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Review Article

Updates in Management of Adults with Traumatic Brain Injury: A Rehabilitation Perspective

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Abstract

Introduction: TBI results in significant mortality and morbidity worldwide and represents a global health problem with huge economic burden for healthcare systems due to increased demand for health care, social and vocational services. It is complex and variable, requiring integrated multidisciplinary care. Empirical evidence for various rehabilitation interventions commonly trialed in TBI survivors are growing.

Objective: This review provides an overview of common TBI-related issues and an update on evidence-based overview of the effectiveness of various types of rehabilitation interventions in the treatment of TBI impairments.

Discussion: Majority of patients with mild TBI have non-specific symptoms that may settle within three months, whereas moderate to severe TBI impairments such as motor function, cognition, language, sensory processing and emotional disturbances can be lifelong, requiring long-term management plan. Overall, there was moderate evidence to recommend a multidisciplinary rehabilitation for management for patients with moderate to severe TBI. There are some beneficial effects of CBT to individuals with acute stress disorder or anxiety symptoms following mild to moderate TBI, and beta blockers to improve aggression in adults with ABI. However, for the majority of rehabilitation interventions used for the management of TBI, such as fitness training, cognitive rehabilitation, psychotherapy for depression, cranial electrotherapy stimulation, perceptual intervention, spasticity interventions, sensory stimulation, HBOT and acupuncture, the evidence is still low or inconclusive. This is mainly due to limited number of robust, methodologically strong studies.

Conclusion: Even though rehabilitation interventions are often routinely provided, many are difficult to standardise, and measuring the settings and intensity of different types of approaches that are effective are still a challenge. The limitation in the methodologically robust studies in TBI rehabilitation needs to be addressed, with more focus on longitudinal data to ascertain long-term care needs, and on patient perspective and caregiver burden. More research is needed in understanding components comprising the 'black box' of TBI rehabilitation, mainly on participatory limitations due to psychological issues, work, family and social re-integration.

Keywords: Traumatic brain injury; Brain injury; Rehabilitation; Rehabilitation intervention

Abbreviations

ABI: Acquired Brain Injury; ADLs: Activities Of Daily Living; BI: Barthel Index; CBT: Cognitive Behavioural Therapy; CCT: Controlled Clinical Trial; CPG: Clinical Practice Guideline; FIM: Functional Independence Measure; GCS: Glasgow Coma Scale; GOS: Glasgow Outcome Scale; GRADE: Grade of Recommendation, Assessment, Development and Evaluation Working Group grade of evidence; HBOT: Hyperbaric Oxygen Therapy; ICF: International Classification of Functioning, Disability and Health; LCF: Level of Cognitive Functioning; PTA: Post-Traumatic Amnesia; PTSD: Post-Traumatic Stress Disorder; QoL: Quality Of Life; RCT: Randomised Controlled Trial; rTMS: Repetitive Transcranial Magnetic Stimulation; TBI: Traumatic Brain Injury; TCA: Tricyclic Antidepressant; US: United States.

Introduction

Traumatic brain injury (TBI) is defined as "*blow to the head, or a penetrating head injury, that disrupts the function of the brain*" [1]. TBI severity can be graded as mild, moderate or severe and more detailed TBI severity classification can be seen in Table 1 [2].

TBI is one of the leading causes of disability and death, and represents a serious public health problem worldwide with loss of economic productivity and increased healthcare utilisation [1,3]. TBI is also known as the "silent epidemic" as longer-term impacts of TBI may not be visible [4,5]. The incidence is highest in individuals in productivity age of 16 to 60 years [3]. However, it is underestimated due to under-reporting of mild TBI cases, as many of these individuals may not present to hospital or seek any healthcare [5,6]. In the United States (US), TBI accounts for 50,000 deaths and 1.1 million

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emergency department presentations annually [1]. It also accounts for estimated one million and 25,000 hospitalisations per year in the European Union and Australia, respectively [1].

Although medical advances, including safety and prevention measures have ominously reduced the mortality rate from TBI, however, there is a corresponding increase in the number of TBI-related injuries, resulting in a significant number of individuals living with disability and chronic symptoms [7]. Depending on the severity of the TBI, the level and area of impairment differs among individuals and include impairments in motor function, cognition, language, sensory processing, emotional disturbances and others [8]. The financial implication and burden of TBI to the society as a whole is significant, with an estimated annual cost of US$60 billion [4,9,10]. In 2008, the total costs of TBI in Australia alone was estimated to be AUD$8.6 billion, with a lifetime cost of AUD$ 2.5 million and AUD$4.8 million per incident of moderate and severe TBI, respectively [11]. Some of the potential consequences of TBI are listed in Table 2 [6].

