FOQUEST IN THE TREATMENT OF ATTENTION HYPERACTIVITY DEFICIT DISORDER (ADHD) - WITH CASE STUDY

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Abstract- ADHD is neurodevelopmental disorder affecting approximately 5.3% of the global population. Patients with ADHD exhibit extensive neurocognitive deficits that lead to impairments in working memory, reaction time, variability, vigilance, response inhibition, intelligence and achievement. Untreated ADHD patients are at a higher risk for social isolation, educational underachievement, lower socio-economic status, criminality, suicide, accidents, various addictions, and comorbid psychiatric disorders. Treatment options include neurotherapy, cognitive training, behavioral therapy and pharmacotherapy. Studies have shown that the stimulants, Methylphenidate (MPH) and Amphetamines, are the most beneficial pharmaceutical treatment options. MPH inhibits neuronal reuptake of dopamine and norepinephrine and reduces dopamine transport binding sites, thus normalizing neurocognitive networks in ADHD patients. Extended-Release treatments have been demonstrated to improve adherence. Foquest is a new MPH Hydrochloride, controlled-release, formulation with an onset of action within one hour and a duration of action of ≤ 16 hours. Health Canada approved Foquest for the treatment of adult ADHD in 2017, and extended approval to children and youth ≥ 6 years of age in March of 2019. In this article, we will explore the efficacy of Foquest as a new treatment option for ADHD patients. We will also present a case study that demonstrates improvement of psychosocial functioning and overall quality of life in an adult ADHD patient treated with Foquest.

Keywords - Attention Deficit Hyperactivity Disorder, ADHD, Methylphenidate, MPH, Foquest

I. INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder that has been clinically documented for over two centuries [1]. After depression and anxiety, ADHD is the most common mental health disorder affecting children and youth worldwide [2]. Studies have shown that ADHD is a highly heritable and chronic disorder that persists throughout the lifespan [1]. Recent studies estimate that 30-70% of children with ADHD continue to exhibit symptoms into adulthood [3].
Adult ADHD patients are more likely to show greater decrease in symptoms of hyperactivity than inattention [4-6]. Currently, ADHD affects 4% of adults and 5% of children worldwide [1], with a pooled prevalence of 5.3% [7].

II. PRESENTATIONS OF ADHD

ADHD patients are subdivided into three presentations by DSM-5: Predominantly Inattentive, Predominantly Hyperactive, and Combined [1]. Historically, boys were diagnosed with ADHD more frequently than girls, at a rate of 3:1 [1]. Females often present with more internalizing and less disruptive symptoms compared to their male counterparts, thus making the disorder more difficult to diagnose in females [8]. According to DSM-IV, ADHD diagnostic rates for female youth were higher since more emphasis was placed on inattentive, compared to hyperactive symptoms of ADHD [9]. Studies now show a trend of increased ADHD diagnosis and treatment in female youth 5-18 years old [10]. In adults, the gender gap is less extreme, ranging from a 1:1 to 2:1 ratio between men and women with ADHD [11]. According to DSM-IV symptomatology, as individuals age, hyperactivity-impulsivity symptoms tend to decline, while inattentive symptoms persist [12]. This shift in meeting criteria for ADHD-C to ADHD-I as individuals age, causes a decrease below diagnostic threshold in hyperactivity-impulsivity symptoms [12]. Thus, the gender gap narrows as fewer men and more women are likely to meet the diagnostic criteria for ADHD in adulthood [11].

III. NEUROCOGNITIVE DEFICITS

Compared to healthy individuals, ADHD patients show neurocognitive deficits in the areas of response inhibition, working memory, reaction time, variability, vigilance, and intelligence/achievement [13]. Neuroimaging studies of ADHD patients have demonstrated impairments in the areas of the brain responsible for executive function and attention, namely the dorsolateral prefrontal cortex, cerebellum, inferior parietal lobule, anterior cingulate cortex,

cingulum bundle and the inferior/superior longitudinal fasciculi of the white matter [14]. Timing deficits correlate with the key inferior fronto-striato-cerebellar and fronto-parietal pathway defects visualized on neuroimaging studies of ADHD patients [15].

