Psychotropics in paediatrics or adolescents

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Introduction

Psychotropic drugs are medications and chemical formulations that cross the blood brain barrier to act on the central nervous system to stimulate the change of mood and behaviour of an individual. Schatzberg and Nemeroff (2009) underscore that it is important to note that these medications are not curative but rather palliative, and although they may improve symptoms associated with various mental disorders, they do not cure the primary cause of the disorders. According to Perry (2007), psychotropic medications include antidepressants, antipsychotic or neuroleptics, attention deficit hyperactivity disorder (ADHD) drugs, and antimanic or anxiolytics among others. This paper aims at discussing the physiological implications of using psychotropic medications in paediatric and adolescent populations with a bias on neuroleptic/antipsychotic, anxiolytic/antianxiety and ADHD drugs.

While there may be reservations regarding the use of psychotropic medication in children and the physiologic effect of these drugs on young people’s central nervous system development, leaving mental disorders untreated is not a viable option as evidently supported by medical literature. This is because untreated mental illness may cause paramount long-term morbidity and even irreversible deficits in socio-emotional and cognitive functioning. Regardless of ethical and legal reservations surrounding the use of psychotropic drugs among paediatric and adolescent patients, analyses of data on their use reveals fast changing trends pointing to increased use. According to Hsia and MacLennan (2009) there was a three-fold increase of the number of children/adolescents taking any psychotropic drug between 1987 and 1996. Adolescent visit to physicians significantly increased

psychotropic prescriptions as evidenced by an increase to 8. 3% of the prescriptions in 2001, up from 3. 4% in 1994 (Hsia & MacLennan, 2009). In 2001, psychotropic prescriptions made up 8. 8% of all psychopharmacological prescriptions among patients aged between 6 and 17 years (Hsia & MacLennan, 2009). In terms of gender, more male paediatrics and adolescents are on these medications compared to their female counterparts. Due to increased incidences of anxiety, depressive, manic, and other psychotropic disorders in paediatrics and adolescents, there has been an increased acceptance and need for use of neuroleptics, anxiolytics and antidepressant drugs in these patients.

Neuroleptics and their implications on paediatrics/adolescent

Neuroleptics, also known as major tranquilizers or antipsychotic drugs are used primarily to treat psychoses and symptoms. In paediatrics and adolescents, they are also indicated in the treatment of other non-psychotic psychiatric disorders. They are the drugs of first choice in treatment of autism and schizophrenia in children and adolescence. Kalyna and Virani (2007) explain that neuroleptics are used in treatment of paediatrics and adolescents with severely aggressive conduct disorders, Tourette’s disorder, and chronic motor or vocal tic disorder. Antipsychotic drugs are also used in the treatment of ADHD but their use has decreased due to increased use of stimulant medications which are more effective for this disorder. Examples of antipsychotic drugs include haloperidol, chlorpromazine, molindone and fluphenazine. Newer formulations include olanzepine, clozapine, quetiapine, risperidone and ziprasidone (Hamrin, McCarthy & Tyson, 2010).

The use of neuroleptics on paediatrics and adolescents has several implications. Side effects associated with long-term use of these medications in this population include akathesia, acute dystonic reactions, parkinsonian symptoms, tardive dyskinesia, anticholinergic symptoms and sedation. They also lower seizure threshold in susceptible subjects and drugs such as Chlorpromazine should not be used in such patients. Tardive dyskinesia is a grave concern and has been reported in about 1 to 20% of paediatrics and adolescents on long-term use of neuroleptics (Kalyna & Virani, 2007). It may occur as early as 5 months after commencement of treatment or may delay to up to 3 years. Since paediatrics and adolescents have more dopamine receptors than adults, they are more sensitive to side effects affecting the central nervous system. Long-term use of neuroleptics should be avoided in this population but …. contends that low doses may be recommended in selected difficult cases.

Other side effects associated with neuroleptics include weight gain, irregular menses and breast enlargement in adolescents. Doran (2013) documents that second-generation anti-psychotic (SGA’s) drugs can cause metabolic disturbances and weight gain in paediatrics and adolescents even during first-time treatment. For instance, in a trial of treatment of schizophrenia with olanzapine, 30% of the paediatric/adolescent subjects gained weight compared to 6% in adult subjects (Doran, 2013). Other SGAs such as risperidone, quetiapine and clozapine also posted similar results with the paediatric/adolescent subjects gaining between 0. 9 to 16. 2 kilograms (Doran, 2013).

