Comprehensive Guide to Post-Traumatic Stress Disorder
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# Post-Traumatic Stress Disorder and Its Interrelationship Between Crush Injury and Pain

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## Abstract

Posttraumatic stress disorder (PTSD) is one of the most relevant disorders of patients with chronic pain, but is often underdiagnosed. There are common factors in chronic pain and PTSD that arise from the avoidance and fear-based processes, and result in overlapping and interactive symptoms. Treatment should take this into account. Every year, millions of people are affected by natural or man-made disasters resulting in crush injuries involving multiple tissues. Crush syndrome is the systemic manifestation of traumatic muscle injury. Early aggressive intravenous fluid administration is needed to prevent myoglobinuric renal failure.

Alongside aggressive resuscitation measures, an aggressive attitude in the administration of strong opioids and ketamine is recommended as well, so that the possibility of the acute pain persisting and becoming chronic can be reduced. Victims suffer acute pain (a combination of nociceptive, neuropathic, and inflammatory pain) after crush injuries that can become chronic pain. Nerve damage with neuropathic pain occurs after crush injury by neuro-immune mechanisms resulting in peripheral and central sensitization. Many of the survivors acquire psychiatric disorders such as post-traumatic stress disorder.

Individuals with pain and PTSD share some common psychological mechanisms such as avoidance. They allow themselves to be controlled by pain and distress that can maintain or exacerbate each other. This results in more health problems, disability, functional impairment, and absenteeism from work.

Psychotherapy [exposure therapy and cognitive behavioral therapy (CBT)] is considered the first-line treatment in the psychological treatment of PTSD and pain. Individuals with severe PTSD or disabling chronic pain (or both) require intensive treatment programs. The pharmacological management of neuropathic PTSD and pain is discussed as well.

## Introduction

Every year, millions of people are affected by cyclones, earthquakes, hurricanes, landslides, tornados, flooding (tsunamis, dam failures) or man-made disasters (wars, terrorist attacks, air and railway crashes, and collapsed poorly constructed buildings) (Gibney et al. 2014). In the first decade of the twenty-first century, 3852 disasters killed more than 780,000 people. Two billion others have been affected, at a total cost more than $960 billion (Bilham 1998; Sever and Vanholder 2013).

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# Crush Injury

The term crush injury denotes damage resulting directly from the crushing force. Crush injuries are common in natural disasters such as earthquakes. Typically, the injury involves multiple tissues, from the skin and subcutaneous to the muscle and tendons and to the bone and joints (Strauss 2012). It is seen after motor vehicle collisions, especially after prolonged immobility and extrications, as well as in victims of assault (Genthon and Wilcox 2014).

Crush syndrome (or traumatic rhabdomyolysis) is the systemic manifestation of traumatic muscle injury with the breakdown of muscle cells, and discharge of contents into the circulation (Genthon and Wilcox 2014). It was first defined after the Battle of London by Bywaters and Beall in 1941 (Genthon and Wilcox 2014). Crush syndrome is the most common cause of death after earthquakes, apart from trauma (Sever et al. 2006; Sever and Vanholder 2013). Characteristics of crush syndrome include the following: hyperkalemia; hypophosphatemia; hypovolemic shock; hypocalcemia; metabolic acidosis; dysrhythmias; acute respiratory distress syndrome; cardiac arrest; heme pigment- induced acute kidney injury (AKI), and disseminated intravascular coagulation (Gibney et al. 2014).

Patients extracted from the rubble firstly appeared unharmed, but then developed increasing swelling and shock; they died of renal failure a few days later (Genthon and Wilcox 2014; Smith and Greaves 2003). Other complications that include non-acute kidney injury-associated hyperkalemia, acute respiratory distress syndrome (from inflammatory mediators), and sepsis, may prove fatal as well (Gibney et al. 2014).

The release of cellular contents into the circulation and the third spacing of large volumes of fluid in the injured muscle leads to metabolic derangements (Genthon and Wilcox 2014). Decreased circulating blood volume causes the initial injury to the kidney. Fluid sequestration, hypovolemia, and hypoperfusion of the kidneys all add to the acute kidney injury (AKI) (Sever and Vanholder 2013).

Edema and bleeding occurs within the restrictions of the fascial envelope, increasing pressure within the skeletal muscle-compartment (Strauss 2012). When the tissue fluid pressure is greater than the capillary perfusion pressure to the muscles and nerves in the compartment, the tissues become ischemic creating a skeletal muscle-compartment syndrome (Strauss 2012).