TBI is complex and variable, requiring integrated multidisciplinary care, including rehabilitation in hospital and the community. The goal of TBI rehabilitation is to maximize patients' physical or functional independence, within limits imposed by residual impairments and is managed by a specialized interdisciplinary health care team. The rehabilitation program often consists of inpatient and community phases [6]. Goal setting incorporating patients' perspectives, is an integral part that can be used to support team communication and decision-making, and to maximise patient-centred and therapy-focused care [12]. Various TBI Clinical Practice Guidelines (CPG) have been published to provide key recommendations, including rehabilitation, based on scientific research to improve health care and patient outcome [2,7,12,13]. Further, empirical evidence for various rehabilitation interventions commonly trialed in TBI survivors are growing. This has reflected in the publications of a number of systematic reviews evaluating rehabilitation interventions in TBI population. This review provides an overview of common TBI-related issues and an update on currently used TBI rehabilitation interventions.

Common Rehabilitation Issues in Traumatic Brain Injury

Following a TBI, the severity of initial impairment is usually subdivided into two main categories: mild TBI and moderate or severe TBI [13]. Individuals with mild TBI can experience a wide range of symptoms, including fatigue, headache, irritability, sleep disturbance, dizziness, nausea, increased sensitivity to noise and light, etc. Many of these symptoms are non-specific and may settle within three months. Evidence suggests that there are no cognitive deficits attributable to mild TBI after three months [2,12]. However, many have persisting physical, cognitive symptoms including post-traumatic stress disorder (PTSD) or low mood, which requires comprehensive assessment, including routine mental state examination, as mood and anxiety disorders can contribute to overall symptom burden following mild TBI [12].

Individuals with moderate or severe TBI can either improve or deteriorate over time as a result of the dynamic nature of disability secondary to TBI. Functional recovery following these injuries can occur beyond two years after TBI. In most cases of moderate or severe TBI, impairment can be lifelong, requiring long-term management plan [13]. Common rehabilitation issues in individuals with moderate to severe TBI are summarized below:

Physical Impairment

Physical deficits such as impaired balance, coordination and sensation, altered muscle tone, impaired muscle control and muscle weakness, which are common in TBI and can impact on a persons' physical functioning and participation [12]. Further, impaired coordination can lead to compromised gross motor and fine motor skills. Spasticity, though not common, can be worsened by emotional factors, positioning and functional demands and can interfere with general functioning and activities of daily living (ADLs) [13].

Cognitive Impairment

Cognitive impairment is common following moderate to severe TBI and result in significant long-term consequences [12]. Affected cognitive domains may include memory, concentration and attention, sensory processing, executive functioning (e.g. planning, self-regulation and problem solving), language and perception of sensory information [12,13]. These impairments can affect a person's ability to self-care or return to community participation and meaningful activities such as work, education, social and leisure activities [12].

Behavioural and Emotional Disorders

Behavioural difficulties among TBI individuals may include inappropriate remarks or vocalisation, non-compliance with medical management, aggression and disinhibition [12]. During the post-traumatic amnesia (PTA) period, self-awareness can often be compromised, and behavioural problems can emerge [13]. All these TBI-related behavior issues not only have considerably impact on patients' daily functioning and quality of life (QoL) but can also impose heavy burden on caregivers and family. It is important to understand that medically remediable causes of agitation should be excluded before rehabilitation therapy [12].

Incidence of mood disorder is considerably higher in TBI survivors compared to their counterparts without brain injury and can occur at any stage after a TBI. Mood disorders are associated with worsening of level of disability following TBI [12].

Communication and Swallowing Disorders

Individuals with TBI generally present with diverse combinations of communication difficulties, with additional cognitive, behavioural and physical deficits [12]. Communication disorders can be caused by motor speech, voice, language, cognitive-communicative and fluency disorders. It is well recognised that even the most subtle communication disorder can interfere with a person's ability to achieve functional goals [13]. Dysphagia is common and a distressing symptom reported by individuals with TBI. The incidence of reported dysphasia varies from 25% to 78%, and is characterized by a combination of oral and pharyngeal stage deficits [12,13]. Further, swallowing can be compromised with co-exisiting cognitive and behavioural deficits. Other negative factors that can impact on swallowing function include prolonged ventilation, endotracheal intubation and presence of tracheostomy [13].

Table 1: Classification of TBI Severity [2].

