

# Summary of the Management of Posttraumatic Stress Disorder in Children and Adolescents

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In children and adolescents posttraumatic stress disorder (PTSD) is associated with significant morbidity including an increased risk for suicide attempts (Jacobson et al, 2008), an increased risk of co-occurring depression, substance use disorders, internalizing and externalizing disorders (Donnelly et al, 1999). Recently, there have been significant advances in our understanding of the pathophysiology of PTSD in the pediatric population and concomitantly, efforts have been made to develop effective diagnostic instruments for pediatric youth with PTSD. Paralleling these advances in our diagnostic and neurobiologic understanding of PTSD in children and adolescents, accumulating evidence suggests that a number of psychotherapeutic and psychopharmacologic interventions may be of benefit. Herein, the extant evidence for these strategies will be reviewed.

## Psychotherapeutic Treatments

At present, the most empirically supported psychotherapeutic intervention for youth with PTSD is trauma-focused cognitive behavioral therapy (TF-CBT), a structured, 12–16 week, individual treatment which includes: (1) psychoeducation; (2) stress reduction techniques; (3) involvement of parents and caregivers; (4) development of a trauma narrative and (5) mastery of the trauma. Additionally, there is evidence from randomized controlled trials which suggest benefit for Child Centered Therapy (Cohen et al, 2004), Nondirective Supportive Therapy (Cohen et al, 2005) and eye movement desensitization therapy (EMDR).

## Psychopharmacologic Treatments

### **Selective Serotonin Reuptake Inhibitors (SSRIs)**

SSRIs in pediatric patients with PTSD have generally failed, in randomized controlled trials, to separate from placebo. In the first randomized controlled trial of an SSRI in youth with PTSD, Cohen and colleagues compared adjunctive sertraline (mean dose 150 mg/day, range 50–200 mg/day) to placebo in patients receiving TF-CBT (Cohen et al, 2007). In this study, no statistically significant differences were observed in the Child Global Assessment Scale scores between the two groups (Cohen et al, 2007), nor were there any differences which were detected between placebo-treated and sertraline-treated patients with regard to intrusive, hyperarousal or avoidance symptoms. However, the study was under-powered to detect such differences and importantly, both patient groups were receiving an active treatment (TF-CBT) which likely made the detection of any sertraline-related improvement especially difficult. Similarly, Robb and colleagues (2010) evaluated sertraline monotherapy in children with PTSD (n=131, duration 10 weeks) and did not observe differences in the UCLA PTSD–I 17-item total score between sertraline-treated patients and those receiving placebo (Robb et al, 2010). Despite these two negative double-blind, placebo-controlled trials of SSRIs in youth with PTSD, some open-label trials suggest benefit. Seedat and colleagues evaluated flexibly dosed citalopram (20–40 mg/day, duration 8 weeks) and observed improvements in Clinician-Administered PTSD Scale (CAPS) total and symptom cluster scores as well as the Clinical Global

Impression Scale (CGI) score (Seedat, Stein, Ziervogel, Middleton, Kaminer, Emsley et al, 2002).

### ***Tricyclic Antidepressants***

Limited data exist concerning tricyclic antidepressants in youth with PTSD. One randomized, double-blind, controlled trial suggests that brief treatment with imipramine may attenuate some PTSD symptoms in children and adolescents aged 2–19 years (Robert et al, 1999); however, a follow-up study which compared this agent with fluoxetine and placebo suggested no difference between fluoxetine, imipramine and placebo (Robert et al, 2008). It should be noted that both trials lasted only 7 days and used non-validated outcome measures.

### ***Antiadrenergic Agents***

Given evidence of noradrenergic hyperactivity in both pediatric (Pervanidou et al., 2007) and adult patients with PTSD (Strawn and Geraciotti, 2008), agents that target this increased noradrenergic tone have been utilized in pediatric patients with PTSD, largely based on extrapolation of data from large, randomized, controlled trials of these medications and adult patients. At present, case reports, raise the possibility that the  $\alpha_1$  antagonist prazosin may be effective in treating youth with PTSD. This agent has been utilized as adjunctive treatment (Brkanac et al, 2003; Fraleigh et al 2009) and as monotherapy in children (Strawn et al, 2011) and adolescents (Strawn et al, 2009). At present, there are neither open-label trials nor double-blind, placebo controlled trials to support the use of this agent in youth with PTSD. Although generally well tolerated in adults, reflex tachycardia and orthostatic hypotension should be closely monitored on all patients treated with prazosin (Strawn, 2010).

Clonidine, a non-selective  $\alpha_2$  agonist attenuates reenactment symptoms in children (Harmon, and Riggs, 1996; Porter and Bell 1999; De Bellis et al, 2001). Guanfacine, which is less potent as an  $\alpha_2$  agonist may reduce nightmares in children with PTSD (Horrigan and Barnhill, 1996). However, there are no double-blind trials of these  $\alpha_2$  agonists in pediatric PTSD. Nonetheless, both clonidine and guanfacine are frequently used in the treatment of youth with ADHD and are generally well tolerated, with common side effects being dry mouth and sedation.