Skeletal muscle can endure up to 2 h of ischemia without permanent injury. At 4–6 h, tissue necrosis develops (Genthon and Wilcox 2014; Sahjian and Frakes 2007). Crushing disrupts the Na/K transporter, allowing calcium into the cell-stimulating intracellular proteases, resulting in cell breakdown (Genthon and Wilcox 2014). Restoration of circulation to the damaged area gives rise to ischemia–reperfusion injury (Genthon and Wilcox 2014). When the external pressure is released, cellular contents (with potassium, phosphorous, and urate) are freed into the circulation (Genthon and Wilcox 2014). The breakdown of cell walls allows calcium and sodium to rush into the cell, leading to hypocalcemia and hyponatremia (Genthon and Wilcox 2014). Large volumes of fluids are sequestered into the tissues.

If the myoglobin levels exceed the protein-binding capacity of the plasma, it is filtered into the glomerular filtrate and precipitates within the tubules, possibly causing heme (nephrotoxic) pigment-associated AKI (Gibney et al. 2014). Myoglobin may harm the kidney in a number of ways. These include proximal cell injury, tubular obstruction, and myoglobin scavenging of nitric oxide instigating vasoconstriction of renal medullary arterioles (Gibney et al. 2014; Khan 2009; Mannix et al. 2006).

The immediate life-threatening finding of crush syndrome for many patients is hyperkalemia that gives rise to dysrhythmias, often developing less than an hour after extrication (Gibney et al. 2014). Comprehensive clinical guidelines are available for the management of crush injury (Gibney et al. 2014). Early aggressive intravenous fluid administration (isotonic saline) even before extrication of the victims and avoidance of potassium-containing solutions (e.g., Ringer lactate, Hartmann's solution, and Plasmalyte) is important to prevent myoglobinuric renal failure (Parekh et al. 2012). Starch-based fluids are linked

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with an increased rate of AKI and bleeding, and should be avoided (Gibney et al. 2014). Active fluid administration prevents crush syndrome (Sever and Vanholder 2013).

Laboratory blood tests include electrolytes, acid–base status, lactate, creatine kinase, blood urea, and creatinine levels (Gibney et al. 2014; Sever et al. 2012). Acidosis, hyperkalemia, and fluid overload may necessitate earlier initiation and more frequent dialysis (Gibney et al. 2014; Sever et al. 2012). Intermittent hemodialysis is most often used. Peritoneal dialysis may be desirable in small children (Gibney et al. 2014). Symptoms of acute compartment syndrome include pain, paresthesia, paresis and pain with stretch. More recently pulse examination, and pink skin color have been added as well (Gibney et al. 2014). This may necessitate a fasciotomy (or amputation if lifesaving). The diagnosis of acute compartment syndrome is made by physical examination and repeated needle sticks that measure intracompartmental pressures over a short period of time (Harvey 2012).

## Posttraumatic Stress Disorder

Many survivors acquire psychiatric disorders such as posttraumatic stress disorder (Dell'osso et al. 2013; Gibney et al. 2014). After control of confounding factors, exposure to the recent Canterbury earthquakes led to a small to moderate increase in the risk for common mental health problems (Fergusson et al. 2014).

Posttraumatic stress disorder (PTSD) is the development of a collection of symptoms after experiencing or witnessing an extreme traumatic event (Bosco et al. 2013). It is a "failure of recovery" caused in part by altered fear learning (Kirkpatrick and Heller 2014). It is a failure to switch off behavioral responses to stimuli associated with trauma (Kirkpatrick and Heller 2014). The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) defines PTSD as having at least one symptom of intrusive reexperiencing, one symptom of avoidance, two symptoms of negative cognition or mood, and two symptoms of arousal that last for more than 1 month after exposure to trauma (American Psychiatric Association 1994; Juang and Yang 2014). A specifier of "with dissociative symptoms" (depersonalization and/or derealization) has been added as well (American Psychiatric Association 1994; Juang and Yang 2014). It represents one of the few mental disorders in which the inciting event or cause is usually known (Kirkpatrick and Heller 2014). Diagnosis of PTSD requires symptoms to continue for more than 1 month (Kirkpatrick and Heller 2014).

Cognitive and avoidance strategies are adopted to avoid distressing emotions (Kirkpatrick and Heller 2014). These limit exposure to safe reminders (the hippocampus is involved in the ability to recall safe episodes) and fear predominates (Kirkpatrick and Heller 2014). Fear learning involves the amygdala and prefrontal cortex as well (Kirkpatrick and Heller 2014). The ventral medial prefrontal cortex (VMPFC) inhibits the amygdala to "overwrite" the original fear, permitting safe episode memories to prevail (Craske et al. 2008; Kirkpatrick and Heller 2014).

