Pharmacological Treatment of Anxiety Disorders in Children and Adolescents

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ABSTRACT:
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Anxiety disorders are among the most common of childhood psychiatric disorders, which may be associated with low self-esteem, substance abuse, depression, social isolation, inadequate social skills, and academic difficulties. The aim of the presented article is to review the drug treatment of anxiety disorders. Selected papers and books regarding to drug treatment of anxiety disorders were reviewed. Currently the selective serotonin receptor inhibitors are the first choice for the short-term treatment of anxiety disorders in children and adolescent, because they have been shown to be effective and safe. It is recommended to begin the treatment with very low doses and increase gradually to avoid side effects and compromise the adherence to treatment. The medication should be administered at therapeutic dosages for least 6 weeks to decide effectiveness of the treatment. The studies on drug treatment of anxiety disorders in children and adolescent are scarce. More well designed, double blind, placebo controlled studies on drug treatment of anxiety disorder are required.

Key words: anxiety disorders, drug therapy, children, adolescent

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INTRODUCTION

Anxiety disorders are among the most common of childhood psychiatric disorders, with a prevalence rate for any anxiety disorder ranging from 5.7% to %17.7 (1-7). Despite this high prevalence rate, treatment studies are scarce, possibly due to the incorrect idea that these disorders are transient or harmless.

Youth with anxiety disorders are at risk for low self-esteem, substance abuse, depression, social isolation, inadequate social skills, and academic difficulties (8-14). Children with anxiety disorders often follow a chronic course and have high rate (15). It has been suggested that separation anxiety disorder (SAD) may be a precursor of depressive disorder, agoraphobia, panic disorder, and any anxiety disorder in adulthood (16-24).

It is now recognized that management of the anxiety disorder in children and adolescents requires multiple-modal approaches including psychosocial and pharmacological interventions. The psychosocial interventions include education of parents and child about the anxiety disorder, consultation with school personnel and primary care physician, and cognitive-behavioral therapies (CBT), and family therapies (25-30). Although the psychosocial interventions, in particular CBT, have been shown to be useful for the treatment of anxiety disorders in youth (29,31-33), these are beyond the scope of this review. The aim of this article is to review pharmacological treatments of generalize anxiety disorder (GAD), social phobia (SP), selective mutism (SM), and SAD in youth.

ASSESSMENT

A crucial step before recommending any treatment for anxiety disorders in children and adolescent is a thorough evaluation of anxiety symptoms as well as other psychiatric symptomatology, family, psychosocial and academic problems, and somatic symptoms that

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Table 1. Pharmacological Studies in Children and Adolescent with Separation Anxiety Disorder, Social Phobia, and Generalized Anxiety Disorder.

