

## CHAPTER 7: PHARMACOLOGICAL TREATMENT OF ADHD

### Principles for Medical Treatment

#### **Thirteen Considerations in Medication Selection in the Treatment of ADHD<sup>209</sup>**

- Age and individual variation
- Duration of effect
- The speed of action of the medication
- ADHD subtypes
- Comorbid symptom profile
- Comorbid psychiatric disorder
- History of earlier medication use
- Attitudes towards medication use
- Affordability
- Medical problems and other medications
- Associated features similar to medication side effects
- Combining stimulants with other medications
- Physician attitude towards ADHD medications.

#### **1. Age and individual variation**

All ADHD medications can be used for all age groups, although not all medications have received the “official” approval for various ages through the process required by the Therapeutic Products Directorate of the Canadian government. Treatment before the age of six, if necessary, should only be done under the direction of a specialist. There is no maximum age to treat ADHD if the general health of the patient permits use of those treatments. Women of childbearing age taking ADHD medications should be advised to talk with their physicians if they plan a pregnancy, as effects of ADHD medications on the foetus and on the baby while breastfeeding are unknown. Individual variation may exist (e.g. effective dosage is not closely correlated with age, weight or symptom severity) accounting for differences in treatment response and wide variation in dosage requirements. Medications don't work equally well for all patients – for some, results are huge; for others, substantial, but not huge; for others, much more modest; and for about 20%, currently available medications don't work very effectively at all, even when different classes of drugs are tried. **Caution: clinicians should not oversell the effectiveness of medications.** Some patients may experience difficulty swallowing pills. Although this can be improved by training, it should also be noted that some medication can be sprinkled on soft food or diluted in water.

#### **2. Duration of effect**

Exposure to tasks that require mental effort changes over the years. Medication use can be titrated to meet increased demands or to cover longer periods of daytime impairment. In childhood there may only be a need to treat during the school hours, though longer duration medications do improve home life, while by adulthood continuous full day and evening treatment may be necessary. Similarly, a patient may need to have individualized treatment based on day-to-day variation. This may be critical for tasks such as driving, where the maximal risk period for young drivers is during the evenings and at weekends.

### 3. The speed of action of the medication

When patients require urgent treatment, psychostimulants are the treatments of choice. However, ADHD is a chronic disorder where long-term management approaches are critical. For ADHD patients in general, ADHD is often perceived as an emergency once it is identified, and faster is seen to be better. However, given the extraordinary rates of low adherence over a year, long-term benefits are more likely if the ultimate goal – once emergencies such as abuse or expulsion from school are dealt with – is not just to obtain reduction of symptoms and better quality of life but also to support long-term adherence by taking into account patient comfort.

### 4. ADHD subtypes

The core symptoms within ADHD (that also determine the subtypes) include inattentiveness, impulsivity and motor hyperactivity. All three of these symptoms are associated with impairment of different sorts. For example, attention problems remain stable and impairing throughout the lifespan and affect academic and organizational functioning. Hyperactivity may diminish in adolescence but is transformed into restlessness, driven behaviour, stimulus-seeking behaviour, and discomfort from always being on the go. This may continue well into adulthood. While adults may present with impairing inattentive symptoms, their childhood progression into adulthood may reveal that some came from an only inattentive background, while others came from a transformation of the combined subtype. It is important to understand the transformation of the clinical symptoms because it may have relevance both in terms of dosing effect as well as emergence of anxiety and other side effects. All of the ADHD medications improve inattention.

### 5. Comorbid symptom profile

The CAP-Guidelines Committee has used a symptom-based inventory to help the clinician determine the possible treatments for each symptom. When comorbid disorders exist, prioritizing the key symptom makes the choice of medication simpler and widens the medication options. For example, aggression may be a part of many of the comorbid disorders the patient has, but focusing on this symptom addresses the major area of impairment.

