Supervised off-label prescribing of methylphenidate in adult ADHD


Abstract

OBJECTIVE:
Off-label prescription is a common practice in psychiatry, raising health and economic concerns. Collegial consultation could allow a framed prescription of treatments that are not authorized in specific indications. Attention Deficit Hyperactivity in adult populations (ADHD) is a striking example of a pathology where off-label prescription is frequent. First considered to be a childhood disorder, the awareness of this condition in adults is increasing, leading to the development of new clinical practices and treatments. However, the adult ADHD diagnosis and its management are still emerging in France despite a high prevalence. Treatment of adult ADHD relies on methylphenidate prescription, but the initiation of this drug is not authorized in adult populations. Methylphenidate is a central nervous system stimulant that is structurally close to amphetamine and acts as a norepinephrine and dopamine reuptake inhibitor. Due to these pharmacological properties, neuropsychiatric and cardiovascular side-effects could occur. Furthermore, its addictive potential has led France to classify it as a psychoactive drug, dispensed via secured prescription. The first prescription and the one-year follow-up are restricted to neurologists, paediatrics, psychiatrists and sleep disorders specialists at hospital. The objective of this article is to propose a multidisciplinary framework for the off-label prescription of methylphenidate in adult ADHD.

METHODS:
The Multidisciplinary Advice Consultation for Exceptional Addiction Treatments (Consultation d'Avis Multidisciplinaire de Traitements d'Exception en Addictologie CAMTEA) was first set up in Lille for the prescription of baclofen in alcohol dependence and was then extended to topiramate in binge eating disorder. This procedure has been adapted to the particularities of ADHD in adult populations, the differential diagnosis (bipolar disorder, depressive disorder, anxious disorder, personality disorder, substance use disorder) and the co-morbidities requiring a full psychiatric and neuropsychological assessment. Moreover, a particular attention has been paid to the monitoring of neuropsychiatric, cardiovascular and misuse risk because of the potential side-effects of methylphenidate.

RESULTS:
The proposed prescription framework is structured into several specialized consultations. A first psychiatric evaluation aims to diagnose adult ADHD, using the French version of the Diagnostisch Interview Voor ADHD 2.0 questionnaire (DIVA 2.0), and to assess the quality of life impact with the Weiss Functional Inventory Rating Scale (WIFRS). It also searches for the presence of differential diagnosis or co-morbidities. The second appointment consists of a pharmacological evaluation that aims to search for contraindications and potential drug interaction. A neuropsychological evaluation based on standardized tests (Wechsler Adult Intelligence Scale [WAIS IV], Conner's Continuous Performance Test 3 [CPT] and the Minnesota Multiphasic Personnality Inventory [MMPI]) is also required to evaluate neurocognitive disabilities and personality features. Once the parameters of the different assessments have been collected, the synthesis is presented during a multidisciplinary meeting in order to assess the risk-benefit ratio for each patient. Several specialties are involved in this multidisciplinary meeting: psychiatry, addictology, general medicine, addictovigilance, pharmacovigilance and neuropsychology. One strategy among three possibilities can be decided: (1) contraindication to treatment with methylphenidate, (2) attention deficit disorder that does not require medication management, and (3) indication of treatment with methylphenidate with the choice of the pharmacological form (immediate or prolonged release). A biological check-up and an electrocardiogram are carried out systematically before any treatment. If the decision is made to initiate treatment, it is started at the lowest dosage and followed by a titration phase. A weekly follow-up is carried out during the titration phase in order to assess treatment efficacy and safety. After treatment stabilization, the general practitioner
can carry out the renewal, and the patient will be reassessed within the framework of the multidisciplinary consultation every 3 months.

CONCLUSION:
When an off-label prescription is being considered, it must comply with the basic rules of good clinical practice, and the benefit/risk ratio should be constantly reassessed. The proposed multidisciplinary framework, adapted to the characteristics of adult ADHD and the pharmacological properties of methylphenidate, appears to be an interesting strategy to meet the requirements of the good clinical practice. The complementary assessments carried out and the collegial framework allow enhancing the patient's follow-up and minimize the drug risk, particularly in the psychiatric, addictive and cardiovascular adverse events. Finally, this framework could also help the monitoring of other off-label treatments for ADHD, such as atomoxetine or guanfacine.