Authors	Study	n	Age	Diagnosis	Drug	Dose	Duration	Results (effectivity)
Berney et al (1981)	Double-blinded and placebo controlled,	51	9-14	SR	Clomipramine	40-75 mg/day	12 weeks	Clomipramine = placebo
Simeon and Ferguson (1987)	Open-label Placebo-drug-placebo crossover,	12	8.8-16.5	OAD	Alprazolam	0.5-1.5 mg/day	4 weeks	Alprazolam > placebo
Bernstein et al (1990)	Double-blinded and placebo controlled,	24	7-18	SR with DD or ANXD	Imipramine Alprazolam	3 mg/kg/d for imipramine; 0.03 mg/kg/d for alprazolam	8 week	Medications = placebo.
Simeon and Ferguson (1992)	Double-blinded and placebo controlled,	30	8-17	OAD, AVD	Alprazolam	0.5-3.5 mg/day	4 weeks	Alprazolam = placebo
Klein et al (1992)	Double-blinded and placebo controlled,	20	6-15	SAD	Imipramine	5 mg/kg/day	6 weeks	Imipramine = placebo
Graae et al (1994)	Double-blinded and placebo controlled,	15	7-13	SAD	Clonazepam	Up to 2mg/day	4 weeks	Clonazepam = placebo, side effects observed frequent.
Black and Uhde (1994)	Double-blinded and placebo controlled,	15	6-11	SM, SP, AVD	Fluoxetine	0.6 mg/kg/day	12 weeks	Effective (on parents' rating) and safe
Birmaher et al (1994)	Open,	21	11-17	OAD, SP, SAD	Fluoxetine	10-60 mg/day	Up to 10 months	Effective and safe
Dummit et al (1996)	Open,	21	5-14	SM	Fluoxetine	10-60 mg/day	9 week	Effective, 3 patients discontinued fluoxetine because of disinhibition
Fairbanks et al (1997)	Open,	16	9-18	SP, GAD, SAD, SPP, PD	Fluoxetine	Up to 40 mg/day (children under) 12 Up to 80 mg/day (adolescent)	6-9 weeks	Effective, and safe
Bernstein et al (2000)	Double-blinded and placebo controlled,	63	13.9 ± 3.6	SR with DD or ANXD	Imipramine	3 mg/kg/d	8 weeks	Imipramine + CBT > Placebo + CBT
Rynn et al (2001)	Placebo-controlled,	22	5-17	GAD	Sertraline	50 mg/day	9 weeks	Effective and safe
Compton et al (2001)	Open,	14	10-17	SP	Sertraline	Mean: 123.21+/-37.29 mg/day	8 weeks	Effective and safe
RUPP (2001)	Placebo-controlled,	128	6-17	GAD, SP, SAD	Fluvoxamine	Up to 300 mg/day	8 weeks	Effective, 8% discontinued fluvoxamine because of adverse effects
Khan et al (2002)	Double-blinded and placebo controlled,	156	6-17	GAD	Venlafaxine XR	Up to 225 mg/day	≤ 8 weeks	Venlafaxine XR > placebo

Legend: OAD: Overanxious disorder; SP: Social Phobia; SAD: Separation Anxiety Disorder; AVD: Avoidant Disorder; SM: Selective Mutism; SR: School Refuser; DD: Depressive Disorder; ANXD: Anxiety Disorder; SPP: Specific Phobia; PD: Panic Disorder; GAD: Generalize Anxiety Disorder

may be easily misinterpreted as side effects of future pharmacological treatment. Multiple informants and several sessions with the child and their parents are useful to obtain an adequate history and mental status examination. Information about premorbid functioning, substance abuse, onset of condition and developmental and psychiatric family history should be obtained.

Considering the age and developmental level of the child, a variety of rating scales may be used to gather information from patients, parents (about their children and themselves), teachers, and significant others (34). Medical history and examination should be done and laboratory should be tests requested if warranted. Since anxiety disorders in youth are often associated with high rates of comorbidity with other psychiatric disorders such as depression (9,35-37), these comorbid disorders should be diagnosed and treated appropriately. Hospitalization may be required for severe cases or if there is high risk for suicide. Since parents of anxious youth usually have psychiatric disorders, to improve the child's prognosis it is recommended to refer them for the treatment as well.

SELECTIVE SEROTONIN REUPTAKE INHIBITORS

All the selective serotonin receptor inhibitors (SSRIs) are well absorbed from the gastrointestinal track after oral administration. Hematology and chemistry testing are usually not necessary before treatment with the SSRIs (38). The preliminary reports suggest that SSRIs are efficacious for the treatment of anxiety disorders in children and adolescents (Table 1) (39-45). The time course of improvement with the SSRIs for anxiety disorders is approximately 4 to 6 weeks. The dosages of the SSRIs are similar to the ones used to treat depression (Table 2), but the length of treatment needed to avoid relapses or recurrences has not been determined yet (43,46).

