

## Post-Traumatic Stress Disorder: A pressing concern of the current era

Dr. Uzma Tabassum

Submitted: 05-04-2022

Accepted: 18-04-2022

### ABSTRACT:

The stress that results from traumatic events precipitates a spectrum of psycho emotional and physio pathological outcomes. Posttraumatic stress disorder (PTSD) is a psychiatric disorder that results from experience or witnessing of traumatic or life-threatening events. PTSD has profound psychobiological correlates, which can impair the person's daily life and be life threatening. Posttraumatic stress disorder can happen to a person after experiencing a traumatic event that has caused them to feel fearful, shocked or helpless. It can have long term effects, including flash backs, difficulty sleeping, and anxiety. PTSD is marked by clear biological changes, in addition to the psychological symptoms and is consequently complicated by a variety of other problems of physical and mental health. Individual reactions to traumatic events vary greatly and most people do not develop a mental disorder after exposure to trauma. PTSD should be considered in any patient exposed to a major traumatic event. Up to 3% of adult has PTSD at any one time. Lifetime prevalence rates are between 1.9% and 8.8%. Studies suggest that, while men are more likely to experience violence, women have a higher chance of having Post traumatic stress disorder. Instead of feeling better as time goes on, the individual may become more anxious and fearful. PTSD can disrupt a person's life for years but treatment can help them recover. Patients with complex PTSD should receive specialist multidisciplinary care. Psychological treatments, particularly trauma focused psychological therapies, can be effective. Although the effect sizes are not as high as for psychological therapies, drug treatments can be effective. The National Institute for Health and Care Excellence and World Health Organization recommend drug treatment second to trauma focused therapy. In single RCTs, amitriptyline, GR205171 (a neurokinin-1 antagonists), mirtazapine, and phenelzine have shown superiority over placebo in reducing symptoms of PTSD.

**Keywords:** Traumatic event, psychiatric disorder, psychological therapies, drug treatment, WHO,

placebo, multidisciplinary care, evidence-based research.

### I. INTRODUCTION:

The twenty-first century rose in a ray of hope. The belief was commonly held that an age of world- wide prosperity was beginning with new millennium. Only a few years ago, people spoke of peace. Today, the general trend in many populations across the globe is fear and anxiety about self and neighbor. PTSD is a mental disorder that may develop after exposure to exceptionally threatening or horrifying events. Many people show remarkable resilience and capacity to recover following exposure to trauma [1]. Post-traumatic stress disorder, PTSD, is the psychiatric disorder that can result from the experience or witnessing of traumatic or life-threatening events such as terrorist attack, violent crime and abuse, military combat, natural disasters, serious accidents or violent personal assaults. Exposure to environmental toxins (e.g. Agent Orange, electromagnetic radiation) may result in immune symptoms akin to PTSD in many susceptible patients [56].

PTSD can occur after a single traumatic event or from prolonged exposure to trauma, such as sexual abuse in childhood. Examples of events that can trigger post-traumatic stress disorder (PTSD) include wars, crimes, fires, accidents, death of a loved one, or abuse of some form. Thoughts and memories recur even though the danger has passed. Predicting who will go on to develop PTSD is a challenge [2]. Subjects with PTSD often relieve the experience through nightmares and flashbacks. They report difficulty in sleeping. Their behavior becomes increasingly attached or estranged and is frequently aggravated by related disorders such as depression, substance abuse and problems of memory and cognition. The disorder soon leads to impairment of the ability to function in social or family life, which more often than not results in occupational instability, marital problems and divorces, family discord and difficulty in parenting. PTSD is marked by clear biological changes, in addition to the psychological symptoms and is consequently complicated by a

variety of other problems of physical and mental health.

Patients with PTSD are at increased risk of experiencing poor physical health, including somatoform, cardiorespiratory, musculoskeletal, gastrointestinal, and immunological disorders [3,4]. It is also associated with substantial psychiatric comorbidity [5], increased risk of suicide [6], and considerable economic burden [7,8]. It was noted that the syndrome resembled more closely an abandonment to emotion and fear, rather than the 'effort' that normal subject engage to overcome challenges [58]. Da Costa reported in 1871 that the disorder is most commonly seen in soldiers during time of stress, especially when fear was involved [57]. The syndrome became increasingly observed during the Civil War and during World War I.

