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Methylphenidate as a treatment for stuttering: a case report

D. DEVROEY, G. BEERENS, E. VAN DE VIJVER

Department of Family Medicine, Vrije Universiteit Brussel (VUB), Brussels, Belgium

Abstract. – INTRODUCTION: A randomized placebo controlled trial with methylphenidate (MPH) was set up to identify the effects of MPH on cognition in healthy young adults (ea. without attention deficit hyperactivity disorder, ADHD). Subjects repeatedly performed tests of the immediate and delayed memory and vigilance tasks after administration of placebo or 20 mg MPH.

CASE PRESENTATION: We report the case of an 18 year old man who participated in the study. He suffered from stuttering since childhood. During the study phase he reported a remarkable relief of the stuttering after the intake of 20 mg MPH.

CONCLUSIONS: For D-amphetamine the beneficial effect on stuttering has been demonstrated but it was never implemented in clinical practice because of important adverse events. MPH, an amphetamine analogue, doesn't present these side effects. For this reason, MPH seems to merit further investigation in a randomized-controlled trial as a possible agent in the treatment of stuttering.

Key Words:
Methylphenidate, Stuttering.

Introduction

Causes of Stuttering

The most common type of stuttering is developmental stuttering. Many young children develop some mild stuttering while they learn to speak. This may last for several months to years. For less than 1% of the affected children the stuttering persists beyond that and may even get worse. More boys than girls suffer from persisting developmental stuttering into adulthood. This affects daily living and health related quality of life is impaired[1]. Some families present more stuttering. Genetic variants have been identified which may predispose speech and language difficulties[2].

Another type of stuttering is psychogenic stuttering that may be caused by emotional trauma. Stuttering may also be caused by brain injuries, including stroke and brain traumas.

Treatment for Stuttering

Most children with stuttering show a spontaneous decrease of the symptoms. No drug therapy has ever shown to be effective without acceptable side-effects. Speech therapy may be effective for stuttering which lasts for more than 6 months. It will not only improve speech but will also make the child feel more comfortable about the stuttering. It is known that stressful social situations can favour stuttering.

Speech-language pathologists can help stuttering children and improve their social skills[3]. For developmental stuttering in adults both treatments (*fluency shaping of speech* and *stuttering management*) are evidence based[2]. Stuttering management is mainly supported by a cognitive learning model of defensive behaviour[2].

The most robust outcome evidence was reported for fluency-shaping approaches of stuttering[4]. Cognitive behaviour therapy and desensitization also reported hopeful results but much of the research focussed not only on the stuttering but also on concomitant disorders such as anxiety. Comprehensive approaches demonstrate the best results because they target improved speech fluency as well as stuttering management[3,4]. Despite several treatment options, most of the stutterers experience important problems in their social and professional contacts.

The Study Setup

Participants

The aim of the present study was to explore the cognitive effects of 20 mg methylphenidate (MPH) in healthy young adults between the age of 18 and 35 years. Participants were excluded if they suffered from diabetes mellitus, hypertension, arrhythmias, thyrotoxicosis, epilepsy and attention deficit hyperactivity disorder (ADHD) or other disorders that could have an impact on concentration. They were also excluded if they had a history of drug abuse or use of psychoac-

Corresponding Author: Dirk Devroey, MD; e-mail: dirk.devroey@vub.ac.be

tive substances, if they had already taken MPH in the past, if they had a history of depression or if they were pregnant. Participants had a regular breakfast but were asked to refrain from all caffeinated and alcoholic beverages and to eat no more than two pieces of fruit 24 hours before drug administration.

Procedure

A double blind, randomized, placebo-controlled design with MPH. The Ethical Committee of the University Hospital of Brussels (UZ Brussel) of the Vrije Universiteit Brussel approved the study protocol.