Table 2. Pediatric Dosage for Anxiety Disorders (43)

	Dose/Day	
Medication	**Children**	**Adolescents**
Fluvoxamine	50-150 mg	100-300 mg
Imipramine	2-5 mg/kg	2-5 mg/kg
Buspirone	10-20 mg	15-60 mg
Venlafaxine	1-4.5 mg/kg	1-4.5 mg/kg
Nefazodone	50-100 mg	100-200 mg
Sertraline	25-100 mg	50-150 mg
Paroxetine	5-20 mg	10-40 mg
Fluoxetine	5-20 mg	10-40 mg
Citalopram	5-20 mg	10-40 mg
Nortriptyline	1-3 mg/kg	1-3 mg/kg
Lorazapam*	0.5-2 mg	2-4 mg
Clonazepam*	0.125-0.5 mg	0.5-2 mg

*Adjunctive alternatives.

Fluoxetine:

Fluoxetine has a long half-life (1 to 4 days) in adults compared with other SSRIs. Norfluoxetine, the primary metabolite of fluoxetine, is at least as potent inhibitor of serotonin as its parental compound, fluoxetine, and it has a long half-life of approximately 7 to 15 days in adults (47,48). Fluoxetine inhibits its own metabolism; its half-life gets longer with increased dosage, and its plasma concentration increases disproportionately (49). Because of these facts, when treating a patient with fluoxetine, it is reasonable to wait at least 4 to 6 weeks before increasing the dose. The usual dosage is 20 mg/day, but some patients may respond to lower dosages (e.g., 5 mg/day). Maximum dosages up to 60 mg/day are sometimes necessary (46).

To date, three open label studies and one double blind and placebo-controlled study of fluoxetine in youth with anxiety disorders have been reported. Open label studies suggested that fluoxetine is efficient for the treatment of children with overanxious disorder (OAD), SP, SAD, and SM (39,41,42). A double blind and placebo-controlled study of fluoxetine (20 mg/day) in 15 children (mean age: 8.5±1.9 years) with SM and SP showed that fluoxetine was significantly better than placebo and well tolerated (50). Recently a double blind randomized controlled trial compared a fixed dose of fluoxetine (20 mg/day) to placebo for the treatment of 74 children and adolescents with SP, GAD, and/or SAD. Approximately 60% of the patients treated with fluoxetine showed much to very much improvement in comparison with 30% of those randomized to placebo (Birmaher et al, personal communication).

Sertraline:

The half-life of sertraline, the parent compound, has been reported to be about 1 day in adult, and 14 hours in youth (Axelson et al, in press). Desmethylsertraline, the principal metabolite of sertraline, has longer half-life, but it is not pharmacologically active. Sertraline exhibits a linear relationship between dose and plasma concentration (49,51). In general, treatment is initiated at 25 mg/day with a target dose of 50 mg day to 200 mg/day (46).

Rynn et al (2001) examined the safety and efficacy of a fixed dose of sertraline (50 mg/day) treatment compared to the placebo for 22 children and adolescents aged 5-17 years with GAD (44). Ten of the 11 patients who received sertraline (90%), but only one of the 11 who received placebo (10%) improved. However, of those patients who improved

while taking sertraline, only two patients were markedly improved, representing a possible remission rate of only 18%. Overall, sertraline was well.

An open label trial of sertraline (mean dose 123.21+/-37.29 mg per day) in 14 children with social anxiety disorder showed that sertraline resulted in significant improvement in symptoms of childhood social anxiety disorder. Sertraline was generally well tolerated (52).

Fluvoxamine:

In adults, the half-life of the fluvoxamine is about 12 to 24 hours (53) and has no active metabolites (51). Fluvoxamine displays a linear relationship between dose and plasma concentration. Fluvoxamine is usually started at 25 mg/day with a target dose of 50 mg/day to 200 mg/day (46).