#### Symptoms and diagnosis:

Symptoms may start within 3 months of an event, but they can begin later. Symptoms include persistent intrusive recollections, avoidance of stimuli related to the trauma, negative alterations in cognitions and mood, and hyper arousal [14,15]. For a person to receive a diagnosis of PTSD, they must meet the criteria that are set out by the American Psychological Association's (APA) Diagnostic and Statistical Manual Fifth edition (DSM-5).

According to these guidelines, the person must:

- Have been exposed to death or threatened death, serious injury or sexual violence whether directly, through witnessing it, by it happening to a loved one, or during professional duties.
- Experience the following for more than one month:
  - One or more intrusion symptoms
  - One or more avoidance symptoms
  - Two or more symptoms that affect mood and thinking
  - Two or more arousal and reactivity symptoms that began after the trauma

Here are some examples of these four types of symptoms:

#### Intrusion symptoms:

- Nightmares
- Flashbacks and a sensation that the event is happening again
- Fearful thoughts

#### Avoidance symptoms:

- Refusing to discuss the event
- Avoiding situations that remind the person of the event

#### Arousal and reactivity symptoms:

- Difficulty sleeping
- Irritability and angry outbursts
- Hypersensitivity to possible dangers
- Feeling tense and anxious

#### Symptoms that affect mood and thinking:

- Inability to remember some aspects of the event
- Feeling of guilt and blame
- Feeling detached and estranged from others and emotionally and mentally numbed
- Having reduced interest in life
- Difficulty concentrating
- Mental health problems, such as depression, phobias, and anxiety

#### Physical symptoms:

Physical effects include sweating, shaking, headaches, dizziness, stomach problems, aches and pains and chest pain. A weakened immune system can lead to more frequent infections. Sleep disturbances can result in tiredness and other problems. There may be long term behavioral changes that contribute to problems and work and a breakdown in relationships. Complex PTSD, which is also referred to as 'disorder of extreme stress', results from exposure to prolonged traumatic circumstances, such as the year-on end threat of insurgent attacks among our military personnel currently in active deployment.

#### Children and teens:

In those aged 6 years or under, symptoms may include:

- Bedwetting after learning to use the bathroom
- Inability to speak
- Acting out the event in play
- Being clingy with an adult

They may also act out the trauma or express it through play, pictures, and stories. They may have nightmares and be irritable. They may find it hard to go to school or spend time with friends or studying. From the age of 8 years and above, children generally tend to display similar reaction to adults.

Between the ages of 12 and 18 years, the person may show disruptive or disrespectful, impulsive or aggressive behavior.

Children who have experienced sexual abuse may likely to:

- Feel fear, sadness, anxiety and isolation
- Have a low sense of self worth
- Behavior in an aggressive manner

- Display unusual sexual behavior
- Hurt themselves
- Misuse drugs or alcohol

#### **Psychological interventions:**

Psychological interventions have been evaluated after traumas concerning a single incident, such as road traffic crash and physical or sexual assaults. Meta-analysis show that brief, trauma focused, cognitive behavioral interventions can reduce severity of symptoms when the interventions is targeted at those with early symptoms [20,21].

Some evidence suggests that high levels of social support are perceived as protective [27]. Consensus guidelines recommend supportive, practical and pragmatic input but avoidance of formal clinical interventions unless indicated [28,29,30].

#### **Screening:**

As part of the diagnostic process, the person may be given a screening test to assess whether or not they have PTSD. The time taken for this can range from 15 minutes to several one-hour sessions. A longer assessment may be used if there are legal implications or if a disability claim depends on it. If symptoms disappear after a few weeks, there may be a diagnosis of acute stress disorder.