A National Comorbidity Study estimated the United States lifetime prevalence of PTSD in adults to be 7.8 %, with women more at risk than men (20.4 % vs. 8.2 %) even though experiencing fewer traumas (Kirkpatrick and Heller 2014; Ditlevsen and Elklit 2012; Kessler et al. 2005). An earlier study by Davidson et al. reported the lifetime and 6-month prevalence of PTSD in the community to be 1.30 % and 0.44 %, respectively (Davidson et al. 1991; Juang and Yang 2014).

The association and interactions between stress hormones and PTSD is well established in both animal and human research (Porhomayon et al. 2014). The hypothalamic-pituitary-adrenal axis function has been investigated in PTSD patients, but no reliable biological markers have been found (Kirkpatrick and Heller 2014).

Primary care PTSD screen (PC-PTSD) can be used for initial screening. It has four items, and has a recommended cut off of three (Gardner et al. 2012; Kirkpatrick and Heller 2014). If positive, further

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evaluation can take place by a psychologist, counselor, or social worker (for symptoms of intrusion/reexperiencing, hyperarousal, and avoidance) (Kirkpatrick and Heller 2014). Patients with PTSD commonly complain of sleep disturbances such as nightmares and insomnia (Khawaja et al. 2014). Neuroticism can be thought as a risk factor for PTSD in people who have been exposed to a traumatic event (Soler-Ferrería et al. 2014).

In children and adolescents PTSD may present as restriction of activities, social withdrawal, sleep changes, and a reduced display of affect or explosive tantrums (Kirkpatrick and Heller 2014). They may complain of headaches and stomachaches as well (Kirkpatrick and Heller 2014; Scheeringa et al. 2011).

## Chronic Pain

The literature examining the association between crush injury and chronic pain remains limited (Cammack and Shipton 2013). Chronic pain is pain lasting for greater than 3–6 months; it persists beyond the healing of the initial injury (Bosco et al. 2013; Merskey and Bogduk 1994). Chronic pain results in a complex interaction of somatosensory, psychological, and social factors (Bosco et al. 2013; Sanders et al. 2005). As the chronicity of pain continues, emotional distress (resulting in depression, irritability, or anxiety), functional limitations, and increased use of the healthcare system occur (Bosco et al. 2013; Sanders et al. 2005). Coping ability may be compromised by maladaptive cognitions. The beliefs that chronic pain is a signal of damage or harm, and that activity should be avoided to recuperate from pain, are common (Bosco et al. 2013; Rainville et al. 2011). This gives rise to avoidant strategies that affect relationships, functioning, and behavior (Bosco et al. 2013).

Posttraumatic stress disorder (PTSD) is one of the most relevant disorders of patients with chronic pain, but is often underdiagnosed (Egle et al. 2014). Individuals with PTSD more often report to be in chronic pain (Bosco et al. 2013). Likewise, the prevalence of PTSD is increased in chronic pain patients (Bosco et al. 2013). PTSD symptoms become more severe with chronic pain (Bosco et al. 2013; Villano et al. 2007).

Chronic pain and PTSD share some common psychological mechanisms, such as anxiety sensitivity, and fear avoidance (Juang and Yang 2014). Fear-based avoidance becomes a common base for the development and maintenance of chronic pain and PTSD (Bosco et al. 2013). The common base of avoidance impedes recovery. It reinforces maladaptive beliefs, ineffective behaviors, distressing symptoms, and functional limitations (Bosco et al. 2013).

Chronic pain and PTSD also share a greater sensitivity to anxiety's physiological symptoms, and to catastrophization (Bosco et al. 2013). Individuals with PTSD or chronic pain may over-attend to potentially threatening stimuli or to potentially pain-inducing stimuli, respectively (Bosco et al. 2013). Hyperawareness of bodily sensations may add to fears and avoidance behaviors (Bosco et al. 2013). The tendency to respond with fear to physical symptoms of anxiety creates a shared susceptibility for the development of chronic pain or PTSD (Bosco et al. 2013).

The functional impact of co-occurring pain and PTSD conditions should not be disregarded. Individuals with pain and PTSD show more health problems and more use of healthcare services, higher pain ratings, more pain-related disability, increased functional impairment, and more frequent absenteeism (Bosco et al. 2013; Hoge et al. 2007). Individuals with chronic pain and PTSD allow themselves to be controlled by pain and distress (Bosco et al. 2013). It seems that in both chronic pain and PTSD, the original injury or trauma initiates a wave of adaptive responses or expected symptomology. However, this becomes maladaptive over time, and maintains both conditions (Bosco et al. 2013).

Depression, mild traumatic brain injury (TBI), and chronic pain create difficulties that coexist with PTSD after major injury (Australian Centre for Post Traumatic Mental Health 2013). Patients will tend to

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ruminate on pain due to its decidedly intrusive and aversive nature. The clinician needs to concentrate on specific questions regarding PTSD and depression to avoid missing vital information (Australian Centre for Post Traumatic Mental Health 2013).