Criteria	Mild	Moderate	Severe
Structural imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of Consciousness	0-30 min	>30 min and <24 hours	>24 hours
Alteration of consciousness/ mental state	up to 24 hours	>24 hours; severity based on other criteria	
Post-traumatic amnesia	0-1 day	>1 and <7 days	>7 days
Glasgow Coma Scale (best available score in first 24 hours)	13-15	9-12	<9

Vocational Issues

Return to employment/education following TBI is known to be challenging in the course of recovery due to various issues. Vocational rehabilitation is considered a very important stage in TBI management, and is correlated to a patients' QoL. As TBI affects mostly young people of working age, unemployment can also result in substantial financial loss to the individual, family and community in large [12]. Therefore, vocational rehabilitation and an interdisciplinary approach is required for successful return to work/ education and societal reintegration [13].

Minimally Conscious or Vegetative State

TBI severity can range from concussion through to persistent vegetative state and minimally conscious state. With advances in medical and neurosurgical interventions, the survival rates and functional outcomes following severe TBI have improved dramatically, potentially increasing the need for comprehensive and effective rehabilitation. Patients in a minimally conscious or vegetative state require complex ongoing medical needs and represent a challenge in terms of assessment and rehabilitation [12].

Cochrane Evidence for Rehabilitation Interventions in Traumatic Brain Injury

Rehabilitation is defined as "a problem-solving educational process aimed at reducing disability and handicap experience by someone as a result of disease or injury" [14]. The overriding objective of TBI care has now extended beyond survival and acute management to reintegration of the patient into home and community. TBI impairments can be complex and can display an extremely varied spectrum, which requires individualised and holistic care, tailored to the needs of the patients and family. This reflects the use of a wide range of rehabilitation interventions (both multidisciplinary and uni-disciplinary modalities), which target to maximize patient function, promote independence and adaptation, and improve patients' QoL. The evidence for the effects of rehabilitation interventions currently used for individuals with TBI is diverse, with many interventions showing beneficial effect, whilst for some, evidence are yet to established. The existing evidence for various specific rehabilitation interventions in TBI, based on the published Cochrane systematic reviews are summarized below, and tabulated in Table 3 [1,3,14-25].

Multidisciplinary Rehabilitation

Turner-Stokes et al (2015) assessed the effects of multidisciplinary rehabilitation following acquired brain injury (ABI), which included TBI, in adults 16-65 years of age [n: 14 randomised controlled trials (RCTs), 5 controlled clinical trials (CCTs), 3480 participants] [14]. The authors reported strong evidence in favour of multidisciplinary intervention and intensive rehabilitation programs for functional recovery in majority of patients with TBI (both mild TBI and moderate to severe brain injury). Strong evidence was also seen in favour of a milieu-oriented rehabilitation model for individuals with severe brain injury, where by comprehensive cognitive rehabilitation was conducted in an environment that involves a peer group of patients. There was limited evidence regarding effectiveness of community-based multidisciplinary rehabilitation, specialist inpatient rehabilitation and early acute care rehabilitation on functional outcome of individuals with ABI [14].

Physical Exercise

It is vital to optimise health of TBI survivors by including regular physical activity, which is one of the key components of management in the acute and subacute phase following injury. A systematic review of by Hassett et al (n: 6 RCTs, 303 participants) evaluating the efficacy of fitness training on cardiorespiratory conditioning in TBI survivors, reported insufficient evidence to draw any definitive conclusions regarding the effects of fitness training on cardiorespiratory fitness [21]. Primary outcome was cardiorespiratory fitness, which was assessed by direct (peak oxygen uptake, minute ventilation) and indirect (peak heart rate, rating of perceived exertion) measures. There was significant heterogeneity amongst the included trials in terms of clinical diversity such as the type of intervention (swimming versus cycling), timing of intervention (acute versus chronic) and outcome measures used. The authors were unable to pool data and study results were mixed. Hence, although physical exercise appears to be a safe and feasible intervention for TBI survivors, the authors couldn't make any definitive conclusions about effects on cardiorespiratory fitness following TBI [21].