#### **Causes:**

PTSD can develop after a traumatic event. Examples include:

- Military confrontation
- Natural disaster
- Serious accidents
- Terrorist attacks
- Loss of loved one, whether or not this involved violence
- Rape or other type of abuse
- Personal assault
- Being a victim of crime
- Receiving a life-threatening diagnosis
- Any situation that triggers fear, shock, horror or helplessness can lead to PTSD

#### **Risk factors:**

It remains unclear why some people develop PTSD while others do not. However, the following risk factors may increase the chance of experiencing symptoms:

- Having additional problems after an event, for example losing a loved one or losing a job

- Lacking social support after an event
- Having a history of mental health problems or substance use
- Past experience of abuse, for example during childhood
- Having poor physical health before or as a result of an event
- Some physical and genetic factors may impact the chance of having anxiety, depression and PTSD.

#### **Brain structure:**

Brain scans have shown that the hippocampus appears different in people with PTSD, compared with others. The hippocampus is involved in processing emotions and memories, and it could affect the chance of having flashbacks.

#### **Response to stress:**

Levels of hormones that are normally released in fight-or-flight situation appear to be different in people with PTSD.

#### **Gender:**

This may play a role. Studies suggest that, while men are more likely to experience violence, women have a higher chance of having PTSD.

#### **When to see a doctor:**

Many people experience symptoms after a traumatic event, such as crying, anxiety, and difficulty concentrating, but this is not necessarily PTSD. Prompt treatment with a qualified professional can help prevent the symptoms from getting worse.

This should be considered if:

- Symptoms persist for more than a month
- Symptoms are severe enough to prevent the person returning to normal life
- The person considers harming themselves

#### **Treatment:**

Treatment usually aims at reducing reactions and to diminishing the acuity of the reactions. Treatment also seeks to increase the subject's ability to manage trauma-related emotions to greater confidence in coping abilities.

The treatment of PTSD is complex, both in terms of available treatments and the myriad of trauma possibilities that cause it. According to experts, combat veterans with PTSD may be less responsive to treatment than other victims of other traumatic exposures [59,60]. Combat-caused PTSD is often associated with other psychiatric disorders, including depression, anxiety, mood disorders and substance abuse disorders. More specifically, 57-

62% of Croatian Balkan War veterans diagnosed with PTSD also met co-morbid diagnoses criteria [61], with most common being depression alcohol, drug abuse, phobias, panic disorders and psychosomatic and psychotic disorders [45]. It is usually believed that most effective treatment results are obtained with both PTSD and other disorders are treated together rather than one after the other. Treatment usually involves psychotherapy and counseling, medication or a combination. Options for psychotherapy will be specially tailored for managing trauma.

#### **Psychological therapy:**

Clinical guidelines recommend trauma focused psychological therapies based on evidence from systematic reviews and meta-analysis [31,32,33]. Individual trauma focused CBT and eye movement desensitization and reprocessing to be equally effective [34].

In exposure therapy, therapists help patients to confront their traumatic memories through written or verbal narrative, detailed recounting of the traumatic experience, and repeated exposure to trauma related situations that were being avoided or evoked fear but are now safe.

Cognitive therapy focuses on identifying misinterpretations that led patients to overestimate the current threat (for example, patients who think assault is almost inevitable if they leave the house). Cognitive therapy focuses on modifying beliefs and how patients interpret their behavior during the trauma, including problems with guilt and shame.

#### **EDMR:**

Standardized, trauma focused procedure. Involves the use of bilateral physical stimulation (eye movements, taps or tones), hypothesized to stimulate the patient's information processing to help integrate the targeted event as an adaptive contextualized memory. Group trauma focused CBT is also effective, but fewer studies have focused on this method [35]. Non-trauma focused CBT-including components such as grounding techniques to manage flash backs (for example, focusing on the here and now by describing items in a room), relaxation training (for example, controlled breathing and progressive muscle relaxation), positive thinking and self talk (for example, repeating positive phrases such as "I can deal with this")- has been found to be superior to waiting list control groups and has shown similar efficacy to trauma focused CBT and EDMR

immediately after treatment, but this is not maintained at follow-up [34].

#### **Self- help program:**

Guided self- help interventions for depression and anxiety disorders are being used as an alternative to face to face therapy as these interventions offer enhanced access to cost effective treatment [40]. Some evidence suggests that internet based guided self-help therapies effectively alleviate symptoms of traumatic stress, but randomized controlled trials (RCTs) have historically been limited to sub syndromal populations [41,42].