Although the conceptual relationships between chronic pain and PTSD have been established, further investigations of the underlying mechanisms involved are needed (Bosco et al. 2013). While chronic pain and PTSD may share comparable psychopathological sequelae in response to chronic fear and avoidance behaviors, their precise etiology and clinical expression may vary (Bosco et al. 2013). There is evidence that they may share related neurobiological features as well (Australian Centre for Post Traumatic Mental Health 2013; Moeller-Bertram et al. 2012; Ramage et al. 2013).

Increasing consideration has been paid to the influence of pain on the maintenance and recovery from PTSD (Australian Centre for Post Traumatic Mental Health 2013). Pain and PTSD can maintain or exacerbate each other. A recent study of United States veterans found that two thirds of those with PTSD met the conditions for chronic pain as well (Australian Centre for Post Traumatic Mental Health 2013; Shipherd et al. 2007). This stresses the importance of including pain as part of a routine assessment for PTSD (Australian Centre for Post Traumatic Mental Health 2013). Effective PTSD treatment has been found to reduce chronic pain (Australian Centre for Post Traumatic Mental Health 2013). Of note is that with chronic pain the expectation of treatment outcome is positively related to the actual outcome itself (Australian Centre for Post Traumatic Mental Health 2013; Goossens et al. 2005).

Chronic pain creates a major hurdle to treating PTSD because it can actively inhibit attention to therapy tasks (Australian Centre for Post Traumatic Mental Health 2013). Pain and PTSD drive each other over time, with pain-activating memories of the event, and hyperarousal magnifying perceptions of pain (Australian Centre for Post Traumatic Mental Health 2013; Forbes et al. 2008). Pain acts as a cue of the trauma that can complicate treatment for both conditions (Australian Centre for Post Traumatic Mental Health 2013). It results in a tendency to avoid situations that increase pain (such as exercise or physiotherapy) (Australian Centre for Post Traumatic Mental Health 2013).

Traumatic events have been associated with an increased prevalence of functional somatic syndromes (Afari et al. 2014). A recent meta-analysis examined the association of reported psychological trauma and PTSD with functional somatic syndromes (fibromyalgia, chronic widespread pain, chronic fatigue syndrome, temporomandibular disorder, irritable bowel syndrome) (Afari et al. 2014). Individuals who were exposed to trauma were 2.7 (95 % confidence interval = 2.27–3.10) times more likely to have a functional somatic syndrome (Afari et al. 2014). PTSD may present with headaches and rheumatic pains as well (Australian Centre for Posttraumatic Mental Health 2013).

Initial assessment should examine both pain and mental health status, and appropriate risk factors. Good communication is important when different providers are involved. In PTSD, there is a scarcity of studies examining a combined pharmacologic and psychological treatment approach (Kirkpatrick and Heller 2014).

## Neuropathic Pain

The recent International Association for the Study of Pain (IASP) Taxonomy working group has redefined neuropathic pain as “pain caused by a lesion or disease of the somatosensory nervous system” (Hurley et al. 2013; IASP et al. 2011). Neuropathic pain is then subdivided into peripheral and central neuropathic pain to line up with peripheral and central somatosensory nervous system damage (Hurley et al. 2013). The mechanism by which crush injury to nerves results in neuropathic pain is complex. It likely encompasses changes in the peripheral nerve, in the dorsal root ganglion, and in the spinal cord (Cammack and Shipton 2013).

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Neuropathic pain has some common clinical characteristics, including pain in an area with partial or complete sensory loss, burning pain, and increased pain after repetitive stimulation (Jensen and Finnerup 2014). Troublesome symptoms are allodynia (i.e., pain elicited by a stimulus that normally does not cause pain) and hyperalgesia (i.e., an increased pain response produced by a stimulus that normally causes pain (Jensen and Finnerup 2014).

Nerve damage after crush injury is depicted by axonal injury followed by Wallerian degeneration (Cammack and Shipton 2013). In this process, the injured axon is surrounded by hematogenously derived macrophages and activated Schwann cells, degrading the myelin sheath (Cammack and Shipton 2013). These cells yield growth factors and cytokines generating a favorable environment for regrowth of damaged axons (Cammack and Shipton 2013; Pham and Gupta 2009). Wallerian degeneration is significant in the development of neuropathic pain; the timing of this process correlates with the development of hyperalgesia in the rat model (Cammack and Shipton 2013; Ramer et al. 1997).