An examination period with a partial sleep deprivation was simulated. The subjects had to remain awake until 2:00 AM. Popular games worked as cognitive distracters. The participants were awoken at 6:00 AM and they all received the same breakfast. After the breakfast participants were orally administered 20 mg MPH or placebo. One hour after the drug administration, the test period of 4 hours started. Participants performed memory tasks, Go/No Go tasks and vigilance tasks.

Methylphenidate

Drug dose was set at 20 mg MPH, immediate release formulation. Identical and unmarked capsules were provided for drug and placebo. After oral administration MPH is almost completely absorbed, with food having little impact on this process. In adults, MPH has a pharmacokinetic profile similar to that of children, reaching a peak concentration at 1.5-2.5h and having an elimination half-life of 2-3.5h[5,6].

The Case

Medical History

The medical history of this young man mentions arrhythmia as a newborn and a hospitalisation for septic shock and a Stevens Johnson syndrome caused by a *Staphylococcus aureus* at the age of 11. Subsequent neurological testing during adolescence (EEG, MRI, sleep investigation) didn't reveal any abnormalities.

The young man had no allergies and was previously treated with minocycline, adapalene and benzoylperoxide for acne.

The young man and his two years older brother both have been suffering from stuttering since their very young childhood. His two sisters don't stutter at all, but his 3.5 year old half-sister (a daughter of his father) also stutters, obviously more than her peers. His mother had a stutter as a child, which stopped during adolescence.

The young man suffered from a severe type of stuttering, making him unable to read one single sentence fluently. For a short period he underwent stuttering therapy based on fluency-shaping approaches. Thanks to several coping strategies, the stuttering became less prominent since the beginning of adolescence. However, in stressful situations – such as exams – it becomes more explicit again.

Since his childhood school results have consequently been above average, in 2010 he successfully started the study of medicine.

Study Participation

The young man received 20 mg MPH in the context of the study but in line with the study protocol he was not aware of this (participants and investigators were blinded). He spontaneously reported that he experienced less speech problems than normal. Usually, stress situations aggravate the young man's stuttering. Our whole study set-up was very stressful for the participants. Parts of it were filmed by Belgian television, creating an additional stress. The day after the study the effects had worn off and he was stuttering as before.

Discussion

The study was not designed to evaluate the effect of MPH on stuttering and no objective tests were performed to confirm this testimonial. However, it is worthwhile to look at this observation, since stuttering has an obvious impact on life quality. We note that the relationship between the severity of stuttering and the quality of life is influenced by the stutterers coping style (emotion-oriented and task-oriented)[1].

It is clear from the medical history that this young man is suffering from familiar stuttering and that emotional factors may have an influence on it.

Former Medication Trials

Today only few reliable therapies are available for stuttering. Physicians insist on more treatment research about stuttering[7]. According to our literature search, MPH was never tested as a treatment for stuttering. Fifty years ago, three studies showed a positive effect of D-ampheta-

mine on stuttering. In 1953, Ginn and Hohman were the first to notice an effect of D-amphetamine on stuttering[8]. They noted that the speech of two of four stutterers improved while using D-amphetamine during a study for behaviour problems in children.

In 1962 a double-blind study investigated the effects of D-amphetamine on 106 mentally retarded patients with speech defects such as stuttering, immature production, oral inaccuracy, lisps and cleft palate, and other conditions such as psychosis, mongolism, aphasia and deafness[9]. In 1957, one of the two authors used D-amphetamine and noticed a considerable reduction in his stuttering. It is this personal experience that lead to the study of 1962. Participants of this study were either given 15 mg of D-amphetamine daily or placebo for a three-month period. Speech improved significantly among the stutterers taking D-amphetamine compared to those in the placebo group. Participants with other speech defects didn't experience an improvement. For three severe, long-term stutterers the improvement spectacularly changed their life course. The observation of an improvement of the stuttering was based on tape recordings which were made before and during the project. They were evaluated by the ward personnel, a speech therapist and the director of the project.

