

MANAGEMENT OF SIDE EFFECTS OF ANTIDEPRESSANTS – BRIEF REVIEW OF RECOMMENDATIONS FROM GUIDELINES FOR TREATMENT OF MAJOR DEPRESSIVE DISORDER

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SUMMARY

The side effects of antidepressants are important because they influence treatment process, patients' satisfaction with treatment and adherence to medications. Because of side effects correction of daily dosage of antidepressants is required in some cases, and sometimes therapy with particular antidepressant must be stopped. For this reason, management of side effects of antidepressants is part of routine clinical practice.

The objective of this paper is to review recommendations from treatment guidelines and recent articles about management of antidepressants' side effects during treatment of major depressive disorder.

Key words: major depressive disorder - side effects – antidepressants - treatment

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INTRODUCTION

The severity of side effects from antidepressant medications in clinical trials has been assessed both through the frequency of reported side effects and through the frequency of treatment dropout. The likelihood of different side effects varies between classes of antidepressant medications, between subclasses, and between individual agents (American Psychiatric Association 2000).

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The objective of this paper is to review recommendations from treatment guidelines and recent articles about management of antidepressants' side effects during treatment of major depressive disorder.

METHODS OF LITERATURE RESEARCH

Literature research included recommendations regarding management of side effects of antidepressants from modern algorithms for treatment of unipolar depressive disorder and recent articles on this subject. Recommendations regarding management of side effects of antidepressants from the following guidelines were considered:

- American Psychiatric Association. Practice guideline for the treatment of patients with major depressive disorder (revision), 2000. (American Psychiatric Association 2000);
- National Institute for Clinical Excellence. Depression: management of depression in primary and secondary care, 2004. (National Institute for Clinical Excellence 2004);
- Qaseem A, Snow V, Denberg TD, Forcica MA, Owens DK; Clinical Efficacy Assessment Subcommittee of American College of Physicians. Using second-generation antidepressants to treat depressive disorders: a clinical practice guideline from the American College of Physicians, 2008. (Qaseem et al. 2008);

- Bauer M, Whybrow PC, Angst J, Versiani M, Möller HJ, WFSBP Task Force on Treatment Guidelines for Unipolar Depressive Disorders. World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Unipolar Depressive Disorders, Part 1: Acute and Continuation Treatment of Major Depressive Disorder, 2002. (Bauer et al. 2002);
- Bauer M, Whybrow PC, Angst J, Versiani M, Möller HJ, WFSBP Task Force on Treatment Guidelines for Unipolar Depressive Disorders. World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Unipolar Depressive Disorders, Part 2: Maintenance Treatment of Major Depressive Disorder and Treatment of Chronic Depressive Disorders and Subthreshold Depressions, 2002. (Bauer et al. 2002).

CONTENT ANALYSIS OF GUIDELINES AND LITERATURE

Monitoring

Independent of the choice of the specific treatment intervention, components of psychiatric management and general "psychotherapeutic support" should be initiated and continued throughout the entire treatment. These components include: determining the treatment plan and treatment setting; establishing and maintaining a therapeutic alliance; monitoring and reassessing psychiatric status (including the patient's risk of suicide); reassessing the adequacy of diagnosis; monitoring the patient's treatment response, side effects and general medical condition, and enhancing treatment adherence by providing education to patients and families (American Psychiatric Association 2000). Careful monitoring of symptoms, side effects and suicide risk (particularly in those aged under 30) should be routinely undertaken, especially when initiating antidepressant medication (National Institute for Clinical Excellence 2004). Titration to full therapeutic doses generally can be accomplished over the initial week(s) of treatment but may vary depending on the development of side effects, the patient's age, and the presence of comorbid

illnesses. Patients who have started taking an antidepressant medication should be carefully monitored to assess their response to pharmacotherapy as well as the emergence of side effects, clinical condition, and safety (American Psychiatric Association 2000).

The American College of Physicians recommends that clinicians assess patient status, therapeutic response, and adverse effects of antidepressant therapy on a regular basis beginning within 1 to 2 weeks of initiation of therapy (Qaseem et al. 2008). Comorbid somatic illness requires attention during treatment process. Hepatic dysfunction and hepatic enzyme induction frequently complicate pharmacotherapy of patients with alcoholism and other substance abuse; these conditions may require careful monitoring of blood levels (if available), therapeutic effects, and side effects to avoid either psychotropic medication intoxication or inadequate treatment (American Psychiatric Association 2000).

