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Child Use of Controlled Substances for Treating Attention Deficit Disorder

By Cheyenne Goodspeed

Abstract

Attention Deficit Disorder is a learning disability that limits attentiveness and increases hyperactivity and impulsivity in affected individuals. On average, more children are diagnosed with this disorder than adults, indicating that the majority of people being treated for this disorder are children. With the recent rise in Attention Deficit Disorder diagnoses in children, more children are being exposed to controlled substances to treat the disorder. Considering the tight restrictions and regulations implemented by the Food and Drug Administration (FDA), many question the safety of these medications used to treat children with Attention Deficit Disorder. This research explores the safety and efficacy of the controlled substances used to treat Attention Deficit Disorder in children. Findings indicate that these medications pose no significant danger to children and drug dependence is not likely. Furthermore, findings also show that the medications used to treat the disorder are effective overall.

Introduction

Attention Deficit Disorder is a learning disability that impacts millions of families across the United States. In an Attention Deficit Disorder fact page, Doctor Fred K. Berger, MD, states, “Attention Deficit Disorder is problem of not being able to focus, control behavior, being overactive, or a combination of these” (1). According to the Centers for Disease Control and Prevention, approximately 6.4 million children in the United States are currently diagnosed with Attention Deficit Disorder. Of those 6.4 million children, approximately four million of these children are prescribed controlled substances to treat the disorder. The amount of children diagnosed with Attention Deficit Disorder continues to increase at an average rate of 5% per year, indicating that the problem of Attention Deficit Disorder has indeed become more prevalent (1). In recent years, individuals have questioned the safety, efficacy and abuse potential of the medications used to treat Attention Deficit Disorder in children. A controlled substance is any drug with abuse potential. All controlled drugs are classified into five categories, ranked from highest abuse potential to lowest abuse potential. The Drug Enforcement Agency (DEA) is responsible for enforcing the laws and regulations surrounding all controlled substances.

According to the Drug Enforcement Agency, Schedule II drugs are defined as, "Drugs with a high potential for abuse, less abuse potential than Schedule I drugs, with use potentially leading to severe psychological or physical dependence. These drugs are also considered dangerous" (1). With the vast majority of prescriptions used to treat Attention Deficit Disorder being classified as Schedule II controlled drugs, many question why these drugs are approved for children.

Controversy

Some argue that controlled substances have little to no negative effects on children taking them and are essential for children with severe Attention Deficit Disorder. On the contrary, others believe that the medications used to treat the disorder are highly addictive and will ultimately cause children to become dependent on these medications. In the article, "Abuse Liability of Medications Used to Treat ADHD", by Scott H. Kollins, PhD, Kollins states, "A considerable amount of literature in a number of species supports the abuse potential of the most commonly used medications to treat ADHD. This abuse potential is the primary reason these products are tightly regulated by the U.S. Food and Drug Administration" (40). The controversy of prescribing children these medications stems from individuals who believe that children should not be exposed to medications deemed highly addictive. On the contrary, many individuals believe that despite the harmful effects of the controlled substances used to treat Attention Deficit Disorder, it is essential that many children be treated with these medications in order to focus, follow instructions, interact with others, and live a normal life. Further into the article, Kollins explains that, "Abuse potential may be lower in longer acting formulations" (40). This supports the argument that some of these medications regulated by the Food and Drug Administration may not be as harmful and addictive as others depending on the dosage amount and dosage form of the drug. This research paper will explore whether these medications are necessary or harmful by researching the positive and negative effects of the drugs used to treat children with Attention Deficit Disorder. The effects of the drugs used to treat Attention Deficit Disorder in children will essentially help answer the underlying question, "Why are controlled substances acceptable for use and prescribed to treat children with Attention Deficit Disorder?"

Clinical Trials

Although the Food and Drug Administration has successfully approved the medications used to treat Attention Deficit Disorder in adults, the Food and Drug Administration has informed consumers that many medications used to treat children have not been approved specifically for children. On the Drug Research and Children Information Page on the FDA's website, the FDA states, "Most drugs prescribed for children have not been tested in children … By necessity, doctors have routinely given drugs to children "off label" which means the drug has not been approved for use in children based on the demonstration of safety and efficacy in adequate, well-controlled studies" (1). In recent years, prescribers have been prescribing off-label controlled substances to children with Attention Deficit Disorder. While some less commonly used medications have been tested on children, some of the most common medications used to treat Attention Deficit Disorder in children have only been tested on adults. By prescribing these controlled substances to children, prescribers may put children at risk for experiencing amplified adverse events. Any possible side effects would be more harmful on children than adults simply because children are continuously changing and developing while adults are not. There are various reasons why many drugs have not been tested on children. One of the primary reasons is