Recently, the RUPP Anxiety Study Group (2001) compared the effects of a flexible dose of fluvoxamine and placebo in a group of 128 children and adolescent (aged 6 to 17) with SP, SAD, or GAD (45). The dose of fluvoxamine was increased by approximately 50 mg per week to a maximum of 300 mg per day in adolescents and 250 mg per day in children less than 12 years of age with a mean group dose of 150 mg/day by the end of the study. Approximately 70% of the anxious youth treated with fluvoxamine and 30% of those receiving placebo showed moderate to very strong response. Five children in the fluvoxamine group (8 percent) discontinued treatment because of adverse events, as compared with one child (2 percent) in the placebo group.

Side effects of the SSRIs:

The SSRIs' studies in children and adolescent with anxiety disorders suggested that the side effects of SSRIs are usually mild and transient. They present the advantage of having fewer anticholinergic and antihistaminic side effects, and lack of serious systemic toxicity in relatively high doses (38). One of the great concerns about SSRIs, like other antidepressants is that they may activate hypomania or mania especially in the youth with a family history of affective disorders. Children and adolescents receiving SSRI therapy should be monitored for the development of hypomanic and manic symptoms. Although previous reports suggesting that SSRIs use is associated with increased suicidal risk (54), Khan and colleagues reported that there is no difference in suicide risk between SSRIs and plasebo (55). The common side effects reported in association with SSRIs include gastrointestinal difficulties (abdominal discomfort, nausea, diarrhea, vomiting, and decreased appetite), central nervous system (CNS) effects (increased motor activity, agitation, disinhibition that is so-called behavioral activation, headache, and insomnia). The other side effects of SSRIs includes decreased appetite and weight, abdominal pain, drowsiness, tremor, restlessness, hypersomnia, increased diaphoresis, delayed ejaculation, anorgasmia, vivid dreams, apathy, seizures, akathisia, ecchymoses, hyponatremia, and allergies. In addition, the serotonin syndrome may occur when SSRIs are combined with MAOs. This syndrome carries the potential for significant morbidity and mortality; it is characterized by symptoms such as confusion, myoclonus, hyperreflexia, diaphoresis, and possibly cardiovascular compromise (56).

SSRIs like other antidepressants and benzodiazepines may cause agitation or disinhibition. Referred to as a loss of the ability to control one's impulses, disinhibition may result in nonspecific behavioral activation including giddiness, agitation, confusion, irritability, insomnia, temper outburst, anxiety, or aggression. Disinhibiton generally occurs immediately after the initial exposure (<30 minutes) to a medication and dissipates commensurate with the plasma half-life of the medication. The disinhibition caused by the SSRIs needs to be differentiated from mania/hypomania induced by these medications (57).

Tricyclic antidepressants:

Absorption from oral administration of most tricyclic antidepressants (TCAs) is incomplete, and the pharmacokinetics of TCAs are characterized by substantial presystemic first-pass metabolism, a large volume of distribution, extensive protein binding, and an elimination half-life averaging about 1 day (up to 3 days for protriptyline) (58).

The reports regarding the use of the TCAs for the treatment of children and adolescent with anxiety disorders are conflicting (Table 1). Moreover most of the reported studies have included children with school refusal whom not necessarily had anxiety disorders. In a 6-week double-blind controlled study of 35 children, aged 6 to 14 years, with anxiety-based school refusal, imipramine was found to be significantly superior to placebo (59). However, Klein et al did not replicate this finding in a group of 21 children with separation-anxiety (60). Bernstein et al, in a double blind controlled study also did not find statistically significant differences among imipramine,

alprazolam and placebo in a small sample (n=24) of school refusers, aged 7 to 18 years, with depression or anxiety disorders (61). Recently, Bernstein and colleagues in a 8-weeks double blind-placebo controlled study comparing imipramine plus CBT versus placebo plus CBT alone found that imipramine plus CBT was better in improving school attendance and decreasing symptoms of depression in 63 school-refusing adolescent with comorbid anxiety and depression (62). Berney et al, in a 12-weeks double blind placebo-controlled study, found no significant differences between placebo and clomipramine in decreasing symptomatology or facilitating in a return to school in 51 school refusers, ages 9 to 14 years old (63). The inconsistent reports noted above may be accounted by the differences in sample sizes, presence or absence of comorbid disorders, dosages, and type and control of concurrent therapies (25).