Cognitive Rehabilitation

TBI can lead to cognitive impairment that affects various aspects of ADLs in TBI survivors. A systematic review (n: 9 RCTs, 790 participants) evaluated the effects of various cognitive rehabilitation in TBI survivors on various occupational outcomes including return to work, independence in daily activities, community integration and QoL [3]. Types of cognitive rehabilitation interventions included interventions for emotional perception and self-awareness, Cognitive Symptom Management and Rehabilitation Therapy (cog SMART), a categorization program, short term Executive Plus program (STEP) and comprehensive cognitive rehabilitation strategies. The control interventions included conventional rehabilitation treatment, no treatment, home based program and different type of cognitive rehabilitation strategy. The authors' reported a moderate–quality evidence for provision of home-based cognitive rehabilitation program (8 weeks) compared to hospital-based program in achieving similar occupational outcomes. There was also moderate quality evidence for

Table 2: Consequences of Traumatic Brain Injury [6].

Consequences	Examples
Neurological impairment (motor, sensory, autonomic)	• Motor function impairment – coordination, balance, walking, hand function, speech
	• Sensory loss – taste, touch, hearing, vision, smell
	• Sleep disturbance – insomnia, fatigue
	• Medical complications – spasticity, post-traumatic epilepsy, hydrocephalus, heterotopic ossification, Sexual dysfunction
Cognitive impairment	• Memory impairment – difficulty with new learning, attention and concentration, reduced speed and flexibility of thought processing, impaired problem-solving skills
	• Problems in planning, organizing and making decisions
	• Language problems – dysphasia, problems finding words, impaired reading and writing skills
	• Impaired judgment and safety awareness
Personality and behavioural changes	• Impaired social and coping skills, reduced self-esteem
	• Altered emotional control, poor frustration tolerance and anger management, denial and self-centredness
	• Reduced insight, disinhibition, impulsivity
	• Psychiatric disorders – anxiety, depression, post-traumatic stress disorder, psychosis
	• Apathy, amotivational states
Common lifestyle consequences	• Unemployment and financial hardship
	• Inadequate academic achievement
	• Lack of transportation alternatives
	• Inadequate recreational opportunities
	• Difficulties in maintaining interpersonal relationships, marital breakdown
	• Loss of pre-injury roles, loss of independence

effectiveness of cognitive rehabilitation strategy (cognitive didactic) compared to functional–experiential cognitive program on return to work outcomes. There was a low quality evidence for cognitive rehabilitation when compared to no intervention in outcomes including return to work, independence in ADLs and no evidence for community integration or QoL, when followed up during the 8-12 week period. There was insufficient evidence to support short to medium term (4 weeks-6 months) beneficial role of cognitive rehabilitation in any occupational outcomes when compared to conventional rehabilitation programs. The authors concluded the need of further trials to draw conclusive evidence for effectiveness of any particular form of cognitive rehabilitation following TBI [3].

Another meta-analyses (n: 13 RCTs, 770 participants) examined the effects of cognitive rehabilitation for executive dysfunction in ABI, including TBI population (n: 395 participants) [23]. Types of cognitive rehabilitation interventions used include restorative, compensatory and adaptive interventions. Control interventions included no intervention or placebo, another cognitive rehabilitation strategy or standard care. Primary outcome was global executive function using assessment batteries such as Behavioural Assessment of Dysexecutive Syndrome (BADS) and Hayling and Brixton Tests. The authors found no conclusive evidence to suggest the favorable effects of cognitive rehabilitation on executive function for TBI survivors. The authors concluded that due to lack of high-quality evidence, cognitive rehabilitation cannot be recommended in regular clinical practice for executive dysfunction in TBI survivors [23].

Pharmacotherapy for chronic cognitive impairment in TBI

Various types of medications have been used to manage different aspects of cognitive functioning in TBI survivors. Dougall et al conducted a systematic review (n: 4 RCTs, 274 participants) examined the effects of centrally-acting medications, including modafinil, an experimental drug (monoamine stabiliser), Atomoxetine and Rivastigmine, on cognition, which were started at least 12 months after TBI [22]. All studies with a placebo control group control group evaluated psychometric measures for memory and cognition as primary outcome measures. Although Rivastigmine was found to be better on one primary measure (verbal memory) than placebo, it failed to show any other beneficial effects on all other cognitive tests. Similarly, a superior result in favor of the experimental drug (monoamine stabiliser) was found on psychometric testing. The authors suggested that due to small number of studies (n: 6), these results should be interpreted with caution. No positive effects were found for modafinil and atomoxetine in improving cognition. All medications were relatively well tolerated. Overall, current evidence for pharmacological treatment in chronic cognitive impairment among TBI survivors is limited to make any definitive recommendations and hence warrant further high quality trials [22].