With neuropathic pain the following become activated on spinal cord and dorsal root ganglion levels, namely, tumor necrosis factor-alpha (TNF-α); cytokine interleukins (IL-1alpha, IL-1beta, IL-2, IL-4, IL-6, IL-10, IL-15, and IL-18); transforming growth factor beta 1 (TGF-beta 1); interferon-gamma (IFN-gamma); fractalkine and chemokine (C-C motif) ligand 2 (CCL2); complement components (C1q, C3, and C5), and metalloproteinases (MMP-2,-9) (Cammack and Shipton 2013; Mika et al. 2013b).

There is activation of immune and immune-like glial cells (and astrocytes) in the dorsal root ganglia and spinal cord that release of pro- and anti-inflammatory cytokines and algesic and analgesic mediators (Cammack and Shipton 2013; Mika et al. 2013b). Neutrophils that are almost absent in uninjured nerves, display marked infiltration around crushed sciatic nerves owing to the neural inflammation (Cammack and Shipton 2013; Thacker et al. 2007). Pain is therefore considered a neuro-immune disorder.

Pain is a sensory and emotional experience. After crush injuries a combination of nociceptive, neuropathic, and inflammatory pain can exist. After spinal processing, some pain messages go up via the thalamus to activate sensory areas of the cortex, where pain intensity and location are coded (Gilron et al. 2013). Others go to areas in the limbic brain where the aversive and affective components of pain are produced. Continuing painful inputs into areas such as the reticular formation and the amygdala can disrupt normal function and lead to comorbidities, such as sleep problems, depression, and anxiety (Gilron et al. 2013). These higher centers then communicate with spinal circuits through descending controls that are either inhibitory or facilitatory. Thus, pain can be controlled by dampening excitatory mechanisms or elevating inhibitory controls.

Continuing peripheral input with peripheral sensitization results in the spinal neurons becoming hyperexcitable. As a result they display reduced thresholds, increased receptive field sizes, ongoing stimulus-independent activity, and greater evoked responses (Gilron et al. 2013). This activity is the origin of allodynia, hyperalgesia, and spontaneous pains found in central sensitization.

There is only limited evidence supporting non-pharmacological treatments in neuropathic pain; these include physical exercise and physical therapies (transcutaneous electrical nerve stimulation and graded motor imagery) (Cammack and Shipton 2013).

A systematic review of available high-quality randomized controlled trials of drugs used to treat neuropathic pain shows that very few patients enjoy complete pain relief, but that 30 % pain reduction is clinically relevant to patients (Farrar et al. 2001; Gilron and Dickenson 2014).

Synergistic interactions of drug combinations in neuropathic pain might provide superior analgesia and fewer side effects than monotherapy by targeting of multiple mechanisms (Gilron et al. 2013). Combining drugs acting at peripheral and central sites of action can be combined. In this way transmission at the peripheral site of neuropathy might be blocked and its central outcomes modulated (Gilron et al. 2013). Drugs used in neuropathic pain include those acting at metabotropic glutamate receptor ligands, at

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**Table 1** Pre-trauma psychosocial risk factors for developing chronic pain. (Based on preoperative psychosocial risk factors (Shipton 2014a))

| | |
|---|---|
| *Pre-trauma risk factors* | |
| | High pre-trauma catastrophizing |
| | High pre-trauma fear |
| | High pre-trauma anxiety |
| | High pre-trauma depression |
| *Post-trauma risk factors* | |
| | Low expectation of return to work |
| | Emotional numbing |
| | Pain hypervigilance or hyperarousal |
| *Social and environmental factors* | |
| | Solicitous responding from significant others |
| | Social support |
| | Stressful life events |
| | Lower education |
| | Lower socioeconomic status |
| | Low self-rated health |

voltage-gated and ligand-gated ion channels, at opioid receptors, as cannabinoid receptor modulators, and as glycine transporter inhibitors (Colombo et al. 2010; Jensen and Finnerup 2014).

## Psychological Treatment of PTSD and Pain

Psychotherapy is considered the first-line treatment (Kirkpatrick and Heller 2014). As PTSD and chronic pain have shared components, concurrent treatment using evidence-based cognitive-behavioral interventions becomes a realistic option (Bosco et al. 2013). Treatments should be directed toward reduction of avoidance, and to the titration of exposure to facilitate habituation (Kirkpatrick and Heller 2014). The pre-trauma psychosocial risk factors for developing chronic pain are discussed in Table 1.

The best evidence for reduction of symptoms regarding trauma-related therapies is exposure therapy and cognitive behavioral therapy (CBT) (Kirkpatrick and Heller 2014). In seven randomized trials clinically significant improvement in PTSD symptoms occurred with exposure therapy; there was evidence for the efficacy of cognitive therapy as well (Institute of Medicine Committee 2007; Kirkpatrick and Heller 2014).