#### **Drug treatment:**

The National Institute for Health and Care Excellence and World Health Organization recommend drug treatment second to trauma focused therapy [33,46]. Effect sizes with drug treatment are similar to those observed from use of antidepressants for depression compared with placebo [48]. Anti- depressants and other medications commonly used are tricyclic antidepressants, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, antianxiety and adrenergic agents and mood stabilizers [64]. Sertraline has been found effective to reduce PTSD symptomatology. Sertraline and Fluoxetine have produced clinical improvements among PTSD patients in randomized clinical trials [65]. Paroxetine, another selective serotonin reuptake inhibitor like sertraline, is also habitually used to treat chronic PTSD [63]. In single RCTs, amitriptyline, GR205171 (a neurokinin-1 antagonists), mirtazapine, and phenelzine have shown superiority over placebo in reducing symptoms of PTSD.

Selective Serotonin Reuptake Inhibitors (SSRIs), such as paroxetine, are commonly used. SSRIs also help treat depression, anxiety and sleep problems, symptoms that are linked to PTSD. There have been some reports that antidepressant medications can cause an increased risk of suicide in individuals under the age of 24.

Sometimes, benzodiazepines may be used to treat irritability, insomnia, and anxiety. However, the National Center for PTSD does not recommend these, because they do not treat the core symptoms and they can lead to dependency.

Post- traumatic stress disorder is associated with depression, anxiety disorders, and drug and alcohol use disorders. Little evidence exists for the effectiveness of psychological

interventions for PTSD with comorbid substance use disorders. Some evidence suggests that trauma focused CBT can be effective with concomitant interventions to stabilize drug or alcohol use, but treatment effects are not as large as for PTSD in the absence of drug or alcohol misuse [54].

#### Tips for non-specialists:

- A traumatic event can precipitate conditions other than PTSD, such as depression, phobic anxiety, and substance use disorders.
- PTSD is associated with comorbidity.
- Sensitive questioning is required to elicit symptoms of PTSD as patients may avoid volunteering their traumatic experiences.
- Patients with PTSD may present in primary care with physical symptoms that are difficult to explain.
- Trauma focused psychological therapy is the treatment of choice for PTSD, although drugs and other forms of psychological treatment can help.
- Patient choice and availability of psychological therapy will influence the treatment given.

#### When to suspect PTSD:

- When patient present with mental or physical symptoms that can not be fully explained after a traumatic event.
- When patients present with characteristics symptoms of PTSD – re-experiencing, avoidance and hypoarousal.
- When patients disclose a history of involvement in a traumatic event.
- When patients present with mental or physical symptoms that are difficult to explain in the absence of a disclosed traumatic event.

## II. DISCUSSION:

Traumatic events are profoundly stressful. The stress that results from traumatic events precipitates a spectrum of psycho-emotional psycho-pathological outcomes. In its gravest form, this response is diagnosed as a psychiatric disorder consequential to the experience of traumatic events. PTSD tends to last for longer and the symptoms are more severe and may not appear until sometime after the event. Many people recover within 6 months, but some continue to experience for several years. During the civil war, a PTSD-like disorder was referred to as the 'Da Costa's Syndrome' [57], from American internist Jacob Mendez Da Costa (1833-1900; Civil War

duty: Military hospital in Philadelphia). The syndrome was first described by ABR Myers (1838-1921) in 1870 as combining effort fatigue, dyspnea, a sighing respiration, palpitation, sweating, tremors, an aching sensation in left pericardium, an exaggeration of symptoms upon efforts and occasionally complete syncope.

In an RCT the alpha-1 adrenoceptor antagonist prazosin was found to reduce nightmares in veterans with PTSD [49], and a further RCT in veterans showed reduction in overall symptom severity [50]. Olanzapine, in contrast with another anti-psychotic, risperidone, has been shown to accentuate the effects of anti-depressants when resistance to treatment is encountered [51] [52].