IV. ADHD RISK FACTORS

Studies have shown that offspring of mothers who smoked during pregnancy or had evidence of childhood lead exposure had double to triple the risk of developing ADHD [16]. Other potential risk factors include maternal gestational obesity or gestational diabetes [17-19], low birth weight, premature birth, male gender, family history of ADHD, maternal use of antidepressant medications during pregnancy, borderline personality disorders, and artificial food additives [20-27].

V. QUALITY OF LIFE IN ADHD

As reflected in the ADHD Rating Scale-5, the six Quality of Life Domains most commonly impaired in children and adolescents are: relationships at home and school, peer relationships, academic performance, behavioral functioning, homework functioning, and self-esteem [28-30]. DuPaul and colleagues report that impairment of academic functioning is most common among children with ADHD [29], with fewer ADHD youths attaining post-secondary graduation compared to their neurotypical peers [31].
Patients with Hyperactive-Impulsive and Combined ADHD presentations frequently exhibit disruptive behavior [32]. Peer relations are frequently impaired in this patient group [28]. Other adverse outcomes associated with ADHD in childhood and adolescence include increased rates of motor vehicle accidents, accidental injuries and substance misuse [33]. Studies show that adults with ADHD underperform academically, attain lower levels of academic achievement, and thus lower rates of professional employment [34]. As such, adults with ADHD are at a greater risk of lower socio-economic status [34].

They also tend to suffer from frequent job changes, antisocial behavior, arrests, difficulties at work, driving violations, difficulties parenting, interpersonal conflicts, and higher rates of spousal separation and divorce [35-42].

Wehmeier and colleagues suggest that the reduced quality of life in adults with ADHD is not only due to inattention, impulsiveness and hyperactivity [43]. They further suggest that the compromised Health Related Quality of Life (HRQoL) in ADHD is due both to deficits with executive function, which is central to the disorder, and to emotional difficulties secondary to coping with ADHD [43].

VI. COMORBIDITIES OF ADHD

Zablotsky and colleagues note that childhood comorbidities of ADHD include learning disorders (33.8%), anxiety disorders (25.1%), mood disorders (19.4%), language disorders (13.2%), Autism Spectrum Disorder (ASD) (13%), Oppositional Defiant Disorder (ODD) (12.8%), sleep disorders (12.2%), intellectual disability (10.8%), and Conduct Disorder (CD) (8.7%) [44].
Weissenberger et al conclude that ADHD patients are more prone to developing food addiction and obesity, substance abuse, electronic media dependencies and conduct and personality disorders [45]. ADHD is also linked to excessive social media, internet and video game usage [45].
Patients with the Predominantly Inattentive ADHD presentation are more likely to experience depression and anxiety while those with the Hyperactive-Impulsive ADHD presentation are more likely to experience CD as children and ASPD as adolescents [45]. 84% of male and 74% of female patients with persistent ADHD have comorbid psychiatric disorders; depression and anxiety are more common in women while personality disorders and substance abuse disorder are more common in men [46]. In adults with ADHD, 80% have at least one coexisting psychiatric disorder [47-48]. According to the National Comorbidity Survey, major depressive disorder, dysthymia, and any mood disorder are more prevalent in adults with ADHD at rates of three, four and six times, respectively [49]. 47% of patients with ADHD have been reported to have at least 1 criminal offence [47].