because children are believed to have minimal financial influence on the pharmaceutical industry. Further into the Drug Research and Children Information page on the FDA's website, the FDA states, "Experts say the historical lack of pediatric drug testing is due to [the fact that] pharmaceutical companies generally have viewed children as a market that would bring only small financial benefits" (1). Conducting studies on children would be conducive to pharmaceutical companies particularly for vaccines and medications specifically for children. Many medications that can be prescribed to adults will only be adequately tested on adults simply because adult individuals have a greater financial impact on pharmaceutical companies. By restricting many clinical trials to adults, the FDA and pharmaceutical companies are considering the group of individuals that would potentially have greater financial influence. Not only is money a key factor in restricting many clinical trials to adults, another issue with conducting clinical trials on children is that they are often unable to provide an "informed consent" to conduct research for these types of medications (2). In most cases, adults who agree to participate in the clinical testing of drugs are able to gain a clear understanding of the process. Many adults are also able to ask important questions and are aware of any potential risks. On the contrary, many children may not fully understand the process of many clinical trials and may be unaware of the seriousness of any potential adverse events. Children who experience adverse events can also potentially threaten the liability of the Food and Drug Administration. The families of children who experience adverse events can potentially take legal action against the Food and Drug Administration. Although the parents of these children have some influence on the child's decision, the ultimate consent must come from the participating individual. By restricting many clinical trials to adults, the FDA and pharmaceutical companies are attempting to avoid uninformed consent given by many children.

Figures

Table 1. The drug development and approval process

Stage	Average no. of years	Population tested	Purpose	Estimated success rate	Capitalized cost (millions USD)
Preclinical (CMC) testing and animal studies	5.5	Laboratory and animal studies	To assess biological activity and safety	5 to 20 out of 5,000 to 10,000 compounds	185.6 (7)
Phase 1	2	20 to 80 Healthy volunteers	Determine drug kinetics, its dosage, and safety in humans	2 to 5 of above	30.5 (8)
Phase 2	2	100 to 300 Patient volunteers	Evaluate the drug for efficacy and safety (adverse events)	2 to 5 of above	41.6 (8)
Phase 3	2 to 4	1,000 to 3,000 Patient volunteers	Larger scale usage to confirm efficacy and to monitor for adverse events from long-term use	2 to 5 of above	119.2 (8)
FDA review	1 to 2		Unbiased independent review process for approval or denial	1 compound selected	1.96 (direct cost) (3)
Phase 4	15	Entire user population	Additional post-marketing surveillance required by FDA or sponsor-initiated	NA	Variable

CMC, Chemistry, Manufacturing, and Controls; FDA, Food and Drug Administration; NA, not available; USD, United States dollar.

Food and Drug Administration Approval Process

Controlled substances have been acceptable for use and prescribed to treat children with Attention Deficit Disorder stems due to elaborate testing through the Food and Drug

Administration. In Arthur Ciociola's article, "How Drugs are Developed and Approved by the FDA: Current Process and Future Directions", Ciociola states, "The US Food and Drug Administration is responsible, among its many other duties, for enforcing the nation's laws designed to protect the health and safety of American consumers" (1). Before introducing a new controlled drug to the market, it is an essential responsibility for the Food and Drug Administration to test all medications for safety and efficacy. According to the Food and Drug Administration drug approval fact page, standard reviews usually take several years to complete. By testing controlled medications, the FDA is ensuring quality and minimizing adverse effects caused by the medication

In Arthur Ciociola's article, "How Drugs are Developed and Approved by the FDA: Current Process and Future Directions", Ciociola provides readers with a table that outlines the phases of the FDA's drug approval process. The first step in the drug approval process is the review of a proposal of a prospective new drug attempting to enter the market. This proposal is called an Investigational New Drug Application and must contain key information about the safety, efficacy, and components of the prospective drug (2). The FDA will review this proposal and if the medication is deemed safe enough to progress to the next phase, the medication will enter into the preclinical testing phase where the drug is tested in the laboratory and on animals (2). After approximately five years in the preclinical phase, the drug is ready to progress into phase one of the drug approval process. Phases one, two, and three of the drug approval process collectively take anywhere from six to ten years and focus on testing the safety and efficacy of the drug on human beings. Useful dosage amounts and adverse events are noted as well in these phases. Next, the FDA will review the trials and either approve or prevent a drug from entering the market. Additional monitoring of recently approved medications is required for a predetermined amount of time upon entering the market (2). Upon completion of phases one, two, and three of clinical testing, the drug will finally move the drug into phase four of testing. Phase four focuses on testing the drug on the entire population. Additional monitoring is required for several years in this phase. Although each phase assesses different aspects of the drug, each phase assesses the safety of the drug, thus ensuring safety in each drug in multiple phases. Testing the safety in each drug demonstrates the emphasis the FDA places on drug safety in human beings. The extensive testing helps explain why the FDA and many prescribers believe controlled substances will cause minimal harm and thus are safe to prescribe to children.