Psychological Intervention

Increased incidence of depression and anxiety is prevalent among individuals with TBI compared with the general population [16,19]. It is important to recognise that depression and anxiety can possibly limit recovery from TBI and is one of the risk factors of suicide after TBI [16]. Gertler et al in a systematic review (n: 6 RCTs, 334 participants) assessed the effect of non-pharmacological interventions for depression among TBI victims, which predominantly included psychological interventions, followed by medical, physical, or

Table 3: Rehabilitation Interventions in Traumatic Brain Injury [1,3,14-25].

Interventions	Study, year	Number of studies, participants	Key findings	Quality of evidence (GRADE)
Multidisciplinary rehabilitation	Turner-Stokes et al (2015)	RCTs:14,CCTs:5,n:3480	Good evidence to suggest that intensive rehabilitation programs are beneficial for patients with moderate to severe TBI and associated with earlier functional gains.	Moderate
Fitness training/ Physical therapy	Hassett et al (2008)	RCTs:6, n:303	Inconclusive evidence to support fitness training in improving cardiorespiratory fitness although appears to be safe and feasible option in TBI survivors.	Very low
Cognitive rehabilitation	Kumar et al (2017)	RCTs:9, n:790	Inconclusive evidence to make recommendations of cognitive interventions on occupational outcomes.	Very low
	Chung et al (2013)	RCTs:13, n:660	Inconclusive evidence to make recommendations of cognitive interventions on executive functioning.	Very low
	Dougall et al (2015)	RCTs:4, n:274	Inconclusive evidence to recommend pharmacological agents in treatment of chronic cognitive impairment following TBI.	Very low
Psychological intervention	Gertler et al (2015)	RCTs:6, n:334	Inconclusive evidence to recommend CBT, mindfulness-based cognitive therapy, supportive psychotherapy, exercise intervention and rTMS on depression following TBI.	Very low
	Soo et al (2012)	RCTs:2, n:44	Good evidence to recommend CBT in individuals of acute stress disorder in mild TBI and combination of CBT and neurorehabilitation for treatment of anxiety symptoms in mild to moderate TBI.	Moderate
	Lane-Brown et al (2009)	RCT:1, n:21	No evidence to recommend the use of cranial electrotherapy stimulation for treatment of apathy in TBI.	Very low
Behavioural intervention	Fleminger et al (2008)	RCT:6, n:102	Good evidence to recommend beta blockers to improve aggression in adults with ABI.	Moderate
Perceptual intervention	Bowen et al (2011)	RCTs:6, n:338	Inconclusive in favour or against perceptual intervention such as functional training, strategy training, sensory stimulation and task repetition for treatment of perceptual disorders in TBI.	Very low
Spasticity intervention	Synnot et al (2017)	RCTs:5 n:105	Inconclusive evidence on the effectiveness or adverse effects of non-pharmacological interventions (e.g. physiotherapy, pseudoelastic orthosis, traditional splint, tilt table standing and electrical stimulation) and pharmacological interventions (e.g. baclofen, botulinum toxin A and tizanidine) for treatment of spasticity in TBI.	Very low
Sensory stimulation	Lombardi et al (2009)	RCT:1,CCTs:2, n:68	Inconclusive evidence to support or refute multisensory stimulation programs for patients in coma or vegetative state.	Very low
Hyperbaric Oxygen Therapy	Bennett et al (2012)	RCTs:7, n:571	No evidence HBOT improve outcomes (QoL) although strong evidence in reduction of risk of dying in TBI when used as adjunctive therapy	Very low
Acupuncture	Wong et al (2013)	RCTs:4, n:294	Inconclusive evidence on the efficacy and safety of acupuncture in acute treatment and/or rehabilitation of TBI survivors.	Very low

High quality: Further research is very unlikely to change our confidence in the estimate of effect,
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate,
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate,
Very low quality: Very uncertain about the estimate,
GRADE:Grade of Recommendation, Assessment, Development and Evaluation Working Group grades of evidence; RCTs: Randomised controlled trials; CCTs : case controlled trials; n : number; TBI: traumatic brain injury; CBT:cognitive behavioural therapy; rTMS:repetitive transmagnetic stimulation; ABI:acquired brain injury; HOBT:hyperbaric oxygen therapy; QoL:quality of life.

other interventions [16]. The non-pharmacological interventions investigated included: psychological therapy [e.g. cognitive behavioural therapy (CBT), mindfulness-based cognitive therapy and supportive psychotherapy], exercise intervention and a combination of repetitive transcranial magnetic stimulation (rTMS) and tricyclic antidepressant (TCA). The authors found no beneficial effect in favour of any evaluated interventions. The included studies were of very low quality with high risk of bias (e.g. lack of blinding of participants or assessors). Another systematic review (n: 2 RCTs, 44 participants) showed a beneficial effects of CBT in ameliorating anxiety symptoms in individuals with mild TBI and acute stress disorder [19]. Further, anxiety symptoms were lower in combined CBT and neurorehabilitation group with individuals with mild to moderate TBI compared to the control group. However, due to limited number of trials available, these results should be interpreted cautiously [16].