VII. ADHD AND SUICIDE

Every year approximately 1 million lives are claimed by suicide worldwide [50]. 60% of these incidences occur in Asia (50).
Among 15-29-year-olds, suicide was the second leading cause of death worldwide in 2016 [51].
Suicide is in the top 10 leading causes of death in all age groups in most of the developed world [52]. After motor vehicle accidents and homicide, suicide is the leading cause of death in adolescents in most of the developed world [52]. Evidence shows that rates of suicidal ideation, self-injury and suicide attempts are significantly increased in the untreated ADHD population [53]. A study found that in adolescents who had attempted suicide, 65% had met the criteria for ADHD but only 22% of the 65% had been diagnosed with ADHD prior to the attempt [54].

Compared to untreated patients, treatment with Methylphenidate (MPH) reduced suicide attempt risk by 59% in those treated for 90-180 days and by 72% in those treated for longer than 180 days [55]. For those receiving MPH less than 90 days there was no apparent protective effect [55].

VIII. ADHD AND CRIMINALITY

The association between ADHD and criminality has been increasingly recognized [56]. Core ADHD symptoms inclining toward social maladjustment and criminal offenses include low self-control, mood instability, emotional impulsiveness and impulsivity [57-60]. Higher rates of delinquency, violent behavior and criminal recidivism have been associated with ADHD Hyperactive-Impulsive and Combined subtypes than the Predominantly Inattentive subtype [61-64]. There is an increased risk in criminal behavior in ADHD individuals with psychiatric comorbidities of CD and Substance Use Disorder (SUD) [56]. The rate of criminality was reduced by 32-41% with the use of ADHD medication [65].

IX. ADHD AND SMARTPHONE USE

A Korean study shows a significant link between smartphone addiction and symptoms of ADHD [66]. Cell phone use in youths 14-20 years of age is high and youth with ADHD are uniquely prone to the negative impacts of cellphone addiction due to their cognitive flexibility, reduced impulse control, and high sensitivity to reward [67-68]. Smartphones enable users to experience the freedom of self-expression, feelings of being in control, and rapid co-occurring stimuli [66]. These provide a high degree of motivation and the immediate reward that adolescents with ADHD crave [69]. The inhibition and self-control deficits of this patient group can lead to excessive smartphone use and worsening symptoms of ADHD [66]. Further investigation is needed to determine how to best combat smartphone addiction, with particular emphasis on smartphone addiction in the ADHD youth population [66].

X. ADHD TREATMENT OPTIONS

Noreika et al propose that treating ADHD neurocognitive timing deficits would likely influence the detrimental behavior patterns commonly experienced by these patients due to its close association with impulsiveness [15]. Non-pharmacological treatment option in ADHD include neurotherapy, cognitive training and behavioral therapy [15]. Rubia's review states that transcranial direct current stimulation (tDCS) offers hope as a non-medical alternative to ADHD treatment [70]. However, limited data is available on the potential detrimental effects of such neurostimulation on non-targeted functions [70].

Studies have shown that stimulant formulations (Amphetamine and MPH) appear to be effective pharmacological treatment options for adults with ADHD as they have been shown to have a favorable response in these patients. [71-72]. Methylphenidate (MPH) formulations act as central nervous system stimulants, much like Amphetamines [73]. However, MPH has greater effect on mental aspects of ADHD while Amphetamines have greater influence over motor activities [73]. The response to stimulants on the behavioral and cognitive symptoms of ADHD reflects activity of the nonadrenergic and dopaminergic systems [73]. MPH inhibits neuronal reuptake of dopamine and norepinephrine, which leads to increased extracellular dopamine concentration in ADHD patients [73]. It is also an inhibitor of monoamine oxidase [73]. MPH also reduces the number of dopamine transport binding sites in the brains of ADHD patients and increase extracellular dopamine [73]. This is regarded as beneficial because dopamine transport binding sites are increased in patients with ADHD [73].

There is variability in the onset and duration of action, as well as the chemical composition within the stimulant MPH and the Amphetamine classes of ADHD pharmacotherapies [74]. MPH functions as a dopamine agonist and psychostimulant that regulates the fronto-striato-cerebellar neurocognitive network in ADHD (15). Treatment with MPH thereby attenuates most timing deficits and normalizes these neurocognitive networks [15]. Other approved monotherapies for ADHD include Amphetamines, Atomoxetine, Clonidine, and Guanfacine [74].