Few longitudinal follow up studies have been done of PTSD, but for many patients PTSD is severe and enduring [5]. There is, however, good evidence that patients may benefit from treatment even when symptoms have been present for many years [34]. The issue of the full prevalence of the pandemic related PTSD remains a matter of future research as symptoms may develop up to 6 months after traumatic event.

Several experimental studies provide hope that better or alternative ways to prevent and treat PTSD are on the way. Simple visuo-spatial tasks such as playing a computer game shortly after a traumatic experience reduce re-experiencing [55].

People with PTSD may have other health problems, such as, depression, anxiety, personality disorder, or the misuse of substances such as alcohol or drugs. Stress alters the regulation of both the sympathetic and parasympathetic branches of the autonomic nervous system, with consequential alterations in hypothalamic control of the endocrine response controlled by the pituitary gland.

People who work in professions where traumatic events are likely to occur, such as the military and emergency services, may be offered training or counseling to help them cope or reduce the risk of PTSD.

## III. CONCLUSION:

In light of current events (e.g. extended combat, terrorism, exposure to certain environmental toxins), a sharp rise in patients with PTSD diagnosis is expected in the next decade. PTSD is a serious public health concern, which compels search for novel paradigms and theoretical models to deepen the understanding of condition to develop new and improved modes of treatment intervention. Stress alters the regulation of both the

sympathetic and parasympathetic branches of the autonomic nervous system, with consequential alterations in hypothalamic control of the endocrine response controlled by pituitary gland. About 3% of adult population has PTSD at any one time [11]. Lifetime prevalence is between 1.9% [12] and 8.8% [7], but this rate doubles in populations affected by conflict [13] and reaches more than 50% in survivors of rape [5]. Post-traumatic stress disorder thought to affect between 7-8% of population, and women are more likely to be affected than men.

The National Center for PTSD (US department of veterans affairs) made public estimates that whereas the lifetime prevalence of PTSD in the US population was 5% in men and 10% in women in the mid-to-late 1990s, the prevalence of PTSD among Vietnam veterans at this same time was at 15.2%. About 30% of the men and women who have spent time in more recent time zones experience PTSD.

Available data from National Center for PTSD suggest that approximately 8% of men and 20% of women go on to develop PTSD and approximately 30% of these individuals develop a chronic form that persists through out their lifetimes. The National Center for PTSD also estimates that under normal and usual socio-political conditions 8% of population will experience PTSD at some point in their lives, with women (10.4%) twice as likely as men (5%) to develop PTSD.

It is usually believed that most effective treatment results are obtained with both PTSD and other disorders are treated together rather than one after the other. The result of recent RCT of the psychedelic 3,4-methylene dioxy methyl amphetamine with psychotherapy for treatment resistant PTSD have been promising [56,57]. Sertraline and fluoxetine have produced clinical improvements among PTSD patients in randomized clinical trials [65]. Paroxetine, another selective serotonin reuptake inhibitor like sertraline is also habitually used to treat chronic PTSD [63].

Previous research indicates that about 80% of individuals with PTSD have atleast one other comorbid disorder [11,12]. Finally, studies indicate that severity of PTSD symptoms in parents is associated with an increase in behavioral and emotional problems in their children [68].

#### REFERENCES:

[1]. Bonnano GA. Loss, trauma and human resilience: have we underestimated the

human capacity to thrive after extremely aversive events? *Am Psychol* 2004;59:20-8. [PubMed] [Google Scholar]

[2]. Karstoft K, Galatzer Levy IR, Statnikov A, Li Z, Shalev AY. Bridging a translational gap: using machine learning to improve the prediction of PTSD. *BMC Psychiatry* 2015;15:30. [PMC free article] [PubMed] [Google Scholar]

[3]. Schnurr PP, Green BL, Kaltman, S. Trauma exposure and physical health. In: Friedman MJ, Kaene TM, Resick PA, eds. *Handbook of PTSD: Science and Practice*. Guilford Press, 2007.