Withdrawal of neuroleptics or lowering of the dosage may lead to withdrawal emergent syndrome with resultant aggravation of psychotic symptoms. This has been reported in paediatrics and symptoms include ataxia, vomiting and nausea. In a study by Vitiello (2008) as high as 51% of the paediatric patients showed the withdrawal symptoms, usually occurring after few days to few weeks after drug withdrawal. Clozapine has been associated with deaths of two paediatric patients with the mechanism being linked to sudden cessation of treatment (Vitiello, 2008). Haloperidol has been demonstrated to interfere with the children and adolescent's daily routine including social and school activities. Neuroleptics increase sedation, lethargy and somnolence in paediatrics and adolescents than in adults; for instance, this was demonstrated in 30% to 49% of paediatric patients being treated with Risperidone in contrast to 7% of adults taking the same drug for bipolar mania (Hamrin, McCarthy & Tyson, 2010).

Anxiolytics and their implications on paediatric/adolescents

Anxiolytics are psychopharmacologic drugs used to treat anxiety disorders in paediatrics and adolescents. Other conditions for which they may used include sleep disorder, aggressive behaviours and psychosis. They include selective serotonin-reuptake inhibitors (SSRIs) benzodiazepines, tricyclic antidepressants (TCAs) and busipirone. Anxiety disorders are greatly predominant in adolescence; between 6 and 20% of children have a type of anxiety disorder (Kalyna & Virani, 2007). Doran (2013) documents that use of benzodiazepines in paediatrics and adolescents has tripled over the last 10 years.

Anxiolytics are recommended to be used only after an aftermath of an event e. g. traumatic event and should be used for short periods (not more than two weeks) to avoid the risk of developing addiction or diminished efficacy. A recent review shows that SSRIs have become the preferred pharmacological intervention for paediatric anxiety disorders. They have very potent anxiolytic effects and their tolerance among paediatrics and adolescents is high. However, this class of psychotropic drugs has been associated with increased suicidal ideation.

A well-documented controversy in paediatric and adolescent psychopharmacology occurred in 2003 when FDA issued public alert warning prescribers of increased ideation and attempts of suicide among patients below 18 years on anxiolytics (Vitiello, 2008). This contributed to a substantial drop in rates of diagnosis and prescription of these drugs among paediatric and adolescent population. Later, after a meta-analysis of numerous clinical trials of nine drugs in this class, it was demonstrated that there was only a marginal increase (0. 7%) increase in the suicidal ideation with no actual increase in completed suicides (Schatzberg & Nemeroff, 2009). However, this has led to adoption of a multidisciplinary approach towards management of paediatric and adolescent depression to encompass both pharmacological and non-pharmacological interventions.

Cardiovascular adverse effects are often reported with most anti-anxiety medications because these drugs act on the autonomic system. Such side effects include increase in heart rate and changes in blood pressure. Although these side effects are generally not of major clinical significance while taking psychotropic medications, tricyclic antidepressants (TCAs) such

as desipramine have been inconclusively linked to sudden death among paediatric patients (Kalyna & Virani, 2007). Therefore, it is imperative for the prescribing physicians to take a comprehensive patient history, as well as monitor the electrocardiograms, heart rate and blood pressure changes of the paediatric and adolescent patients before and during treatment with psychotropic agents such as TCAs. Lamotrigine manifestly increases the risk for severe skin reactions and hives in paediatrics and adolescents (Dulcan, 2010).

Another critical consideration in anxiolytic use of drugs in these subjects is drug interactions. Drugs that inhibit the cytochrome P450 enzyme system could have adverse effects on the subjects if concomitantly administered with anxiolytics (Perry, 2007). Antifungal drugs and some antibiotics such as erythromycin when co-administered with SSRIs such as fluoxetine can cause cardiac arrhythmias (Perry, 2007). Others such as imipramine and Lamotrigine can cause toxic delirium (Hamrin, McCarthy & Tyson, 2010). The prescribers must document all medications that may have drug-drug interactions with psychotropics as well as those that have direct or indirect effect on the cytochrome P450 enzyme system.