Side effects of TCAs:

Numerous of the TCAs side effects are reasoned by blockade of cholinergic, histaminic, and adrenergic receptors. TCAs have "quinidine-like" effect on cardiovascular system, which may result in slower intracardiac conduction and increased heart rate, flattened T waves, prolonged QT intervals, and depressed ST segments on electrocardiograms (EKGs) (56, 64). A number of case reports proposed the sudden unexplained death occurring in children stable on TCA medications (65-68). At least two of them due to imipramine and desipramine metabolite accumulation which has been shown by a postmortem study (69). Impaired metabolism was caused by a genetically determined "slow metabolizer" phenotype of cytochrome CYP2D6, and/or concurrent therapy with phenothiazines in these cases, which warrants physicians to treat all patients as if they were poor metabolizers for the drugs, especially in combined pharmochotherapy (69). It would be helpful to predict which patients are at greater risk for the development of serious adverse effects to TCAs. Potential factors include pre-existing abnormalities in the ECG, such as a bundle branch block or other conduction problem, a prior history of cardiac arrhythmia and a family history of early onset cardiac disease. It appears appropriate to show special concern in the presence of these factors, but it is not currently clear whether these factors convey an additive risk to the development of catastrophic cardiovascular adverse effects (70). Varley offers following proposal: (i) initial utilization of alternative agents, with TCAs as secondary or tertiary agents; (ii) informed consent/assent by the patient and family which should include mention of the reports of sudden death and discussion of the controversy as to the relationship of TCAs, if any, to sudden deaths; (iii) vigilance regarding the emerging literature; (iv) systematic ECGs, serum concentrations and vital sign monitoring (Table 3). Blood levels should be obtained 10 to 12 hours after the last oral dose (46).

Table 3. An Example of a Tricyclic Antidepressant Protocol (70)

Obtain baseline ECG to assess for pre-existing arrhythmias or cardiac conduction delays
⇓
Begin TCA treatment at 1 mg/kg/day (0.5 mg/kg/day for nortriptiline)
⇓
Advance dose no more rapidly than every 5 days. Repeat ECG at 3.0 mg/kg/day and at any subsequent dose increases with the following parameters
⇓
PR interval <0.18 sec in children <10 years
PR interval <0.2 sec in children >10 years
QRS complex <0.12 sec
Corrected QT interval <0.45 sec
⇓
Vital signs monitoring:
Baseline postural pulse and blood pressure
Regular monitoring of postural pulse and blood pressure
⇓
Obtain serum concentrations after steady state if TCA dosage <3mg/kg/day
If dosage exceeds 3 mg/kg/day, obtain serum concentration at 3 mg/kg/day, and at ceiling dose. Serum concentration should not exceed 500 mg/L.

TCA seems more likely to induce maniform states (mania or hypomania) than SSRIs (71,72). Other side effects of TCA include anticholinergic side effects like dry mouth, constipation, blurred vision, urinary retention; sedation due to serotonergic, cholinergic, and histaminergic activities; weight gain reasoned by histamine H_1 receptors; autonomic side effects partly because of alpha-1 adrenergic blockade like orthostatic hypotention; delirium possibly reasoned by anticholinergic effects; seizures, myclonus, dizziness, cognitive disturbance, agnulositosis, leukositosis, leukopenia, eosinophilia, hyperprolactinemia, galactorrhea, anorgasmia, ejaculatory disturbances, inappropriate secretion of antidiuretic hormone, nausea, vomiting, hepatitis, skin rashes, speech blockage, paresthesia, peroneal palsies, and ataxia (46,56,73,74). As a consequence of anticolinergic activities, TCA aggravate the precipitation of glaucoma requires emergency treatment with a miotic agent. TCA should not be administered during a course of electroconvulsive therapy, primarily because of the risk of serious adverse cardiac effects.