Health Risks

One of the most important factors in determining why Schedule II drugs are prescribed to treat children is exploring the overall safety of these drugs. One of the primary concerns surrounding the safety of controlled drugs is the potential health risks controlled medications pose to adults. In the article, "Long-term Efficacy and Safety of Treatment with Stimulants and atomoxetine in Adult ADHD: A review of Controlled and Naturalistic Studies", the authors state, "Regarding adverse events, it is reassuring to know that the adverse events most commonly reported with long-term ADHD medication treatments are relatively minor. It is also reassuring to know that long-term treatment does not markedly exacerbate or cause psychopathology, although there is some risk for increases in nervousness, irritability and sleep disturbance" (16). One of the top reasons the FDA any many prescribers are comfortable treating children with off-label controlled substances is that the controlled medications do not cause psychological disorders, or make them worse. The medications prescribed for Attention Deficit Disorder also have minimal reported

side effects. The most common side effects associated with these controlled substances – such as sleep abnormalities, decreased appetite, and stomach irritability - are essentially not life threatening to children and would not pose an increased threat in children than in adults. These side effects can also be reversed quickly. Due to few reported minor side effects and the reversibility of the side effects, prescribers are comfortable using these controlled substances to treat children with ADHD. Further into the article, the authors state, “Post-marketing reports of adverse events prompted the FDA in 2007 to require manufacturers of drugs approved for the treatment of ADHD to develop Medication Guides with detailed information for clinicians and parents on possible adverse effects and precautions that can be taken to avoid them. Package inserts of all stimulant drugs for the treatment of ADHD have also been amended to include warning language around specific risks” (5). In 2007, the FDA required manufacturers to provide clinicians with Medication Guides along with the drugs approved to treat ADHD. It is then the responsibility of every clinician to dispense these Medication Guides along with the prescription of any medication used to treat ADHD. By providing the parents of pediatric patients with Medication Guides, the FDA ensures that the parents are informed and well aware of any potential side effects. Medication Guides include particular warnings about potential risks and side effects for the parents’ further discretion.

Abuse Potential

Not only are health risks a major concern, the risk of abuse potential in children is a major concern as well. Introducing children to potentially abusive substances can be seen as unethical and can pose a threat to children as well as their future. In the article, "Stimulant ADHD Medication and Risk for Substance Abuse", the authors state, “One reason for the persistent concern for subsequent substance abuse derives from the fact that stimulant medications increase dopamine concentration in the nucleus accumbens” (1). Many illegal and controlled substances are tightly monitored and controlled by the government simply because of the high abuse potential. The primary function of anti-depressants, ADHD medications, and illegal substances is to increase dopamine in the brain. Dopamine is a hormone that causes happiness and satisfaction. Along with many illegal substances, controlled substances such as anti-depressants and ADHD medications function by increasing dopamine in the brain. The feeling of happiness is what encourages individuals to overuse and abuse these drugs. Exposing children to controlled substances that increase dopamine can potentially influence children to abuse these medications. Further into the article, "Stimulant ADHD Medication and Risk for Substance Abuse", the authors exhibit and discuss their research findings about the abuse potential of controlled substances. While explaining their research, the authors state, “[Our] results are most congruent with the hypothesis [that] the longer an individual takes the medication, the lower the risk for substance abuse to some extent due to less chance of short-term substance-related and psychiatric problems”(5). Another common cause for drug abuse comes from the practice of taking medications for a short amount of time and suddenly stopping the medication. Abruptly stopping any intense medication allows symptoms to return. Once taking the ADHD medication, prescribers encourage patients to continue taking the medication for longer durations. Patients who continue taking the medications will experience more results and fewer side effects. This situation decreases the risk for abuse potential as well. In the article, "Abuse Liability of Medications used to Treat Attention-Deficit/Hyperactivity Disorder (ADHD)", Kollins explains that, “…Abuse potential may be lower in longer acting formulations” (40). Although significant amounts of research indicate little to no abuse potential, prescribers often prescribe long-acting

medications in opposition to short-acting medications. Short-acting medications are absorbed and released in one's body quickly. With such quick release and absorbance, the formulation is used and released quickly. This prompts one to require more doses in order to experience true effectiveness. By taking short-acting medications, patients are developing a practice of consuming multiple pills in order to feel adequate results. On the contrary, long-acting medications are absorbed and released in one's body at a significantly slower rate. By releasing small doses throughout the day, the patient is not required or tempted to take more doses of the medication. Long-acting medications discourage the practice of continuously consuming medications to reach results. In the article, *Stimulant ADHD Medication and Risk for Substance Abuse*, researchers found no association between ADHD medications and increased rate of substance abuse. In the study, researchers identified and studied approximately 38,753 individuals who were diagnosed with Attention Deficit Disorder. In the study, researchers analyzed whether there was a correlation between increased drug abuse and the medications used to treat the disorder. Results of this study yielded opposite effects contrary to popular belief – the longer the patient remained on the medication, the less likely the patient was to develop drug dependence.