Education

Successful treatment of depressed patients with antidepressants includes the education of the patients and their families regarding available treatment options, the time it takes to see a response, early side effects and what to do about them, and the expected course of treatment. To reduce early side effects that might interfere with medication adherence, a slow start with medication is particularly wise for TCAs (Bauer et al. 2002). Patients and, where appropriate, families and caregivers should be provided with information on the nature, course and treatment of depression including the use and likely side-effect profile of medication (National Institute for Clinical Excellence 2004). Education regarding available treatment options will help patients make informed decisions, anticipate side effects, and adhere to treatments (American Psychiatric Association 2000). All patients who are prescribed antidepressants should be informed, at the time that treatment is initiated, of potential side effects and of the risk of discontinuation/withdrawal symptoms (National Institute for Clinical Excellence 2004).

The choice of antidepressant

The initial selection of an antidepressant medication will largely be based on the anticipated side effects, the safety or tolerability of these side effects for individual patients, patient preference, quantity and quality of clinical trial data regarding the medication, and its cost (American Psychiatric Association 2000).

When an antidepressant is to be prescribed in routine care, it should be a selective serotonin reuptake inhibitor (SSRI), because SSRIs are as effective as tricyclic antidepressants and are less likely to be discontinued because of side effects (National Institute for Clinical Excellence 2004). The American College of Physicians recommends that when clinicians choose pharmacologic therapy to treat patients with acute major depression, they select second-generation antidepressants on the basis of adverse effect profiles, cost, and patient preferences (Qaseem et al. 2008). Patients started on low-dose tricyclic antidepressants should be carefully monitored for side effects and efficacy, and the dose gradually increased if there is lack of efficacy and no major side effects (National Institute for Clinical Excellence 2004). Choosing an antidepressant depends on various factors that should be considered: prior experience with medication (response, tolerability, adverse effects), concurrent medical conditions and concomitant use of nonpsychiatric medications, a drug's short and long-term side effects, atypical features of the depressive episode, clinical subtype of depression, physician's experience with the medication, patient's history of adherence to medication, history of first-degree relatives responding to a medication, patient preferences, and the cost and availability of specific antidepressants (Bauer et al. 2002). In the investigation that aimed to review systematically the comparative harms of second-generation antidepressants for the treatment of MDD in adults by including both experimental and observational evidence, adverse event profiles were similar among second-generation antidepressants. It was concluded that different frequencies of specific adverse events might be clinically relevant and influence the choice of a treatment (Gartlehner et al. 2008).

Augmentation and discontinuation

Augmenting an antidepressant with another antidepressant should be considered for patients whose depression is treatment resistant and who are prepared to tolerate the side effects (National Institute for Clinical Excellence 2004).

Patients receiving combined antidepressant medication and psychotherapy should be monitored closely for treatment effect, side effects, clinical condition, and safety (American Psychiatric Association 2000).

Where patients are treated with one antidepressant augmented by another, careful monitoring of progress and side effects is advised and the importance of this should be explained to the patient. Particular care should be taken to monitor for serotonin syndrome (National Institute for Clinical Excellence 2004). Short-term and long-term side effects are major contributors to treatment discontinuation. If the initial treatment must be discontinued due to intolerable side effects, a switch to a different treatment is called for (Bauer et al. 2002).

Older patients

In general, older patients, medically frail patients, or patients with decreased ability to metabolize and clear antidepressant medications will require lower doses; in such patients, reduction of initial and therapeutic doses to 50% of usual adult doses is often recommended. Doses will also be affected by the side effect profile of medications and the patient's ability to tolerate these (American Psychiatric Association 2000). When prescribing antidepressants – in particular tricyclics – for older adults with depression, careful monitoring for side effects should be undertaken (National Institute for Clinical Excellence 2004).

Compliance

The long-term side effects and tolerability of medications are key considerations in maximizing adherence to treatment. Side effects should be as minimal as possible. Even mild to moderate side effects during maintenance treatment may lead to

noncompliance, with the consequence of symptom worsening and increased risk of recurrence (Bauer et al. 2002). Although some patients taking antidepressant medication experience side effects, this may not be the most frequent reason for immature discontinuation of treatment. The patient's beliefs about the disorder and beliefs about antidepressants, including lack of conviction that the medication is needed and fear of dependence of antidepressant medicine, have a great influence on adherence to treatment (Hansen & Kessing 2007). Using medications with a more favorable side effect profile than the TCAs may facilitate patient compliance with pharmacotherapy, as long as these agents are effective in the maintenance treatment of depression. The "newer" antidepressants are associated with fewer long-term side effects than the older tricyclics and tetracyclics (Bauer et al. 2002)

In the study that evaluated adherence to antidepressants in the continuation and maintenance phase in remitted recurrently depressed patients, it was concluded that non-adherence to continuation and maintenance antidepressant treatment in recurrent depression was frequent, like in other chronic diseases, and a potential risk of recurrence. Doctors continuously have to be aware of this problem and should keep on discussing it with their patients (Ten Doesschate 2008).

CONCLUSION

Monitoring of side effects should be undertaken during treatment with antidepressants. Patients who are prescribed antidepressants should be informed of potential side effects. Potential side effects should be considered when selecting an antidepressant.

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