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LITERATURE REVIEW

CAN METHYLPHENIDATE USE IN CHILDREN/ADOLESCENTS FOR TREATMENT OF ADHD LEAD TO DEVELOPMENT OF BRUXISM: CRITICAL ANALYSIS OF LITERATURE

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Abstract

Aim: This current short review aims to evaluate if there is any association between methylphenidate usage in children with attention deficit hyperactivity disorder (ADHD) and development of Bruxism.

Materials and methods: Prospero registered (CRD42024538678). PubMed, Scopus, Web of Science, Google scholar was searched using pre-specified search strategy. Clinical studies, case-reports and case series are included for the data synthesis. Exclusion criteria is narrative and systematic reviews.

Results: A total of 135 titles were screened rigorously by two independent evaluators and after duplicate exclusion, removal of irrelevant titles, 10 articles were included for full text analysis out of which 8 qualified for final data synthesis.

Conclusion: Most of the studies included in the current review suggests that there is an association between methylphenidate usage and development of Bruxism in children with ADHD but the evidence is weak as most of the included studies are case reports and more studies are required to confirm the same.

Keywords: *ADHD, Adolescents, Children, Bruxism, Methylphenidate.*

INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) refers to a persistent pattern of inattention and/or hyperactivity-impulsivity that hinders functioning and development.[1] ADHD is often diagnosed in children, although symptoms can persist into adulthood if therapy is not obtained. The projected global pooled prevalence of ADHD was 5.29% to 11%, highlighting the mounting burden that ADHD is placing on healthcare systems.[2,3] Genetic, Viral infections, smoking during pregnancy, nutritional deficiencies, and alcohol exposure in the fetus have all been investigated as potential causes of the condition.[4,5] The main cause of the cognitive and functional difficulties associated with ADHD is aberrant brain development. Smaller dorsolateral prefrontal cortex and anterior cingulate gyrus are observed in ADHD patients, which impairs goal-directed behavior. In addition, children with ADHD have less front striatal activation.[6,7,8] The brain's anatomical and functional variations are a contributing factor to issues with executive functioning, impulse control, and attention. These neurological deficits may cause individuals with ADHD to struggle with decision-making, organization, and time management.[9,10,11] Children with ADHD need more support for oral hygiene and eating habits, and their dental health is a concern. They have a higher prevalence of caries and gingival inflammation, and are at higher risk for dental trauma. Parents report toothache, bruxism, bleeding gums, and oral trauma. Oral health problems being the most relevant clinical comorbidity and ADHD being the psychological comorbidity.[7,12] ADHD can be treated using combination of non-pharmacological and pharmacotherapy and behaviour therapy and support.[13] The mainstay of treatment for ADHD is pharmacological therapy. Stimulant and non-stimulant medications are used for the treatment of symptoms associated with ADHD. Stimulants are the most commonly prescribed medications for ADHD and these usually are effective in majority of the ADHD affected population (70-80%). Stimulant medication act by increasing the levels of neurotransmitters such as dopamine and norepinephrine thereby improving attention and thinking. Alpha agonists and antidepressants are examples of non-stimulant treatments. While selective norepinephrine reuptake inhibitor atomoxetine has shown promise in several studies, it is not nearly as effective as stimulants. Patients who do not respond well to stimulant medication are put up on non-stimulant medication.[14] Methylphenidate-based and amphetamine-based medications are the examples for stimulant medication used in children with ADHD. Atomoxetine, Guanfacine, and Clonidine are the commonly used non-stimulant medication for use in children with ADHD. Methylphenidate is the most common medication prescribed for ADHD worldwide.[15] Methylphenidate improves function and attention by inhibiting dopamine and noradrenaline transporters, which helps to lessen ADHD symptoms in children and young adults. Additionally, it lessens impulsivity and hyperactivity. Headaches, insomnia, exhaustion, and decreased appetite, weight loss are the most common adverse effects of ADHD. Methylphenidate, can have side effects that impact oral health. Methylphenidate, can reduce saliva production, leading to dry mouth, increased caries susceptibility, oral ulcers. Multiple published case reports have reported the development of bruxism in children and adolescents with ADHD on methylphenidate. The aim of this current review is to evaluate if there is any association between methylphenidate use and development of bruxism.