Cognitive behavioral theory suggests that thoughts affect feelings and behavior, and as a result level of functioning (Bosco et al. 2013). The degree of accuracy or inaccuracy of cognitions remains a critical factor in CBT (Bosco et al. 2013). CBT facilitates a shift to more adaptive cognitions, emotional processing, and behaviors. This enables rehabilitation and recovery from both chronic pain and PTSD to occur (Bosco et al. 2013). Cognitive restructuring, however, allows for distorted cognitions to be challenged by opposing evidence (Bosco et al. 2013). Hyperawareness of physiological sensations need to be reduced as well by educating about "the fight or flight" response, and by addressing avoidance behavior (Bosco et al. 2013).

Interdisciplinary pain programs that offer psycho-educational sessions (particularly on the tendency to catastrophize), relaxation training and biofeedback, breathing exercises, and physical therapy (to increase strength, flexibility, confidence, and self-efficacy) are effective in altering these processes (Bosco et al. 2013; Gatchel et al. 2007; Murphy et al. 2013). These constituents are similar to the cognitive-

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**Table 2** Peri-traumatic risk factors for developing chronic pain. (Based on "Perioperative risk factors for developing chronic pain" (Shipton 2014a))

| | |
|---|---|
| *Pre-traumatic risk factors* | |
| Pre-traumatic pain state and demographics | Younger age |
| | Female gender |
| | Pre-traumatic pain distant from injury site |
| Genetics | Genetic polymorphisms |
| | Pharmacogenomics |
| *Procedural risk factors* | |
| | Open versus minimally invasive surgical procedure |
| | Site (e.g., thoracotomy, sternotomy, major limb amputation) |
| | Duration of surgical procedure |
| | Damage to nerves occurs by surgical section, compression, stretching, ischemia |
| *Post-procedural risk factors* | |
| | Red flags (infection, bleeding, organ rupture, compartment syndrome) |
| | Unrelieved and severe pain |
| | High post-procedural use of analgesics |
| | Surgical procedure performed in a previously injured area |

behavioral approaches to PTSD treatment in terms of behavioral change, direct or indirect challenges to maladaptive beliefs, and behavioral activation in order to reengage in fun activities (Bosco et al. 2013). For example, within the Veterans Health Association stepped care model for pain management and rehabilitation, there is an interdisciplinary, outpatient program that provides integrated chronic pain and PTSD treatment (Bosco et al. 2013; Rosenberger et al. 2011). Outcomes data to date reveal broad-based physical, emotional, and functional gains by patients with good levels of treatment satisfaction.

Exposure therapy involves graded exposure to situations that cause a fear response, letting the individual become desensitized to fear cues (habituation) (Kirkpatrick and Heller 2014). Situational exposure exercises can be apportioned when feared and avoided stimuli have been identified (Bosco et al. 2013). "Safety behaviours" are actions that protect from the disquiet associated with anxiety-provoking stimuli. Identifying and ceasing these may prove beneficial as well (Bosco et al. 2013).

Other therapies that show good evidence for symptom treatment include cognitive processing therapy and motivational interviewing (Institute of Medicine Committee 2007; Kirkpatrick and Heller 2014). By decreasing avoidance behaviors in chronic pain and PTSD, daily functioning and quality of life is improved (Bosco et al. 2013).

The peri-traumatic risk factors for developing chronic pain are discussed in Table 2.

Individuals with severe PTSD or disabling chronic pain (or both) require intensive treatment programs. These include the "Trauma Recovery Program" in PTSD, or a 2–3-week "Multidisciplinary Persistent Pain Rehabilitation Program," on an inpatient or outpatient basis (Bosco et al. 2013). The "Trauma Recovery Program" provides evidence-based treatments for PTSD that include physical exercise, eye movement desensitization and reprocessing (EMDR), and cognitive processing therapy (CPT) (Bosco et al. 2013).

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**Table 3** Prevention and management of risk factors in acute posttraumatic pain for developing chronic pain. (Based on "Prevention and management of risk factors in acute perioperative pain for developing chronic pain" (Shipton 2014b))

| | |
|---|---|
| *Acute post-traumatic pain management* | |
| | Address victim attitudes and concerns |
| | Supply relevant victim information |
| | Use standardized pain evaluation and treatment protocols |
| | Aggressively optimize analgesia in acute injury period and extend into recovery period as far as possible |
| | Identify patients with modifiable risk factors for development of acute persistent and ultimately chronic pain and follow up |
| *Acute procedural pain management* | |
| | Use least painful procedural approach with acceptable exposure |
| | Prevent nerve and tissue damage |
| | Provide protective multimodal opioid-sparing analgesic pharmacotherapy |
| | Add afferent neural blockade where appropriate |
| | Use local anesthesia at incision sites |
| *Acute post-procedural pain management* | |
| | Measure pain levels at rest and with movement |
| | Aggressively optimize analgesia with protective multimodal opioid-sparing analgesic pharmacotherapy (consider use of gabapentin if nerve damage) (keep pain levels $>$ 5/10 on days 1–5 post-procedure) |
| | Use an multidisciplinary enhanced<br>Post-procedural recovery assessment team |
| | Early initiation of oral feeding and mobilization where possible |
| | Perform a neurological examination if neuropathic pain is suspected |
| | Continue analgesia well into post-procedural period |
| Discharge plan | Individualize discharge analgesic packages and follow-up |