### 6. Comorbid psychiatric disorders

When there is a comorbid disorder along with ADHD, it is generally advised that the treatment may be determined by the more severe disorder first <sup>CB</sup>. A variety of strategies have been used to determine sequence of treatment including diagnostic certainty, patient preference, the primary disorder and the disorder with greatest impairment, or the disorder most likely to respond to treatment <sup>CB</sup>. However, major mood disorders like depression, bipolar disorders and substance abuse disorder should be identified and treated prior to ADHD <sup>CB</sup>. Residual symptoms may require additional treatments. It is important to review drug-to-drug interactions to ensure that there is no risk to the patient. It is not unusual for patients to be on more than one medication to deal with “complex ADHD”.

### 7a. History of earlier medication use

In 65% to 75% of cases, patients will respond to an approved ADHD medication at the first trial<sup>210</sup>. Patients who do not respond to one stimulant may respond to another (e.g., methylphenidate versus amphetamine). The same seems to be true for side effects; one may be better tolerated than the other for common side effects like appetite, sleep suppression, headache, tics, etc. The treatment response percentage increases when more than one medication is tried. If there is a lack of improvement or substantial side effects, another ADHD drug should be considered. If a patient is responding well to one medication, it is strongly advised that the patient not be tried on another medication to see if there is a better response.

## **7b. Family history of medical treatment**

A family history of prior positive medical treatment should also be considered as well as negative experience with a specific medication. Although there is no good research data on these aspects, it is understandable that a positive response to a specific treatment in a family member could increase positive expectations for this treatment while the contrary can occur for a negative outcome.

## **8. Attitudes towards medication use**

All patients and their families need to be educated. The choice of medication should follow the principles of informed consent. Information on informed consent is available on the totallyadd website (<http://totallyadd.com/informed-consent>). Emotional biases against the use of ADHD medications are often due to misinformation regarding side effects and guilt about having 'caused' the problem through 'bad' parenting. Alternatively, excessive expectation of medication improvement may be present and lead to disappointment. It is important for families to access reliable and valid sources and to rely on parent support groups. Medical treatments are there to facilitate treatment of the patient's full range of concerns. Also, parents that are at risk for diversion (e.g. substance abusers) should not be given short-acting stimulants for their children. Patients should be educated about the risks of diversion of medication to friends.

## **9. Affordability**

All patients should have access to optimum treatment. Unfortunately, some medications are beyond the financial reach of a significant number of patients without extended health insurance. Some medications can be supported through special access programs, but access is often limited by the extensive paperwork required and the constricted time for which medication is supplied. Most medications are covered by third party insurers. However, sometimes patients may have to rely on generic medications that may not be as effective. CADDRA continues to advocate for a resolution of this problem at the government level.

## **10. Medical problems and other medications**

It is important for the clinician to do a thorough medical assessment including physical examination before prescribing medications. The CADDRA Guidelines provide templates that can guide the clinician. Many conditions look like ADHD (e.g. thyroid, hearing deficits, vision problems, etc). It is important for clinicians to be aware of any medical risk the patient may have that affects suitability for a medication (e.g. blood pressure problems, interactions with other medications, cardiovascular risk, etc.). When in doubt, a specialist referral is indicated.

## **11. Associated features similar to medication side effects**

All medications may cause side effects. Most side effects are usually improved over two or three weeks of continuous use. One of the most common reasons for non-adherence is related to a lack of physician awareness or understanding of side effects, or patients' reluctance to explain their discomfort. Some pre-existing conditions like tics, sleep problems, very low weight, headaches, GI problems or dysphoria may be aggravated by ADHD medications (although some of these very symptoms might actually be improved by the ADHD medications as well). Patients should be told up front about how to tell if they are getting too much medication, e.g. feeling too "wired", too irritable or too serious during the time medication should be active. In those cases, there is a strong chance that the dose is too high or that the specific medication may not be a good fit for that patient. However, if any symptoms from this triad of too "wired", too irritable or too serious is experienced later in the day, or they are dysthymic at the time when medications would be expected to be wearing off, it is likely that those symptoms are not from an excessively high dose but from rebound, where the medication is wearing off too fast and the patient is

"crashing". An understanding of the side effect profile of each medication may afford a better 'fit'.