Efficacy

Not only is safety essential for the acceptance of controlled substance use in human beings, the overall efficacy of these drugs are an extremely important factor as well. In Sharon Wigal's article, "Efficacy And Safety Limitations Of Attention-Deficit Hyperactivity Disorder Pharmacotherapy In Children And Adults", Wigal states, "Examination of the evidence demonstrates efficacy for both long and short-acting stimulant medications… [Researchers] found that the relative benefit of clinical response for shorter-acting stimulants was greater than for patients taking longer-acting stimulants" (22). As previously mentioned, short-acting formulations are immediately absorbed and released into an individual's body, making it mandatory to take more than one dose throughout the day. Conversely, long-acting formulations are single-dose medications that are absorbed and released into one's body over the duration of the day. Although longer-acting formulations decrease the risk for abuse potential, these formulations have been proven to be less effective in relieving the symptoms of ADHD in children. On the contrary, studies show that short-acting stimulants are more effective in ADHD symptom relief. This is problematic for pediatric patients that want effective results as well as low abuse potential risk. Although choosing between long-acting and short-acting formulations can be challenging to pediatric patients and their families, individuals must remember that all stimulant drugs have been proven to be effective in some aspect. In the article, "Attention-deficit/hyperactivity disorder (ADHD) in Children", the Mayo Clinic Staff explains how children benefit from taking these medications by stating, "Currently, stimulant drugs are the most commonly prescribed medications for ADHD. Stimulants appear to boost and balance levels of brain chemicals called neurotransmitters. These medications help improve the signs and symptoms of inattention and hyperactivity — sometimes dramatically" (1). In all, the FDA and many prescribers are comfortable treating children with controlled stimulant medications due to their powerful impact on children and their everyday lives. Stimulant medications play an important role in balancing chemicals in the brains of children with ADHD. When chemical neurotransmitters are balanced, children experience an improvement in patience, memory, organization, and attention. By improving these aspects in a child, the child is now able to normally interact with peers and family.

Conclusion

Due to the amount of detailed testing conducted on adult human beings, the FDA allows prescribers to treat children with ADHD using controlled substances. The extensive trials conducted by the FDA aid in explaining why prescribers believe these medications are equally safe for children as for adults. Although some studies show that the most commonly used controlled substances prescribed to treat children are effective in improving the social and academic aspects in pediatric patients' lives, the above research suggests that there are two significant problems remaining that may be argued by individuals who question the safety of these controlled substances. The first problem is that many medications are approved, but not necessarily approved for children. Although studies have shown that there are minimal reported side-effects and the potential for drug abuse is low, any adverse events that may occur in adults will likely cause more harm to children taking controlled substances to treat Attention Deficit Disorder. Contrary to this belief, studies have shown that the side effects associated with these medications are not life threatening and are quickly reversible. To further prove the safety of these medications used to treat children, researchers can consider conducting more clinical trials on children, producing results that are specific to children rather than adults. The second problem is that using long-acting formulations may decrease drug abuse potential, however these formulations have also been proven to be less effective. Individuals may argue that this is problematic to families that want to see improvement in symptoms as well as low abuse potential. Although long-acting formulations have been proven to be less effective than short acting formulations, long acting formulations have also proven to be sufficiently effective in treating ADHD overall. Since long acting formulations have been less associated with abuse potential and effective overall, families may consider this option to lessen the chance of drug abuse in the child while simultaneously combatting the disorder. In essence, the FDA has approved these medications because individuals are more likely to benefit from the drug and less likely to experience adverse effects and drug dependence. Ultimately, the benefits of these medications outweigh the negative aspects and therefore, are safe to prescribe to children.

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Cheyenne enjoys hiking, traveling, meeting new people, and experimenting with different foods. She also enjoys reading, shopping, volunteering, and cooking. Cheyenne finds interest in the brain and in the nervous system and she often enjoys keeping up with current research about developments in neuroscience. In 2014, Cheyenne became a nationally certified pharmacy technician. This experience increased her passion for medicine and influenced her to pursue a medical career.

Cheyenne's future goals include pursuing a career in neurology. She plans to utilize her education to help children overcome various neurological disorders and she also plans to contribute to improving public health in her community.