Benzodiazepines

The benzodiazepines are usually used as anxiolytics, hypnotics, anticonvulsants, and muscle

relaxants. (75). This group of medications are in general absorbed and metabolized more rapidly in children than in adults (76,77), indicating that children may require multiple doses to maintain a therapeutic blood level (46).

Despite the history of robust benzodiazepines anxiolytic impact in adults, controlled studies, open label studies, and case reports of benzodiazepines for pediatric anxiety have not been impressive (43). A small open label study suggested that alprazolam was efficacious for the treatment of children with OAD and/or avoidant disorder (78). Bernstein et al, in a double controlled study did not find statistically significant differences between imipramine, alprazolam and placebo in a small sample (n=24) of school refusers (61). Simeon et al, in a double controlled study, did not find statistically significant differences between alprazolam (doses 0.5-3.5 mg/day) and placebo in a small sample (n=30) of children and adolescent with anxiety disorders, aged 8 to 17 years (79). Graae et al, in a double controlled study, also did not find statistically significant differences between clonazepam (doses up to 2mg/day) and placebo in a small sample (n=15) of children with anxiety disorders, aged 7 to 13 years (80).

Side effects of benzodiazepines:

As in adults, sedation is the most common side effect observed in children. This side effect is dose-related and generally resolve as tolerance develops (81,82). Other side effects include irritability, agitation, nausea, constipation, dry mouth, dizziness, headache, blurred vision, abdominal pain, disinhibition, and tiredness. No data have been published regarding the risk of physiological and psychological dependence in children and adolescents. However, it is recommended that benzodiazepines be prescribed for youth for only short periods of time (i.e., weeks rather than months) because of the theoretical potential for dependence (81). It is also recommended that benzodiazepines should be used as adjunctive to other treatments.

Other Pharmacological treatments

Recently a double blind randomized controlled trial compared a flexible-dose of venlafaxine XR (37.5-225 mg/day) to placebo for the treatment of 156 children and adolescents with GAD. Response rates were significantly higher in the venlafaxine XR group (64%) than in the placebo group (40%). Venlafaxine was found to be effective and well-tolerated treatment for children and adolescent with GAD. The most common adverse effects of venlafaxine XR were asthenia, anorexia, weight loss, hyperkinesia, and epistaxis (83). The other adverse reactions of venlafaxine in adults were sweating, nausea, constipations, vomiting, somnolence, dry mouth, dizziness, nervousness, anxiety, tremor, blurred vision, hypertension, abnormal ejaculation or orgasm, and impotence. In addition, a venlafaxine withdrawal syndrome involving mainly gastrointestinal and CNS symptoms was described. The drug should be gradually tapered over 2 to 4 weeks and over a longer period when required (56). Further studies are needed to show reliability of venlafaxine for the treatment of anxiety disorders in youth.

Although no studies using paroxetine, citalopram, bupropion, nefazodone, MAOIs, buspirone, and beta-blokers, have been reported in youth, these compounds have been found for the treatment of the anxious adults (46,84-87).

Hydroxyzine, an antihistaminic medication, was found to be effective compared to the placebo in a small study for adults with anxiety disorder (88-90), but no studies has been done in children with anxiety disorders. Antihistamines may induce drowsiness, agitation, and cognitive and affective side effectes (46,91).

CONCLUSIONS

Currently the SSRIs are the first choice for the short term treatment of anxiety disorders in children, because they have been shown to be effective and safe. However, other medications, such as the benzodiazepines, may be used alone or sometimes in combination with SSRIs.