ADHD drugs and their implications on paediatrics/adolescents

Stimulants used in management of ADHD are some of the most used psychotropic drugs among paediatrics and adolescents. However, trepidation persists due to concerns of the adverse effects of these drugs on the growth rate in paediatrics. Use of stimulant psychotropic drugs has been associated with stunted growth rates. The Multimodal Therapy of ADHD study

demonstrated that stimulant psychotropic drugs, especially in high doses, reduce growth velocity and weight (Gelder et. al, 2009). This is due to appetite loss, a common adverse effect associated with these stimulant drugs. However, in most cases normal growth seems to rebound once the psychostimulant agents are withdrawn with no significant suppression of ultimate height attained. Nevertheless, some studies have revealed that pyschostimulants continue to suppress growth in early and late adolescence. Rosenberg and Gershon (2002) explain that pyschostimulants such as methylphenidate may permanently cause stunted growth by affecting epiphyseal closing of long bones if used between ages 17 and 21 years. However, Cheng and Myers (2010) outline that suppression of growth could be because of the underlying mental disorder, for instance, ADHD rather than the treatment.

One disconcerting physiological implication of ADHD drugs especially in paediatrics being treated for hyperactivity or outbursts is the aggravation of the condition with the medication, a phenomenon referred to as paradoxical response. Doran (2013) explains that in a small number of paediatric/adolescent patients may severely increase nervousness and agitation instead of reducing it (disinhibition). These subjects may become giddier, act sillier or even manic. Similarly, some younger patients may be more depressed after being put on antidepressants. Studies have shown paediatrics and adolescents getting more moody and agitated after receiving mood treatment psychotropic drugs in ADHD treatment (Kalyna & Virani, 2007). Others on stimulants may become more hyperactive and fail even to respond to sleep-inducing drugs. Research by Hamrin, McCarthy and Tyson

(2010) shows that if a paediatric or adolescent patient shows paradoxical effect to one class of psychotropic drugs, there is a 50% of similar reaction if he or she is given another drug of the same class.

Paediatrics and adolescents have a lower albumin binding capacity and reduced adipose compartment, leading to a higher percentage of unbound compound than adults. Similarly, their drug biotransformation rates are higher, and this could reduce the half-life of the drugs relatively increasing the risk for toxic metabolite levels. This may contribute to physiological rebound effect where the paediatric and adolescent patients present with exacerbation of symptoms than original symptomatology (Dulcan, 2010). This often occurs when drug plasma levels decrease due to increased hepatic elimination and subsequent renal excretion. The subjects show symptoms such as hyperactivity, irritability, insomnia, over talkativeness, excitability and non-compliance (Dulcan, 2010). Schatzberg and Nemeroff (2009) explain that this can be remedied by adding a small afternoon dose or using slow-release preparations. The physician may also opt to use short- and long acting medications.

Other implications of ADHD drugs on paediatrics and adolescents are the drug’s adverse effects. In a meta-analysis review, 32% of the doctors were concerned with decreased appetite and loss of weight association with these drugs. Half of them raised concerns about disturbed sleep while 22% were apprehensive of the increased anxiety. Other physicians indicated that they were concerned about possible diversion of ADHD drugs and felt burdened by prescribing these controlled drugs for paediatrics and adolescents. There is a high potential for abuse of controlled stimulant drugs used in ADHD

treatment which can be achieved by crushing and snorting the medication. However, this abuse potential has been addressed through extended release formulations and introduction of skin patches which are less susceptible to abuse.

Conclusion

Psychopharmacological treatment in paediatrics and adolescents is an area of on-going ethical discussion, as these subjects affected by mental disorders are a vulnerable class of patients. The use of psychotropic drugs in children below 8 years is under-researched; this is because most of these drugs are developed and researched in adults. In addition, it could also be due to existing ethical and legal considerations that hamper access of research to such studies. Paediatrics and adolescents with psychotic disorders will classically be put on psychotropic drugs while those with other disorders will be put on non-pharmacological treatment. Sometimes, both approaches may be used simultaneously. Logically, the benefits of pharmacological intervention must outweigh potential risks associated with use of these drugs in these young people. An important consideration is the proof of the efficacy and safety of the drug for the age of the patient and the specific disorder. Psychopharmacotherapy in paediatrics and adolescents requires a holistic, multidisciplinary approach. Pharmacovigilance in use of psychotropic agents among these subjects as well as their long-term efficacy and adverse effects are indispensable. It is evident that paediatric and adolescent patients are, to say the least, more vulnerable to adverse effects of psychotropics than adults are. With the increasing adoption of psychopharmacological interventions in treatment of paediatrics and

adolescents with mental disorders, novel research is vital to come up with clear evidence-based recommendations on use psychotropics in these subjects.

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