## Pharmacological Treatment of PTSD and Pain

The prevention and management of risk factors in acute post-traumatic pain for developing chronic pain is reviewed in Table 3. A combination of acute nociceptive pain and neuropathic pain is experienced in crush injury. Alongside aggressive resuscitation measures, an aggressive attitude in the administration of strong opioids and ketamine is recommended, so that the eventual onset of chronic pain can be reduced (Angeletti et al. 2012; Cammack and Shipton 2013). Opioids and tramadol/tapendadol would normally be reserved as second-line treatments but become appropriate first-line agents in certain clinical situations such as acute neuropathic pain (Attal et al. 2010; Cammack and Shipton 2013; Dworkin et al. 2010). Another primary analgesic used is paracetamol. Nonsteroidal anti-inflammatory drugs are contraindicated in crush injury owing to the acute kidney injury (Cammack and Shipton 2013). It is known that the shortage of opioid or non-opioid pain-relieving medications in the first hours after a natural disaster is connected to availability and transport (Cammack and Shipton 2013; Guetti et al. 2013).

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**Table 4** Pharmacotherapy of neuropathic pain

| **Pharmacotherapy of neuropathic pain** (Four lines are based on guidelines of International Association for the Study of Pain (IASP), the European federation of IASP chapters, and the Canadian pain society) | |
|---|---|
| **Drug groups** | **Drug medications** |
| **First line** | |
| Tricyclic antidepressants | Amitriptyline, doxepin, imipramine, desipramine, nortriptyline |
| Serotonin-noradrenaline reuptake inhibitors | Duloxetine, venlafaxine, milnacipran |
| Gabapentinoids | Gabapentin, pregabalin |
| **First line localized** | |
| Topical with allodynia | Lignocaine patch or gel |
| **Second line** | |
| Opioids (can become first line in acute neuropathic pain) | Morphine, oxycodone, fentanyl, hydromorphone |
| | Tramadol, tapendadol |
| **Third line** | |
| Anticonvulsants | Mexiletine, lamotrigine, valproate, oxycarbazine, topiramate |
| Antidepressants | Bupropion; selective serotonin reuptake inhibitors (fluoxetine, citalopram, paroxetine) |
| **Fourth line** | |
| | Topical capsaicin (0.025 %, 8 %), memantine, dextromethorphan |
| **Others** | |
| Alpha-2 adrenergic agonists | Clonidine, dexmedetomidine, topical clonidine |
| Cannabinoids | Nabilone |
| Botulinum toxin-A | |

# Practice and Procedures

## Treatment of Neuropathic Pain

The pharmacotherapy of treating neuropathic pain is discussed in Table 4.

Tricyclic antidepressants (amitriptyline, doxepin, imipramine, desipramine, nortriptyline) (Mika et al. 2013a), serotonin-noradrenaline reuptake inhibitors (duloxetine, venlafaxine, milnacipran) (Mika et al. 2013a), gabapentinoids (gabapentin, pregabalin) (Moore et al. 2014; Toth 2014), opioids (McNicol et al. 2013), cannabinoids (Fine and Rosenfeld 2014), lamotrigine (Vestergaard et al. 2001), mexiletine (Wallace et al. 2000), lidocaine (lignocaine) gel (Derry et al. 2014), and botulinum toxin-A (Jabbari and Machado 2011) have been found to relieve dynamic mechanical and cold allodynia and hyperalgesia in neuropathic pain conditions (Jensen and Finnerup 2014). More invasive interventions include epidural (or transforaminal) steroid injection and peripheral nerve or spinal cord stimulation (or neuromodulation) (Dworkin et al. 2013; Gilron and Dickenson 2014).

Future drugs for neuropathic pain that have reached phase II or III clinical trials include the following: (Gilron and Dickenson 2014) NMDA antagonists; vanilloid receptor antagonists; calcium channel antagonists; potassium channel agonists; novel opioid receptor agonists; a novel sodium channel antagonist; histamine H3 receptor antagonists; a α-2b adrenoreceptor agonist; serotonin modulators; a novel acetylcholine receptor agonist; a orexin receptor antagonist; a cannabinoid CB2 receptor agonist; a nitric

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oxide synthase inhibitor; an apoptosis inhibitor; an angiotensin II antagonist; and a fatty acid amide hydrolase inhibitor.

