CORRESPONDENCE

Treatment of Depressive Disorders

by Priv.-Doz. Dr. med. Tom Bschor, Dr. med. Mazda Adli in volume 45/2008

The Value of Psychotherapeutic Methods in Treating Depression

The CME article is biased in its unilateral evaluation in favor of pharmacological therapy with antidepressants and at the expense of psychotherapeutic therapeutic options. The stipulated division of therapy into phases thus implies a psychopharmacological approach; the authors cite a publication that is 35 years old and published by the pharmaceutical industry. The treatment setting that is discussed subsequently does include basic therapy provided by the general practitioner, as well as "psychiatric referral," but up to this point, no psychological or medical psychotherapists or psychosomatic specialists are mentioned. What follows is somewhat blurred, when an algorithm of whatever preference would be helpful here: in mild and moderate depressive disorders—the vast majority—the authors prefer monotherapy, whether as pharmacotherapy or psychotherapy; the differential indication in the authors' view being availability of service provision and patient preference. Even psychosomatically oriented compendia (1) offer more helpful, more objective approaches. The decisive effective factor of specific psychotherapy (which includes both psychoanalytical and cognitive behavior therapies)—the therapeutic relationship (2)—is stripped of its value and misunderstood in its essence if the authors stipulate the "conversation with an empathic and understanding physician", sensing "the physician's acceptance of his or her worries and fears and should feel relieved as a result of the therapeutic interview" as the basis of depression treatment beyond specific psychotherapy. Outside the setting of specific psychotherapy these are platitudes that every patient would desire and appreciate.

A more honest title of the article would have restricted itself to pharmacological therapy, as the authors themselves do in their "algorithm-based stepwise treatment regimen" for depressive disorders; psychotherapy does not exist here. The opportunity was sadly missed, to provide a summarizing overview of psychotherapeutic approaches in depressive disorders and of their value and differential indications (as done in locations that are not always easily accessible[3]).

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Some Additional Points

I wish to add to this excellent, compact, and up to date research article by making the following observation:

- Lithium, as is correctly stated, is effective in preventing recurrence in unipolar depression. Its indication is crucially supported, however, especially for patients with preceding suicide attempts, by the efficacy that has been shown for lithium only in numerous studies, in preventing suicidal acts and lowering the excess mortality of depressive patients (1).
- In the "supportive strategies" it would be useful to mention that not only activating but also relaxing physiotherapeutic methods—such as appropriate and scientifically investigated massage techniques—have clear antidepressant effects (2, 3).

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Misleading Statements

The article contains statements under the subheading "Phytotherapy (St John's wort)" that are unbalanced and partly misleading.

A current meta-analysis that would be deserving of this title would have been the Cochrane review 2008 (Issue 4, CD000448, "St John's wort for major depression"), rather than reference 5. The critique of therapeutic studies intentionally does not mention the fact that changeable results with regard to efficacy in this field of application are not merely characteristic of St John's wort preparations but of all antidepressants.

The current discussion about this phenomenon, which was overdue, is mainly based on the surprising therapeutic successes with St John's wort. We wish to mention the 2008 newsletter of the Drug Commission of the German Medical Association (1) and our article "Phytotherapie: Eine erhaltenswerte Alternative", which appeared in *Deutsches Ärzteblatt* (2).

The selective explanation of the potential for interaction, which occurs not only with St John's wort but with other foodstuffs and medications, including synthetic antidepressants, is also lacking in balance. More relevant for clinical practice would have been the remark that undesirable side effects of the medication in total are reduced by the order of 10 for St John's wort extract compared with all other antidepressants. To test teratogenicity as part of embryotoxicity, clear legal regulations apply: the original effective substance (here: total extract of St John's wort; extraction medium ethanol) has to be administered at high dosage to a minimum of 2 species for the duration of pregnancy.

The Federal Institute for Drugs and Medical Devices (BfArM) is in possession of all such findings with a commercially available extract of St John's wort; the specialist toxicological evaluation did not provide any indication of teratogenicity. The incorrect counterstatement has now been published in *Deutsches Ärzteblatt*, complete with CME points, and publicized to all doctors.

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Literature Is Subject to Publication Bias

We noticed that compared with pharmacotherapy, psychotherapy is presented in a relatively casual fashion, as a quasi adjuvant option. A detailed algorithm for how to proceed step by step does not even include the option of switching to psychotherapy or even using it as a primary approach. It is also unusual that in case of suicidal idea-

tion, referral to a psychiatrist is the only option that is recommended. A substantial share of the care, including suicidal patients, is actually delivered not by psychiatrists or neurologists but, in addition to general practitioners, by medical and psychological psychotherapists.

The most recent guidelines from the UK National Institute for Health and Clinical Excellence (NICE) generally recommend psychotherapeutic intervention and not medication for the initial treatment of mild depression.

Two main aspects of psychotherapeutic treatment of depression were not even mentioned: the clearly lower dropout rate and the higher sustainability of psychotherapeutic treatment, with lower rates of relapse and more positive developments after concluding the therapy (1).