Extended-Release (ER) pharmacotherapies provide day-long coverage, thereby improving adherence [75]. ER formulations are easier to ingest while offering protection from medication abuse, rebound symptoms [75]. Overall, long-acting ADHD pharmacotherapies improve treatment outcomes by improving medication adherence [76].

XI. FOQUEST

In December of 2017, Health Canada approved Foquest as a pharmacological treatment option for adult ADHD patients ≥ 18 years of age [73]. In March of 2019, Health Canada broadened the approval of Foquest for use on ADHD patients ≥6 years of age [77]. Foquest is an MPH Hydrochloride, controlled-release, capsular formulation that offers ADHD patients a one-hour onset and a 16-hour duration of action [77]. It is the first MPH product of its kind approved for use in Canada, which provides symptom control throughout the day [78]. In adult ADHD patients, Foquest's safety was demonstrated to be similar to the safety profile of other MPH formulations, with nausea and dry mouth symptoms most commonly reported [73]. The most common side effects in children included decreased appetite, insomnia, headaches and abdominal pain [77].

XII. CASE STUDY – XXI

Mr. XXI is a 27-year old male who is a 2nd-year university student with a full-time job and a history of ADHD. According to Mr. XXI, he was having "pretty bad" symptoms of inattention and poor concentration,

which caused him problems at work as well as with his social and family life. He lives with his fiancé and 5-month old twins. His fiancé, who is a Psychologist, also felt that his ADHD symptoms were getting worse. He was making careless mistakes at work and having difficulties in maintaining consistent focus. He rated himself "often" to "very often" on the ADHD Self-Reporting Scale (ASRS-V1.1) on 12 out of 18 categories.

Upon starting treatment with 25mg of Foquest daily, Mr. XXI's symptoms began to notably improve. After four months of treatment, his symptoms improved significantly, and his self-rating of symptoms became "often" to "very often" on only 3 out of 18 ASRS-V1.1 items. On the Sheehan Disability Scale, his impairment of work improved from marked to moderate, social life from marked to mild, and family life from marked to moderate. His total score of Sheehan Disability Scale improved to 12 out of 30 from 21 out of 30.

Regarding work, Mr. XXI stated that he became "more productive and ambitious", "less fearful", and "had greater follow-through and better planning". Regarding his family life, he stated that he is now "more understanding and empathic", "has higher tolerance", "is no longer getting easily irritated", and "has definitely improved in communication". Regarding his social life, he stated that he is "getting better at listening to people, understands better, interrupts less, communicates better, and demonstrates greater interest in people by asking more questions". When asked about his experience with the Foquest treatment, Mr. XXI experienced considerable improvement and requested a dosage increase as he felt that there was room for further improvement. Mr. XXI is now receiving 35mg of Foquest daily and has rated himself "very satisfied", stating that he would recommend Foquest to other patients.

XIII. DISCUSSION

ADHD is a neurodevelopmental disorder that significantly decreases the quality of life of those affected and places a substantial strain on their families and education systems. Despite the recent focus on recognizing inattentive ADHD symptoms, females remain more likely than males to be undiagnosed, and therefore untreated for ADHD, because they usually present with more internalizing and less disruptive ADHD symptoms and comorbidities. Among the approved ADHD pharmacological monotherapies, Amphetamines and MPH have been shown to significantly reduce ADHD symptoms in adult patients. Particularly, Amphetamines provide a greater reduction of motor activity symptoms while MPH offers a greater reduction of the mental symptoms of ADHD. Foquest may be a promising new MPH treatment option for ADHD patients, due to its extended duration of action and a safety profile comparable to that of other MPH formulations. Our case study demonstrates the improvement of psychosocial and occupational functioning and overall quality of life in an adult ADHD patient treated with Foquest.

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