### Treatment of PTSD

Medications are generally most effective in decreasing hyperarousal and improving mood. Depression has been suggested to be a potential mediator between pain and PTSD (Attal et al. 2010; Bosco et al. 2013; Kirkpatrick and Heller 2014). A meta-analysis of seven randomized treatment trials with selective serotonin reuptake inhibitors (SSRIs) in improving symptoms of PTSD found a relative risk ratio of 1.59 (with a 95 % confidence interval of 1.39–1.82), demonstrating strong efficacy compared to placebo (Kirkpatrick and Heller 2014; Stein et al. 2006).

Serotonin-noradrenaline reuptake inhibitors (SNRIs) also can be effective for improvement in PTSD symptoms. These medications include venlafaxine and duloxetine (Kirkpatrick and Heller 2014; Stein et al. 2013). Prazosin decreases nightmares and improves the quality of sleep (Kirkpatrick and Heller 2014; Calohan et al. 2010). Mirtazapine (a noradrenergic and specific serotonergic antidepressant) can be useful in treating insomnia symptoms associated with PTSD and depression (Kirkpatrick and Heller 2014; Blier et al. 2010).

Medications shown to be ineffective in PTSD include amitriptyline and nortriptyline, and the gabapentinoids (gabapentin, pregabalin) (Jeffreys et al. 2012; Kirkpatrick and Heller 2014). Benzodiazepine medications can be ineffective and carry a high risk of abuse and dependence (Kirkpatrick and Heller 2014).

## Conclusion

There are common factors in chronic pain and PTSD that arise from the avoidance and fear-based processes, and result in overlapping and interactive symptoms (Bosco et al. 2013). Treatment should take these interactions into account. Awareness and management of risk factors is imperative. Treating fear avoidance is important, as it is the core component in both chronic pain and PTSD. Hope for recovery should be offered to patients through some key therapeutic messages (Kirkpatrick and Heller 2014). Such messages could include the following: asking for support from those who listen; communicating their experiences; identifying themselves as survivors; engaging in healthy behaviors (such as sufficient sleep, good nutrition, and avoidance of substance use); and reinstating the usual activities of daily living (Kirkpatrick and Heller 2014).

## Key Facts of Crush Injuries

- Every year, millions of people are affected by natural or man-made disasters causing crush injuries resulting in crush syndromes.
- Aggressive resuscitation measures including intravenous fluids, strong opioids, and ketamine are recommended in crush syndromes.
- Nerve damage occurs after crush injury resulting in peripheral and central sensitization.
- Many survivors of crush injuries acquire psychiatric disorders such as posttraumatic stress disorder.
- Avoidance and fear-based processes in PTSD and chronic pain from crush injuries provide overlapping and interactive symptoms facilitating a common treatment plan, including psychotherapy, pharmacological management, and treating programs.

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- Looking toward the future, there are several new drugs developed for neuropathic pain form conditions that include crush injuries that have reached phase II or III clinical trials.
- In PTSD from crush injuries, there is a paucity of studies examining combined pharmacologic and psychological treatments and this needs initiation.

## Summary Points

- Posttraumatic stress disorder (PTSD) is one of the most relevant disorders in patients with chronic pain.
- Common factors occur in chronic pain and PTSD arising from avoidance and fear-based processes providing overlapping and interactive symptoms.
- Every year, millions of people are affected by natural or man-made disasters causing crush injuries resulting in crush syndromes.
- Aggressive resuscitation measures including intravenous fluids, strong opioids, and ketamine are recommended in crush syndromes.
- Nerve damage with neuropathic pain occurs after crush injury by neuro-immune mechanisms resulting in peripheral and central sensitization.
- Many survivors acquire psychiatric disorders such as posttraumatic stress disorder.
- Individuals with pain and PTSD share some common psychological mechanisms such as avoidance.
- Psychotherapy (exposure therapy and cognitive behavioral therapy) is considered first-line treatment in the psychological treatment of PTSD and pain.
- Individuals with severe PTSD or disabling chronic pain (or both) require intensive treatment programs.
- Pharmacological management consists of serotonin reuptake inhibitors, serotonin-noradrenaline reuptake inhibitors in PTSD, and a combination of tricyclic antidepressants, serotonin-noradrenaline reuptake inhibitors, gabapentinoids, opioids, cannabinoids, lamotrigine, mexiletine, lidocaine gel, and botulinum toxin-A in neuropathic pain.

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