## 12. Combining stimulants with other medications

When a clinician feels that a second medication is needed, it is suggested to begin with an ADHD medication that is known to combine safely with the second medication. For example, in the selection of an ADHD medication for a patient with severe anxiety disorder, a psychostimulant could be combined with an antidepressant (note: there are some limitations with atomoxetine). Younger children should be referred if this is being contemplated.

## 13. Physician attitude towards ADHD medications

Information on ADHD is rapidly evolving (i.e. understanding of comorbidity, adult ADHD, medical treatments, biological underpinnings, etc). It is imperative that physicians seek out reliable sources of information and continue to upgrade their clinical skills. The CADDRA Guidelines, website, conference, continuing medical education courses and other updates are designed to expose clinicians to the latest advances in assessment and treatment for ADHD across the lifespan. Patients today are often as educated about their health conditions as their doctors, and physicians need to be comfortable working with the knowledgeable patient and/or family. Such comfort can be achieved through an open attitude, experience and quality continuing education.

### ADHD Medication Chart

The Canadian ADHD Medication Chart contained in the sleeve of the CAP-G binder provides information on the dosage and appearance of ADHD medications and is a useful tool when discussing medication options with patients and their families. It is available in a Canada-wide and a Quebec version, and the most recent update is always available on the CADDRA website. The charts were originally developed by the Continuing Medical Education Team at Laval University in Quebec City in collaboration with the organizational committee for the Conference on the Pharmacological Treatment of ADHD in April 2007.

## Specific Medication Selection Guidelines and Monitoring

### STEP 1

#### **Feedback and Expectations (refer to Chapter 1, Visit 4 for more details)**

Use principles of informed consent to ensure the patient is adequately educated when addressing medication questions.

### STEP 2

#### **Specific Medication Selection: Considerations**

One central philosophy within CADDRA is to treat each patient as a unique being and to use the clinical advice within the "Thirteen Considerations for Medication Selection" as the guide.

***Practice Point: There are some practical questions that begin the selection process:***

***a) Is medication indicated in your age group? Generally speaking, the first choice should be a medication that has an approved indication by Health Canada for ADHD within the specified age group.***

*Even though some ADHD medications are not officially approved by Health Canada for a specific age group, many doctors may decide to use them based on scientific evidence and expert consensus.*

**b) What impairment do you have and at what time of the day? Is it mainly during work hours, meetings, exam times, leisure times, driving periods, morning routines, etc.?** *Ensure the patient is medicated when it is necessary and that you understand and are responding to his/her individual needs.*

**c) What medication do you prefer? Have you ever taken any medications before or heard of something you might want to try?** *Patients respond better to the medications they most strongly believe in. It also addresses the notion that patients must be educated and they should have a partnership in the treatment agenda.*

**d) Is a family member on some medication for ADHD?** *If yes, then consider trying the same medication first. (Note: there is no evidence at this time about a possible role for such a pharmacogenetics-based approach.)*

**e) Do you have third party coverage or do you plan to pay for the medication?** *Many of the current medications are expensive, so there should be an open discussion related to government plans, third party insurance coverage, direct payment, co-payment plans and limited benefit plans.*

**f) Do you have trouble swallowing a pill?** *If yes, then that will limit certain medications choices, though one should make an attempt to train the individual to swallow a capsule.*

**g) Do you require urgent treatment?** *If yes, then a stimulant is likely your first choice due to its speed of intervention. However, the treatment of ADHD is a long-term plan so while there may be urgent issues, the patient should be cautioned about rapid fixes.*