Children, compared to adults, have greater hepatic capacity, more glomeruler filtration, and less fatty tissue. Therefore children eliminate many psychotropic drugs more rapidly than adults. Because of children's quick elimination, the half-lives of many medications may be shorter in children than adults (56). It is recommended to begin the treatment with very low doses and increase gradually to avoid side effects and compromise the adherence to treatment. The medication should be administered at therapeutic dosages for least 6 weeks to decide effectiveness of the treatment. Since fluoxetine has a longer half-life, titration may require a longer trial period. The discontinuation of the medication should be slow (e.g. for at least 4 to 6 weeks) to avoid withdrawal adverse effects. When several medications are administered, drug interactions should be kept in mind, and lower doses should be considered if the

medications used interact with the same cytocrome P450 coenzyme system. The duration of drug therapy in youth with anxiety disorder has not been ascertained yet and continuation and maintenance studies are warranted. More well designed, double blind, placebo controlled studies on youth are required. Studies are also needed to test and compare the effects of antidepressants versus CBT, the only type of psychotherapy that has been shown in randomized controlled trials to be effective for the acute and continuation treatment of youth with anxiety disorders (24).

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Anxiety disorders are the most prevalent psychiatric disorders in youth. They are associated with severe disability, and are considered gateway disorders-- as they predict adult psychiatric illnesses.Â Childhood obesity affects about a third of children and adolescents in the U.S. and confers a significant risk for current and future health impairment, and eating-related conditions such as loss of control eating and binge eating disorder. Obesity in early/mid-childhood is common and may reflect a distinct, high-risk, early-onset form.Â The pharmacological treatment of pediatric OCD is also studied here. Investigators: Marco Grados, M.D., MPH, Mark Riddle, M.D. Schizophrenia. Classification of anxiety disorders among children and adolescents. There have been some recent changes to the classification of anxiety disorders.Â Selective serotonin reuptake inhibitors (SSRIs) are regarded as the pharmacological treatment of choice for anxiety disorders in children and adolescents because of their effectiveness and safety profile. It is important to note that benzodiazepines have not been systematically evaluated in children and adolescents and, in view of concerns about dependency and side effects,48 their use is not recommended.21. Anxiety disorders often emerge during childhood and adolescence. At some point during childhood, about 10 to 15% of children experience an anxiety disorder. Children with an anxiety disorder have an increased risk of depressive and anxiety disorders later in life. Anxiety disorders that can occur in children and adolescents include. Agoraphobia. Generalized anxiety disorder.Â Anxiety disorders in children are treated with behavioral therapy (using principles of exposure and response prevention), sometimes in conjunction with drug therapy. In exposure-based cognitive-behavioral therapy, children are systematically exposed to the anxiety-provoking situation in a graded fashion.Â Drugs for Long-Term Treatment of Anxiety and Related Disorders. Drug. Uses. Anxiety and related disorders in children. The term â€œanxiety disorderâ€ refers to a group of mental illnesses that includes generalized anxiety disorder (GAD), obsessive-compulsive disorder (OCD), panic disorder, posttraumatic stress disorder (PTSD), social anxiety disorder (also called social phobia), and specific phobias.Â Prescription medications can be effective in the treatment of anxiety disorders. They are also often used in conjunction with therapy. In fact, a major research study found that a combination of CBT and an antidepressant worked better for children ages 7 to 17 than either treatment alone. Medication can be a short-term or long-term treatment op-tion, depending on how severe your childâ€™s symptoms are and how he or she responds to treatment. Antipsychotics in children and adolescents with schizophrenia: A systematic review and meta-analysis. Indian Journal of Pharmacology.45:439-46. doi:10.4103/0253-7613.117720. REASON FOR EXCLUSION: Wide inclusion criteria (in terms of participant age and study design).Â Authors: L Tarsitani and C Barbui Question: Are antipsychotics effective and safe for treatment of psychotic disorders in adolescents compared to placebo? Bibliography: Kumar A, Datta SS, Wright SD, Furtado VA, Russell PS (2013). Atypical antipsychotics for psychosis in adolescents.