Further, any discussion of pharmacotherapy for depression should include two recent publications that have attracted much attention. Turner et al showed that the literature on antidepressants is subject to notable publication bias (3). Whereas 99% of all studies with positive results for antidepressants are published, this is the case for only 26% of studies with negative outcomes. This has led to an overestimation of the effect size of antidepressants in meta-analyses by about a third. Kirsch et al did not find differences in efficacy between placebo and antidepressants in mild and moderate depression (2).

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Stable Therapeutic Effects Thanks to Psychodynamic Therapy

In their article, the authors cite two of my own publications (1, 2). They write: "Other studies and meta-analyses have involved patients with a mixture of diagnoses, so that it is difficult to draw any specific conclusions about the effectiveness of these types of treatment for depression ... ." This statement is not correct with regard to my own two articles. It is not the case that patients with different diagnoses were investigated in these studies, but uniquely patients with depressive disorders. I cited a

series of randomized controlled studies that showed that psychoanalytic therapy was as efficacious as cognitive behavioral therapy. A meta-analysis also showed that psychoanalytically based therapy was as effective in depressive disorders as cognitive behavior therapy (2).

An older meta-analysis that the authors also cite does not even claim to be drawing conclusions about depressive disorders ([e6] in the article). A more recent meta-analysis that was published in JAMA in October 2008 found that long term psychodynamic therapy is more efficacious in complex disorders than shorter forms of psychotherapy (3). "Complex disorders" included patients with multiple psychiatric diagnoses, chronic psychological disorders, or personality disorders. A substantial proportion of patients in the real world does not have merely one psychiatric diagnosis but several (3). Long term psychodynamic therapy yielded large and stable therapeutic effects, especially in patients who had primarily complex depressive and anxiety disorders (3).

What is strange is that psychoanalytically based methods are always blamed for a lack of evidence. However, any evidence that is provided is firmly ignored.

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Opipramol As Nighttime Medication

The CME article addresses primarily general practitioners and family doctors. As a specialist physician in private practice with many years' experience in collaborating with referring colleagues I wish to draw attention to an option for initial treatment that has been tried and tested in the general practice setting.

No mention was made of prescribing the sedative tricyclic antidepressant opipramol, especially as nighttime medication.

This drug can be used even today, and at very low dosage, to treat early awakening, the particularly tormenting symptom of most forms of depression, with few side effects. Another "tricyclic option" that should have a place in general practice is trimipramine; the fact

that it comes in the form of drops makes it particularly suitable when starting treatment.

Following the authors' recommendations would mean that the only antidepressant with the desired sedative effect is the "modern" drug mirtazapine, although this often causes restless leg syndrome in elderly patients.

The highlighted "nonresponder" rate of 30–50% applies for this drug too. There are more than enough patients nowadays—even those of an advanced age—for whom the absolute contraindications of tricyclic antidepressants do not apply and in whom the undesired side effects are limited.

Supported by such medication, even the general practitioner or, in more severe cases, the psychiatrist can prescribe a stimulating antidepressant without having to fear sleep deprivation and inner unrest.

The tricyclic antidepressants and the art of differential therapy should not be altogether sacrificed on the altar of guideline conform medicine (1). This is even more so because in the near future, pharmacogenetics will enable us to predict desirable and undesirable effects even in antidepressants.

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In Reply:

Opipramol is licensed merely for the treatment of generalized anxiety disorders and somatoform disorders. A recommendation for the treatment of depression in the context of our CME certified article is therefore out of the question. We cannot find a general recommendation against tricyclic antidepressants in our article, and this was not our intention anyway. We do not share the recommendation by Leutgeb, to use a combination of two antidepressants for primary treatment, especially in elderly patients.

We thank Müller-Oerlinghausen for his additional points.

We welcome Schulz's mention of the new Cochrane review of St John's wort. As stated in *Deutsches Ärzteblatt*, our manuscript was submitted in June 2008. The Cochrane review was published in October 2008. We object to any accusation of intentional omission.

We thank Schauenburg for his additional explanations. Our article discusses psychotherapy on nearly 1 1/2 pages, so that we cannot quite understand why he has accused

us of sidelining the subject. The figure is a therapeutic algorithm exclusively for somatotherapy of depression. We agree that this should have been made more explicit in the figure legend. Our article discusses the importance of the therapeutic relationship for psychotherapy in more detail in the section entitled "Psychotherapy." The paragraph selected by Waldmann, however, comes from the section entitled "Basic treatment strategy," where we intended to provide a more general overview.

Leichsenring quotes us incorrectly. Our criticism relating to inclusion of patients with different diagnoses (not only depression) in meta-analyses and review articles on psychoanalytical/psychodynamic psychotherapy relates only to his 2005 article, not, as he claims in his reader's letter, his 2001 article. His 2005 review includes—in addition to depressive disorders—anxiety disorders, post-traumatic stress disorders, somatoform disorders, bulimia nervosa and anorexia nervosa, border-

line personality disorder and other personality disorders, as well as substance dependence and misuse.

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