**h) Does the patient have comorbid disorders that require more complex interventions?** *If yes, the current agenda is to initiate the ADHD medication first and see what residual symptoms are left over that require further management. Anticipate drug-drug interaction issues.*

***If the patient is expressing suicidal or homicidal thoughts these need to be addressed as a priority.***

### STEP 3

#### Monitoring

- Establish a schedule for visits and contact with the patient and parents
- It is useful to establish an objective measure within the patient's domain. For example, the teacher may want to observe a five minute on-task behaviour. An adolescent may target their ability to sustain attention in their most difficult tasks. An adult may use a specific target that needs to change, like hourly work production. Formal observational rating scales help to quantify specific medication changes, particularly at school and home. The CADDRA Clinician ADHD Baseline/Follow-up Form and the ADHD Checklist can be used to evaluate change
- During the titration phase, weekly contact with the patient reporting in either by phone, email, fax or visit is recommended. However, the patient should be seen every three to four weeks for a review of medication doses during the titration period and to check physical health, review side effects, family functioning, patient and family well being, coping strategy management, behavioural treatment and other therapies when indicated.

## STEP 4

### Titration

- Recommended starting dose and schedule for dose increases is a guide only
- Start low and go slow but continue to increase the dose until the desired goals of treatment have been reached. An alternative though uncommon titration strategy is to test the patient on two different doses of the medication and then pick the dose level that gives the maximum response and fewest side effects (similar to the MTA strategy). Another alternative is conducting a limited placebo-control trial with different doses each week and evaluating comparisons. The latter strategy requires the cooperation and technical expertise of the local pharmacy. Regardless of the titration schedule, optimal treatment means that the symptoms have decreased and that there is improvement in general functioning. Sometimes side effects limit the dose titration (refer to Side Effect Management, Supporting Document 7C). The threshold maximums are consistent with the off-label standards established by the American Academy of Child and Adolescent Psychiatry
- It is useful to alert the patient in advance that a peak effect may occur in the first week and a plateau effect may occur over the subsequent three weeks. Sometimes patients interpret this as a tolerance to the medication and request a higher dose. In fact, if the patient improves in their functioning at the plateau dose, they are likely dose-optimized.

## STEP 5

### Managing Side Effects

1. In educating patients about medication it is important to provide the realistic view that individuals have different risk/benefit profiles on medication, ranging from those who cannot tolerate or benefit from medication at all, to those who have full remission with no side effects.
2. While our evidence base on medication allows us to provide patients with a great deal of information on medication options, it is also important to remind patients and parents that all individuals are unique and may require doses that are smaller or larger than are usually recommended. It is important to point out that agreeing to a “trial” of medication is not a decision to use it forever. A trial is an experiment that carries minimal if any risks that would extend beyond a very brief period of time, and can be discontinued at any point.
3. Patients who are good stimulant responders, but whose medication is limited by side effects, should be managed by the techniques described below or switched to a different medication regimen that minimizes that particular problem.
4. Patients who are not responding to medication and obtaining little benefit, but do not have major side effects, may require non-medication strategies.
5. If the patient does not respond to any of the first line medications, augmentation strategies or (off label) use of second line medications such as bupropion, clonidine, guanfacine, modafinil or imipramine may be helpful, but a specialist referral should be made. In the rapidly changing field of ADHD, treatment with new medications with different side effect profiles and possibly differential effectiveness in particular patients is becoming possible.
6. If a change in medication is thought necessary, switch medication during long vacations or during the summer to avoid possible side effects that may impair school performance in the short-term. However, sometimes switching medications requires a more immediate intervention due to the urgency of the situation.
7. If a period off medication or on a reduced dose to minimize side effect is required, it should be done during long vacations, the summer, or on long weekends to minimize impact on school performance. Clinically, it is observed that interrupting medication every weekend may in fact increase side effects. Taking the medication each day will help develop a tolerance toward side effects. Some medications (e.g. bupropion, imipramine) need to be taken continuously to maintain clinical effect.