Another systematic review evaluated effectiveness of various interventions for apathy in TBI survivors [15]. Only one RCT (n:21 participants) met the inclusion criteria, which evaluated the effectiveness of cranial electrotherapy stimulation (CES) compared to a sham or no treatment control groups. Five factors of the Profile of Mood States (POMS) including fatigue/inertia, tension/anxiety, depression/dejection, anger/hostility and confusion/bewilderment were measured as the primary outcome measure. Although CES group demonstrated decreased inertia, which is a component of apathy, there were no changes in both control groups and no between –group differences. The authors concluded evidence regarding the effectiveness of CES treatment for apathy is still inconclusive. More robust trials examining different treatment options for apathy would be valuable to provide high quality evidence to guide daily clinical practice [15].

Behavioural Intervention

Agitation and aggression are often the most troublesome psychiatric symptoms following TBI. Agitation may be seen frequently in the acute stage of recovery, often related to PTA, whereas aggression is generally observed when the patient is no longer in PTA and has regained cognitive awareness. Fleminger et al (n: 6 RCTs, 102 participants) examined the effects of psychotropic medications for agitation and/or aggression following ABI, including TBI in participants over 10 years of age [25]. Medications that were used for behavioural interventions include beta-blocker (propranolol and pindolol), central nervous system stimulant (methyphenidate) and anti-parkinsonian medication (amandatine). Two RCTs (Brooke 1992 and Greendyke 1989) found propranolol to be effective in the early and late phase of recovery. Although beta-blockers have the best evidence in management of behavioural difficulties, these studies were underpowered with small sample size, used low doses and did not report any long-term adverse effects. Other psychotropic mediations did not show firm evidence of their efficacy. It is therefore pertinent to choose medications that are well tolerated with fewer adverse effects and to recognise the need for better evaluations of drugs for behavioural interventions [25].

Perceptual Rehabilitation

TBI can lead to perceptual disorders that may cause significant distress and hinder a person's ability to perform ADLs independently. Perceptual rehabilitation includes functional training, strategy training, sensory stimulation and task repetition. Bowen et al (n: 6 RCTs, 338 participants) examined the evidence of non-pharmacological interventions for improvement in ADLs six months post intervention compared to no treatment [17]. Only 2 trials included participants with TBI, however the authors argued that perceptual interventions would be similar among the people with stroke or TBI. Primary outcomes were measured using the Barthel Index (BI), Functional Independence Measure (FIM), and the Assessment of Motor and Process Skills (AMPS). All studies included sensory stimulation (e.g. tasks requiring visuo-perceptual processing with occupational therapist assistance), while one study included functional training, but none included task repetition. No trials explored the effect of interventions on long-term functional outcomes. The authors found insufficient evidence in favour or against any perceptual interventions. They concluded that individuals with impaired perception should continue to receive rehabilitation therapy according to currently available published clinical practice guidelines [17]. There is a need for robust trials in future to include long-term functional outcomes and potential harmful effects of these interventions.

Spasticity Intervention

Spasticity can lead to musculoskeletal issues such as reduced range of movement, muscle contracture, involuntary spasms, joint stiffness, reduced range of movement, skin breakdown and pain. It can negatively impact on a person's functional independence and community participation. Management of spasticity can be challenging in the TBI population due to concurrent behavioural and cognitive difficulties that can affect their tolerance or participation in therapy. Synnot et al in a systematic review (n: 5 RCTs, 105 participants) assessed the effects of different interventions (both pharmacological and non-pharmacological) for skeletal muscle spasticity in TBI [24]. Non-pharmacological interventions (e.g. physiotherapy, pseudoelastic orthosis, traditional splint, tilt table standing and electrical stimulation) and pharmacological interventions (e.g. baclofen, botulinum toxin A and tizanidine) were evalauted in these studies. The authors reported that the effectiveness of these interventions were unclear due to limited number and low quality studies. The authors concluded that there is a need for well-designed and larger randomised controlled trials using appropriate functional outcome measures to evaluate effectiveness of interventions for spasticity to be used regularly in clinical practice [24].