MATERIALS AND METHODS

Prospero registered (CRD42024538678) Search strategy is depicted in Table-1 (Table-1: Search strategy). Electronic searches were performed in the databases: PubMed, Scopus, Web of Science, Google scholar. The search was conducted from inception to 1 march 2024. The search was performed using combination of terms (((Methylphenidate) OR (ADHD)) OR (Attention deficiency Hyperactive disorder)) AND (bruxism). Research gate was also consulted and cross references were also consulted on this topic to extract all the available literature. Clinical studies and case-reports and case series are included for the data synthesis. Exclusion criteria is narrative and systematic reviews.

Table 1. *Search Strategy*

Search terms	PubMed	(((Methylphenidate) OR (ADHD)) OR (Attention deficiency Hyperactive disorder)) AND (bruxism)
	Scopus	Methylphenidate AND Bruxism
	Web of Science	Methylphenidate AND Bruxism
Search Dates	Inception to 1 March 2024 Last search was performed on 1 March 2024	
Selection criteria	Inclusion	Clinical studies, Case-control studies, Cross sectional studies, Case reports, In-Vitro Studies
	Exclusion	Narrative and systematic reviews

RESULTS

Extensive literature search was carried out using pre-defined search strategy was carried out. A total of 135 titles were screened rigorously by two independent evaluators and after duplicate exclusion, removal of irrelevant titles, 10 articles were included for full text analysis out of which 8 qualified for final data synthesis. Figure 1: PRISMA flow chart shows 8 articles that were included for final data synthesis. The characteristics of included studies are presented in Table 2.