[4]. Gupta MA. Review of somatic symptoms in post-traumatic stress disorder. *Int Rev Psychiatry* 2013;25:86-99. [PubMed] [Google Scholar]

[5]. Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Post traumatic stress disorder in the national comorbidity survey. *Arch Gen Psychiatry* 1995;52:1048-60. [PubMed] [Google Scholar]

[6]. Tanielian TL, Jaycox LH, eds. *Invisible wounds of war: psychological and cognitive injuries, their consequences*. RAND, 2009.

[7]. Bisson J. Post-traumatic stress disorder. *BMJ* 2007;334:789-93. [PMC free article] [PubMed] [Google Scholar]

[8]. Muldoon OT, Lowe RD. Social identity, groups, and post-traumatic stress disorder. *PolitPsychol* 2012;33:259-73. [Google Scholar]

[9]. Mc Manus S, Meltzer H, Brugha T, Bebbington P, Jenkins R, eds. *Adult psychiatric morbidity in England, 2007: results of a household surveys*. NHS Information Centre for Health and Social Care, 2008.

[10]. American Psychiatric Association. *Diagnostic and Statistical manual of mental disorders, 5<sup>th</sup>edn*. American Psychiatric Publishing, 2013.

[11]. World Health Organization. *The ICD-10 classification of mental and behavioral disorders: clinical descriptions and diagnostic guidelines*. WHO, 1992.

[12]. Kleim S, Kroger C. Prevention of chronic PTSD with early cognitive behavioral therapy. A meta-analysis using mixed-effects modeling. *Behav Res Ther* 2013;51:753-61. [PubMed] [Google Scholar]

- [13]. Roberts NP, Kitchenier NJ, Kenardy J, Bisson JI. Early Psychological interventions to treat acute traumatic stress symptoms. *Cochrane Database Syst Rev* 2010;3:CD007944. [PubMed] [Google Scholar]
- [14]. Inter-Agency Standing Committee. IASC guidelines on mental health and psychosocial support in emergency settings. IASC, 2007.
- [15]. Williams R, Bisson J, Kemp V. Principles for responding to people's psychosocial and mental health needs after disasters. OP94. Royal College of Psychiatrists, 2014.
- [16]. American Psychiatric Association. Practice guidelines for the treatment of patients with acute stress disorder and post traumatic stress disorder. APA, 2004.
- [17]. Barrera TLM. A meta-analytic review of exposure in group cognitive behavioral therapy for post traumatic stress disorder. *ClinPsychol Rev* 2013;33:24-32. [PubMed] [Google Scholar]
- [18]. Jonas D, Cusack K, Forneris C, et al. Psychological and pharmacological treatments for adults with post traumatic stress disorder (PTSD). AHRQ comparative Effectiveness Review 2013, Report No:13-EHCO11-EF.
- [19]. Courtois CA, Ford JD. Treating complex traumatic stress disorders: an evidenced-based guide. Guilford Press, 2009.
- [20]. Cloitre M, Courtois CA, Charuvastra A, Carapezza R, Stolbach BC, Green BL. Treatment of complex PTSD: Results of ISTSS expert clinician survey on best practices. *J Trauma Stress* 2011;24:615-27. [PubMed] [Google Scholar]
- [21]. Lewis G, Araya R, Elgie R, Harrison G, Proudfoot J. Self help interventions for mental health problems. In: Briefing DOHE, ed,2003.
- [22]. Kar N. Cognitive behavioral therapy for the treatment of post-traumatic stress disorder: A review. *Neuropsychiatr Dis Treat* 2011;7:167-81. [PMC free article] [PubMed] [Google Scholar]
- [23]. World Health Organization. WHO guidelines on conditions specifically related to stress. Geneva: WHO,2013.
- [24]. Leucht S, Hierl S, Kissling W, Dold M, Davis JM. Putting the efficacy of psychiatric and general medicine medication into perspective: review of meta-analyses. *Br J Psychiatry* 2012;200:97-106. [PubMed] [Google Scholar]
- [25]. Raskind MA, Peskind ER, Hoff DJ, et al. A parallel group placebo controlled study of parazosin for trauma nightmares and sleep disturbance in combat veterans with post-traumatic stress disorder. *Biol Psychiatry* 2007;61:928-34. [PubMed] [Google Scholar]
- [26]. Stein MB, Kline NA, Matloff JC. Adjunctive olanzapine for SSRI-resistant combat-related PTSD: a double-blind, placebo-controlled study. *Am J Psychiatry* 2002;159:1777-9. [PubMed] [Google Scholar]
- [27]. James EL, Bonsall MB, Hoppitt L, et al. Computer game play reduces intrusive memories of experimental trauma via reconsolidation-update mechanisms. *PsycholSci* 2015;26:1201-15. [PMC free article] [PubMed] [Google Scholar]
- [28]. Vojdani A, Thrasher JD. Cellular and humoral immune abnormalities in Gulf War veterans. *Environ Health Perspect*. 2004;112:840-6. [PMC free article] [PubMed] [Google Scholar]
- [29]. Da Costa JM. On irritable heart: a clinical study of a form of functional cardiac disorder and its consequences. *Am J Med Sci*. 1871;61:17-52. [Google Scholar]
- [30]. Myers ABR. On the Etiology and Prevalence of Diseases of Heart among Soldiers. London:John Churchill and sons;1870. [Google Scholar]
- [31]. Foa E, Keane T, Friedman M. Effective treatment for PTSD. NY: The Guilford Press;2000. [Google Scholar]
- [32]. Bradley R, Greene J, Russ E, Dutra L, Westen D. A multi-dimensional meta-analysis of psychotherapy for PTSD. *Am J Psychiatr*.2005;162:214-27. [PubMed] [Google Scholar]
- [33]. Kozaric-kovasic D, Kocijan-Hercigonja D, Grubisic-Ilic M. Post-traumatic stress disorder and depression in soldiers with combat experience. *Croat Med J*.2001;42:165-70. [PubMed] [Google Scholar]
- [34]. Kozaric-Kovacic D, Kocijan-Hercigonja D. Assessment of post-traumatic stress disorder and comorbidity. *Mild Med*. 2001;166:78-83. [Google Scholar]
- [35]. Hamner M, Robert S, Frueh B. Treatment resistant post-traumatic stress disorder:

- strategies for intervention. *CNS spectr.*2004;9:740-52. [PubMed] [Google Scholar]
- [36]. Stein DJ, Zungu-Dirwayi, Van Der Linden GJ, Seedat S. Pharmacotherapy for post-traumatic stress disorder. *Cochrane Data base Syst Rev.*2000;4:CD002795. [PubMed] [Google Scholar]
- [37]. Davidson J, Malik M, Sutherland S. Response characteristics to anti-depressants and placebo in post-traumatic stress disorder. *IntClin Psycho pharmacol.* 1996;12:129-6. [PubMed] [Google Scholar]
- [38]. Galatzer-Levy IR, Nickerson A, Litz BT, Marmar CR. Patterns of life time PTSD comorbidity: a latent class analysis. *Depress Anxiety.* (2013)30:489-96. Doi:10.1002/da.22048 [PubMed] [Cross Ref] [Google Scholar]
- [39]. Rytwinski NK, Scur MD, Feeny NC, Youngstrom EA. The co-occurrence of major depressive disorder among individuals with post-traumatic stress disorder: a meta-analysis. *J Trauma Stress.* (2013)26:299-309. Doi: 10.1002/jts.21814 [PubMed] [Cross Ref] [Google Scholar]
- [40]. Parsons A, Knopp K, Rhoades G, Allen E, Markman H, Stanley S. Associations of Army father's PTSD symptoms and child functioning: within and between family effects. *Family process.* (2018)57:915-26. Doi:10.1111/famp.12358 [PubMed] [Cross Ref] [Google Scholar]
- [41]. Litz BT, Engel CC, Baryant RA, et al. A randomized, controlled proof-of-concept trial of an Internet-based, therapist-assisted self-management treatment of post-traumatic stress disorder. *Am J Psychiatry* 2007;164:1676-83. [PubMed] [Google Scholar]
- [42]. Krystal JH, Rosenheck RA, Cramer JA, et al. Adjunctive risperidone treatment for antidepressant resistant symptoms of chronic military service-related PTSD: a randomized trial. *JAMA* 2011;306:493-502. [PubMed] [Google Scholar]