Coma and Vegetative State Management

Individuals with non-traumatic brain injury who are in a coma or vegetative state have a worse prognosis than individuals with TBI. Lombardi et al (n: 1 RCT, 2 CCTs, 68 participants) assessed the effectiveness of sensory stimulation in patients in coma or vegetative state. Outcome measures used include duration of unconsciousness, Glasgow Coma Scale (GCS), Level of Cognitive Functioning (LCF), Glasgow Outcome Scale (GOS), Disability Rating Scale and adverse events. Different types of sensory stimulation interventions [e.g. Intense Mutisensory Stimulation Program (IMS), Formalised Non-Intensive Stimulation Program and Sensory Regulation Program] were compared with standard rehabilitation treatment. The findings showed no consistent evidence to support or refute multisensory stimulation programs for patients in coma or vegetative state, mainly due to poor overall methodological quality of studies. The authors suggested for future larger RCTs to improve evidence on effectiveness of these treatment modalities [20].

Adjunctive Treatment

It is hypothesize that Hyperbaric Oxygen Therapy (HBOT) may improve disability and reduce mortality by reducing swelling and improving oxygen supply to the injured brain. Bennett et al (n: 7 RCTs, 571 participants) conducted a systematic review to assess the effects of adjunctive HBOT for TBI patients. Mortality and functional outcome using Glasgow Outcome Score (GOS) were the primary outcome measures and secondary outcome measures included progress of Glasgow Coma Scale (GCS), activities of daily living, adverse events and cost effectiveness. Although pooled data showed a significant reduction in the risk of dying, improvement in the final GCS and a decrease in proportion of people with unfavorable outcome in GOS, there was no evidence to suggest an improved functional outcome or ability to perform ADLs. Routine adjunctive use of HBOT is yet to be recommended for TBI and warrants further high methodologically robust, larger RCTs to provide evidence for effectiveness of this in clinical practice [18].

Complementary Therapy

Acupuncture may have a role in TBI rehabilitation given the neurological pathophysiology. A systematic review (n: 4 RCTs, 294 participants) comparing the effectiveness of needle acupuncture or electro-acupuncture plus additional therapy for TBI survivors reported efficacy of acupuncture in TBI survivors [1]. Participants were mostly recruited from inpatients and/or outpatient clinics in China and included people of any age or gender with mild to severe

TBI. Functional outcome assessed by Barthel Index, Functional Independence Measurement or Fugl-Meyer assessment were the primary outcome measures in this study. Others primary outcomes included mortality, morbidity and GOS. Given the difference in the types of acupuncture treatment and their combinations with different additional treatments, a conclusive judgment on the efficacy and safety of acupuncture in TBI survivors could not be drawn and more evidence is needed to be recommended in daily clinical practice. No adverse effects have been reported [1].

Discussion

TBI results in significant mortality and morbidity worldwide and represents a global health problem with huge economic burden for healthcare systems due to increased demand for health care, social and vocational services. The consequence of TBI is variable and complex, and can impact significantly on a person's ADLs, psycho-social function and QoL. There is a significant burden to the family and the carers. Symptoms of mild TBI often resolve after three months. Conversely, moderate to severe TBI may result in physical and functional deficits, impaired cognitive skills, psychological and behavioural disorders and communication and swallowing disorders, which require specific coordinated long-term multidisciplinary care, including rehabilitation [6].

This review provides an evidence-based overview of the effectiveness of different types of rehabilitation interventions in the treatment of TBI impairments. Despite extensive research of the Cochrane Library database, only limited number of reviews were identified, and a large number of reviews were mainly focused on rehabilitation interventions for treatment of patients with ABI, specifically in stroke. Overall, there was moderate evidence to recommend a multidisciplinary rehabilitation for management for patients with moderate to severe TBI. There were some beneficial effects of CBT to individuals with acute stress disorder or anxiety symptoms following mild to moderate TBI, and beta- blockers to improve aggression in adults with ABI. However, for the majority of rehabilitation interventions used for the management of TBI, such as fitness training, cognitive rehabilitation, psychotherapy for depression, cranial electrotherapy stimulation, perceptual intervention, spasticity interventions, sensory stimulation, HBOT and acupuncture, the evidence is still low or inconclusive. This is mainly due to limited number of robust, methodologically strong studies.