Figure 1. *PRISMA flow chart*

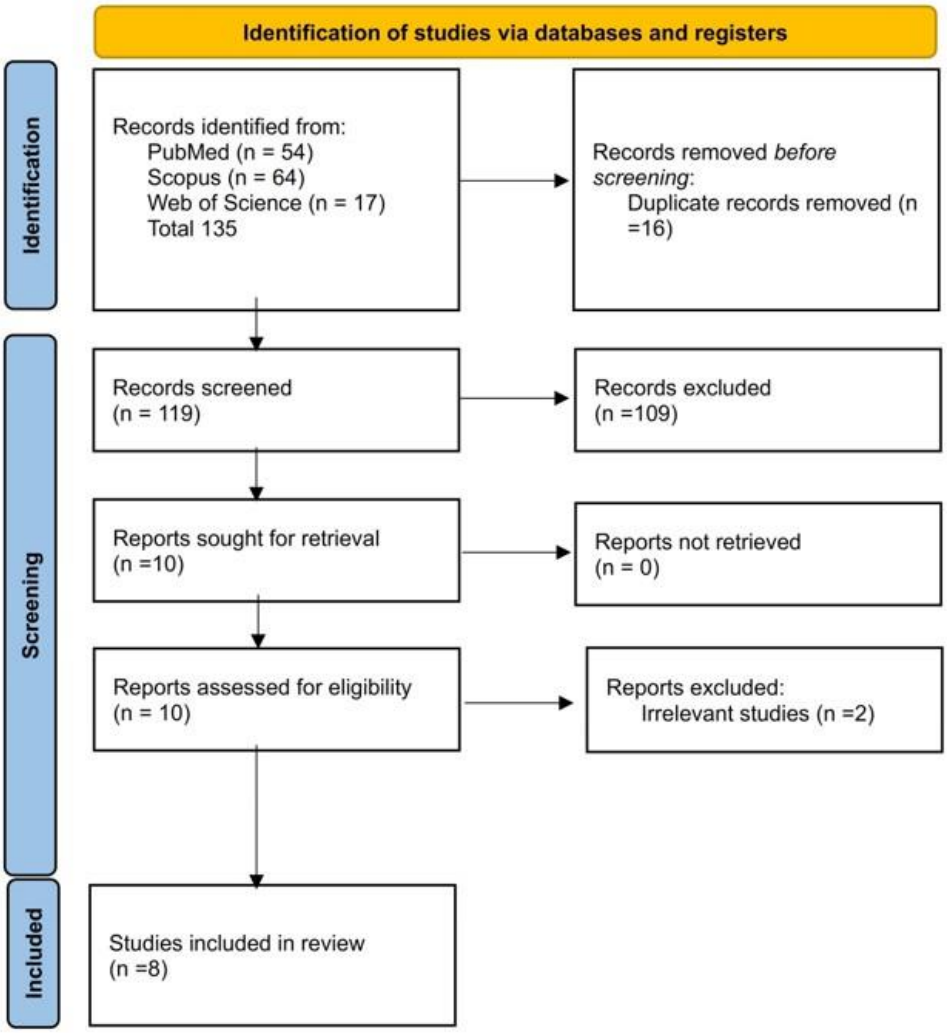

Table 2. *Characteristics of Included Studies*

№	Author-year	Type of study	Age of the Subjects	Medication used	Condition	Evaluating criteria	Dosage of Drugs	Oral Characteristics	Miscellaneous
1	Gara and Roberts 2000.[10]	2-Case reports	4-6 years	Methylphenidate + Valproic acid	Severe ADHD and Epilepsy	Diagnostic and Statistical Manual of Mental Disorders, 3rd ed., revised (American Psychiatric Association 1987).	5mg Methyl-phenidate	bruxism with intermittent sucking clicks, agitation, unusual tongue movements (folding, protruding, and writhing) in addition to intermittent bruxism. Rapid onset of dyskinesia which correlated with the peak plasma level of Methylphenidate was reached	-
2	Perlman et al 2023.[11]	Cross-sectional study Retrospective study	4-12 years	Methylphenidate			Not mentioned		No significant association between sleep bruxism and history of Ritalin (Methylphenidate usage)
3	Mendhekar and Andrade 2008.[12]	Case report	9 year old child	Methylphenidate	Mixed type of ADHD	DSM-IV (American Psychiatric Association 1994) diagnosis of ADHD, mixed subtype was made;	10mg Methyl-phenidate initially and then later dose increased to 15mg	Sleep Bruxism lasted an average of about 20 minutes per night. The parents reported that sleep bruxism subsided the very night they discontinued using methylphenidate	-
4	Naguy et al 2019.[13]	Case report	9 year old child	Methylphenidate	Mixed type of ADHD	DSM-IV (American Psychiatric Association 1994) diagnosis of ADHD)	18mg Methyl-phenidate per day	Sleep Bruxism was reported on day 5, parents have reported audible teeth gnashing during sleep that has never been noticed before	Clonidine 75 µg qHS was given to the child. Two days later, bruxism entirely abated. Clonidine was well tolerated.
5	Sivri and Bilgic 2015.[14]	Case report	9 year old child	Methylphenidate	Mixed type of ADHD	DSM-V (American Psychiatric Association 2013) diagnosis of ADHD)	18mg Methyl-phenidate per day	Awake Bruxism was reported due to the use of Methylphenidate	-
6.	Gau and Chiang 2009.[15]	Case control study	281 Subjects aged 11-17 years	Methylphenidate	persistent ADHD, subthreshold ADHD	DSM-IV criteria	Not mentioned	Sleep bruxism was observed in 51% in persistent ADHD, and 39.7% in subthreshold ADHD taking Methylphenidate	-
7.	Malki et al 2004.[16]	Case control study	24 subjects with ADHD receiving medication and 6 subjects with ADHD not on medication	Methylphenidate was used in more than half of the subjects	-	-	Not mentioned	Children with ADHD on medication showed increase in the prevalence of bruxism	-
8.	Chin et al 2019.[17]	Case control study	71 children with ADHD and 30 controls were	Methylphenidate (0.3- 0.7 mg/kg/ dose) for a duration of 6	ADHD with predominantly inattentive presentation	-	0.3- 0.7 mg/kg/ dose for a duration	Children with ADHD on methylphenidate showed higher	The incidence of bruxism was 41.67 % and 28.57% in

			included. Children aged 6-12 years.	months.	(ADHD-I) and predominantly hyperactive/ impulsive or combined presentation (ADHD-C) were included for this study.		of 6 months	incidence of Bruxism than healthy controls	ADHD C type and I type respectively after 6 months of treatment with methylphenidate