Propranolol has been evaluated in youth with PTSD and also in double-blind trials as a potentially promising agent for secondary prevention of PTSD in youth. Famularo and colleagues reported improvement in 11 children with childhood abuse-related PTSD who had significantly fewer symptoms when receiving propranolol (Famularo et al, 1988). No other studies have investigated propranolol for treatment but rather this agent has received attention as a means of secondary prevention of PTSD. There are 2 published double-blind controlled trials of propranolol in the secondary prevention of PTSD in adults that demonstrated efficacy (Pitman et al, 2002; Vaiva et al, 2003). However, randomized pediatric trials of propranolol for secondary prevention have failed to observe effectiveness in preventing PTSD symptoms. In children and adolescents (aged 10–18 years) exposed to trauma or violence, 2.5 mg/kg/day (maximum dose 40 mg BID; duration of treatment 10 days) was not associated with differences in CAPS–CA scores or in the number of patients meeting criteria for PTSD or subthreshold criteria for PTSD at 6 weeks follow-up (Nugent et al, 2010). In a second study propranolol was evaluated as a means of preventing the post-thermal burn hypercatabolic sequelae and inci-

dence of subsequent development of Acute Stress Disorder (ASD) was evaluated retrospectively (Sharp et al, 2010). In this study, there was no difference in the incidence of acute stress disorder between the two groups (Sharp et al, 2010). However, factors that were not controlled for in the study include mechanism of burn, hemodynamic instability (the medical indication for the use of propranolol) as well as opiate use, which may have some moderating effects on the development of PTSD in adults (Nugent et al, 2010; Pitman and Delahanty, 2005).

### **Atypical Antipsychotics**

There are currently some reports suggesting benefit of atypical antipsychotics in youth with PTSD. However, careful consideration of risks and benefits must accompany the use of this class of medications in treating youth with PTSD. One case series suggests that in young children with serious thermal burns and acute stress disorder, open-label risperidone treatment may be associated with reductions in all symptom clusters of acute stress disorder (Meighen et al, 2007). With regard to PTSD in adolescents, case report level evidence also suggests that adjunctive risperidone also results in significant symptomatic and functional improvement (Keeshin and Strawn, 2009). Lastly, Horrigan and colleagues found that in an open label treatment with risperidone resulted in remission of PTSD symptoms in 13 of 18 adolescents (Horrigan and Barnhill, 1999). To date, one study has examined the efficacy of quetiapine in youth with PTSD. In this study, adolescents (n = 6, 15–17 years) were treated with flexibly dosed quetiapine (50–200 mg/day) over a 6-week period and demonstrated improvement in Traumatic Symptom Checklist for Children (TSCC) posttraumatic stress t-scores and in symptoms of anxiety, depression and anger (Stathis et al, 2005).

### **Mood Stabilizers**

Several open-label studies have suggested benefit for some mood stabilizers in youth with PTSD. Specifically, carbamazepine has been evaluated in children (ages of 8 and 17 years) with sexual abuse-related PTSD (Looft et al, 1995) and over the course of an inpatient treatment, 22 of the 28 patients were asymptomatic, while the remaining 6 also demonstrated improvement (Looft et al, 1995). In addition, divalproex has been evaluated in an open-label trial of youth with PTSD (Steiner et al, 2007). Twelve adolescent boys (mean age 16+1 years) with comorbid conduct disorder and PTSD received either high or low dose divalproex. Patients receiving high dose (e.g. therapeutic doses) had improvements in CGI score over the course of treatment (Steiner et al, 2007).

### **Conclusions**

There is ample evidence to support the use of trauma-focused psychotherapies (e.g. TF-CBT) as first line interventions in youth with PTSD. With regard to medication data, RCTs do not support the use of SSRIs for the treatment of PTSD, nor propranolol for secondary prevention of PTSD. Open-label trials and case series suggest that antiadrenergic medications including prazosin and clonidine, the mood stabilizer carbamazepine and possibly the second generation antipsychotics quetiapine and risperidone may be of benefit for some pediatric patients with PTSD and these agents may be considered in children and adolescents who fail or are partial responders to first-line treatments for PTSD such as TF-CBT. Certainly, when treating physicians deem it clinically appropriate to initiate a trial of pharmacotherapy or to augment evidence-based psychotherapy in pediatric patients with PTSD, medications should be chosen in consultation with the patient's family and

to target specific symptoms that cause the most impairment to the child. Finally, when using medications in the treatment of PTSD, side effects, objective evidence of benefit as well continued need should be regularly re-evaluated.

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