There are limitations regarding the completeness of literature review and interpretation of findings in this review. A literature search was performed only in the Cochrane Library database, we might have missed many relevant articles. However, our aim was to capture the highest quality reviews of RCTs relevant to TBI rehabilitation interventions and the Cochrane Collaboration sets the standards for research synthesis and provides more robust and comprehensive standardised protocol for review process. Due to the standardisation of included Cochrane reviews, critical appraisal of methodological quality of these reviews was possible using the validated tool such as Grade of Recommendation, Assessment, Development and Evaluation Working Group (GRADE) [26]. Adverse events and economic benefits of the interventions were not reported in any of the included reviews.

The Way Forward

Despite significant improvements in the coordination and organization of trauma care and services, many have not extended to include rehabilitation services. The sequelae of TBI and impact on everyday life are not yet broadly reported and there are minimal data on longer-term outcomes, particularly in participatory domains. Majority of TBI survivors, specifically those with good initial outcomes or those who do not have and/or do not know regarding access to longer term care, including rehabilitation, frequently get lost in the transition. This has resulted in fragmented or non-existent long-term care continuum of these patients, even in developed countries. There is a growing body of evidence, to show that TBI survivors have a range of issues (physical, emotional, psychosocial and/or environmental) associated with these injuries that persist over a longer period [27]. One study reported that at 10 years following TBI, although mobility outcomes had improved in 75% of the patients, over two third (40%) of patients required more support than before their injury. TBI-related issues that were evident at 2 years post-injury such as fatigue, balance, communication and cognitive problems, and relationship challenges, persisted until 10 years post-injury [28]. Another study examining factors associated with residual disability and restriction in participation over a longer term (up to 5 years post-injury) in a group of severely impaired trauma patients found persistent impairments including: pain, headache, dizziness, paresis, falls, bowel/bladder issues and sensory-perceptual deficits [29]. Further research is needed to delineate the long-term effects of cumulative disability, specifically psychosocial (over time) in TBI survivors.

TBI survivors form a diverse group with marked clinical heterogeneity and varied levels of disability. Hence, it is difficult to analyse and compare clinical outcomes due to inconsistent use of appropriate outcome measures and variability in the types of rehabilitation. Many existing outcome instruments used in TBI populations do not fully capture its complex constructs and often do not incorporate patient (and carers') perspective [30]. For example, generic functional measures used in general rehabilitation settings (e.g. the Functional Independence Measure or Barthel Index) may not be sufficiently sensitive to capture the relevant gains following intervention, and have floor/ceiling effects. Further, health related QoL is difficult to define in complex patient populations, like TBI survivors, as many factors might influence QoL [30].

The International Classification of Functioning, Disability and Health (ICF) provides an improved framework which takes into account the effect of contextual factors when measuring disability and participation. Rehabilitation for TBI survivors can utilise the various categories within specific domains of the structured ICF framework such as "activity and participation and "environmental factors" for targeted intervention and therapy. The problems listed can be linked with concepts within specific ICF categories in various domains to provide information considered important by persons with TBI for incorporation in care programs. Further, the linked ICF categories within the structured framework of these domains can provide a common language for more effective communication and agreement amongst the treating multidisciplinary clinicians. A recent expert consensus determined the ICF TBI Core sets, which lists

most relevant categories in various ICF domains, which need to be addressed in multidisciplinary care settings. These core sets can then be used to facilitate clinical care and agreement, and in the future may assist in outcome development using ICF item banking and scale development [31].

Variability in the types of rehabilitation program currently used and their outcomes in TBI survivors need review (nationally and internationally), to highlight areas for improved data collection and to identify future clinical needs for planning health service provision. More evidence is needed to support specific rehabilitation modalities and interventions to improve evidence-based practices, which include types of interventions and settings, their intensity and duration and associated cost. Innovations that offer new paradigm shifts in the delivery of more timely, cost-effective, patient-centered and transparent services, such as telerehabilitation are need to be explored in this population.

The limitation in the methodologically robust studies in TBI rehabilitation needs to be addressed, with more focus on longitudinal data to ascertain long-term care needs, and on patient perspective and caregiver burden. More research is needed in understanding components comprising the 'black box' of TBI rehabilitation, mainly on participatory limitations due to psychological issues, work, family and social re-integration.

Conclusion

There is increasing awareness of various rehabilitative approaches in TBI survivors, including multidisciplinary rehabilitation, CBT for acute stress disorder or anxiety symptoms and beta-blockers to improve aggression. Overall, rehabilitation approach for TBI survivors requires a holistic approach and should be goal-oriented to target patient and family/carer priorities. Even though rehabilitation interventions are often routinely provided, many are difficult to standardise, and measuring the settings and intensity of different types of approaches that are effective are still a challenge. More extensive research is needed to determine the effectiveness of other specific rehabilitation interventions.

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