In 1965 an uncontrolled study with D-amphetamine on 28 mentally retarded stutterers demonstrated an improvement of the stuttering by 14 participants, after one month[10]. The 14 non-responding participants were administered trifluoperazine for one month. Eight of them showed an improvement of the stuttering. For most of the participants, improvement was sustained at least six months after treatment was discontinued. D-amphetamine showed to be more effective in patients with functional retardation than in those with organic retardation.

Besides D-amphetamine, other substances have been tested on stuttering patients in the past. Oxprenolol, a non-selective beta-blocker was compared to placebo. Study drugs were administrated twice, with a six weeks interval. During the six weeks subjects were randomized into two groups: half of them underwent no treatment, the other half had intensive speech therapy. Speech therapy showed to be effective for stammering but oxprenolol alone didn't improve stuttering[11].

A double-blind trial with bethanechol, a parasympatomimetic choline ester, failed to prove bethanechol superior to placebo. However, two of the patients who did respond favorably to bethanechol kept a more fluent speech after taking the drug for six months[12].

Tiapride, a dopamine antagonist, did not influence stuttering among 10 to 17 year old patients with severe stuttering problems[13].

Clomipramine, a serotonin re-uptake blocker, was superior to desipramine, a tricyclic antidepressant, for stuttering severity, degree of preoccupation with stuttering, resistance to stuttering and expectancy of stuttering[14].

The alpha 2-receptor agonist clonidine did not improve stuttering in children who were 6 to 13 years old[15].

Paroxetine seemed to be useful in qualitative management of stuttering symptoms. In a randomized, placebo-controlled study paroxetine did not affect the percentage of stuttered words. But stuttering-associated facial movements during speech were significantly reduced in subjects treated with paroxetine[16].

Olanzapine, a dopamine antagonist and atypical antipsychotic, was statistically superior to placebo on the three ratings of stuttering severity: the objective measure of stuttering severity (SSI-3), the clinician based global impression (CGI), and the subject-rated self-assessment of stuttering (SSS) ($p < 0.05$)[17]. Despite that olanzapine was a promising medication for the treatment of stuttering only little research confirmed the effect, probably because of its poorly tolerated adverse effects.

Significant improvement in fluent speaking was found for pimozide, a selective dopamine (D-2) antagonist. Fluency improvement seems more likely to be mediated by dopaminergic rather than serotonergic mechanisms, but dopamine antagonists may be considered a risk for treatment of stuttering due to the side effects[18].

The results of a small randomized study suggest that risperidone may be effective in the treatment of developmental stuttering. Risperidone was well tolerated[19].

Almost all classes of neurological agents have been studied for the treatment of developmental stuttering. Although a few of them showed very hopeful results, none appeared to be acceptable as a treatment for stuttering, mainly because of the unacceptable side-effects which didn't weigh up to the advantages of the treatment.

Future Research

To the best of our knowledge, most of the studies concerning therapies for stuttering, focussed on mentally retarded and D-amphetamine.

However, the results of these studies in combination with the actual case report should encourage us to set-up a double-blind placebo-controlled trial comparing placebo to MPH among young, healthy, stutterers with developmental stuttering.

Biological links between developmental stuttering and amphetamine-like agents should be explored.

Subjects should be rated on the SSI-3, the CGI and the SSS. Video-taping should be made at baseline and under study medication to objectively evaluate stuttering and motor activity. Subjects should also be monitored for potential side-effects.

Conclusions

Stuttering affects daily living and quality of life of adolescents with developmental stuttering. Persistent developmental stuttering also has an impact on adults. Treatment focuses on speech therapy but is often insufficient to permit stutterers to have a normal quality of life. During a double-blind randomized-controlled study comparing placebo to MPH we observed that a participant with developmental stuttering who received 20 mg MPH was relieved from his stuttering during the activity of the study medication. In view of the former studies with D-amphetamine and because of the fact that MPH is an amphetamine analogue, MPH seems to merit further investigation among single subject and eventually in a randomized-controlled trial as a possible agent in the treatment of stuttering.

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