that can be used in the chronic phase of aggression is provided as buspirone, clonazepam, carbamazepine, valproic acid, lamotrigine, oxcarbazepine, lithium, TCA (amitryptiline), SSRI (Trazadone, Fluoxetine, sertraline, citalopram), beta blockers, amantadine, and methylphenidate (6,43).

CONCLUSION

Cognitive and behavior disorders after TBI can be very challenging and disruptive in the process of recovery and rehabilitation. Lack of evidence-based practices and clinical trials in this field is alarming. A multi-disciplinary and timely manner approach can change the outcome and improve understanding the mechanism and effectiveness of treatment plans. While there are several recommendations to manage post-traumatic aggression, a well-organized and standard plan for monitoring and measuring the outcome is missing.

First, assessment of the aggression and its risk factors during its acute phase of onset should be considered with a plan to reduce the environmental factors, training caregivers and using the right medication based on patients' background and structural lesions and physiological condition.

Second, the patient should be monitored during recovery from the acute to chronic phase by psychological assessment test, imaging, electroencephalogram biomarkers to adjust the treatment plan accordingly.

A multi-disciplinary approach and providing a holistic neuro rehabilitation plan will cause a better outcome in post-traumatic aggression.

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I do my best to review this article in accordance to my knowledge

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