DISCUSSION

The current review intends to explore the association/ relationship between methylphenidate usage and development of Bruxism in children with ADHD. Total of 8 articles (4 case reports, 3 case control studies, 1 cross-sectional retrospective study) were evaluated for the data synthesis and exploration.[16-25] The outcome we sorted for is "Bruxism" in children with ADHD under methylphenidate. Most of the studies included were case reports[16,18-20] and case-control studies[21-25], one study is a cross-sectional retrospective study.[17] The children in most of the studies included were ranged between 4 to 12 years in most of the included studies, Chin et al., 2018; Emodi-Perlman et al., 2023; GARA & ROBERTS, 2000; Malki et al., 2005; Mendhekar & Andrade, 2008; Naguy et al., 2019; Sivri & Bilgiç, 2015 except in the study by Gau and Chiang 2009 where they have evaluated subjects between 11-17 years.[21-25] The dosage of methylphenidate used ranged from 5mg to 18 mg per day in the included studies. Duration of methylphenidate usage was not mentioned in the included studies clearly. In most of the included studies there as significant evidence of bruxism in children who were on methylphenidate for ADHD.[16,18-25] Only in the study by Perlman et al 2023 the authors reported no association between bruxism and methylphenidate.[17] Sleep bruxism was reported due to methylphenidate usage in the studies by Gara and Roberts 2000,[16] Mendhekar and Andrade 2008,[18] Naguy et al 2019,[19] Gau and Chiang 2009,[21] awake bruxism was reported only in the study by Sivri and Bilgic 2015.[20] Apart from all these effects bruxism can be seen in 31% of children and adolescents with ADHD.[26-28] Bruxism is a parafunctional oral activity that involves gnashing, grinding, and clenching teeth. It is a sleep-related movement disorder and is associated with microarousals, which may trigger abnormal motor episodes during sleep.[29] The basic mechanism behind this involves causing bruxism by affecting masseter activity through dopamine (DA) or serotonin (5-hydroxytryptamine/5HT) pathways, either directly or indirectly.[15] Methylphenidate users' have higher levels of extracellular dopamine in their brains may cause changes in the dopaminergic system, leading to bruxism. Exploring how methylphenidate affects dopamine levels can aid in identifying treatment options for bruxism linked to this medication.[30-34] Also, there are numerous complications of bruxism in ADHD children, so there is a need to research the incidence and risk factors associated with bruxism, which can lead to prevention and early detection of the disorder in such patients.[35] Appropriate treatment for ADHD can potentially lower the occurrence of bruxism and improve the quality of life for affected children.

LIMITATIONS AND DIRECTIONS FOR FUTURE RESEARCH

The studies that were included were mostly case reports so the quality of evidence is very low hence we recommend a prospective case control study with adequate sample size is required.

CONCLUSION

Most of the studies included in the current review suggests that there is an association between methylphenidate usage and development of Bruxism in children with ADHD but the evidence is weak and more studies are required to confirm the same.

AUTHOR CONTRIBUTIONS

Conceptualization, S.T. and L.A.; Methodology, M.R., K.Y. and S.T.; Formal analysis, S.T. and L.A.; Investigation, S.T., L.A. and M.R.; Data curation, K.Y. and G.M.; Writing—original draft preparation,

S.T., L.A., M.R.; Writing—review and editing, S.T., M.M.M., M.C. and G.M.; Visualization, G.M. and M.M.M..; Supervision, M.C. and G.M.; Project administration, M.C. and G.M. All authors have read and agreed to the published version of the manuscript.

DECLARATIONS

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding for the research in question.

Ethical approval

The study was approved by the Institutional Ethics Committee and was conducted in accordance with the Declaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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