

Introduction

Routine Use of Atypical Antipsychotic Agents

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It is readily apparent that there are significant gains on many fronts in the war against schizophrenia. The explosion in neuroscience, particularly genetics, pharmacology, molecular and classical biology, as well as new imaging techniques combine to produce many gains. These developments have given rise to optimism in an often pessimistic field. For the clinician, these scientific advances yield a wide array of new antipsychotic agents that at the very least have fewer side effects than the prior agents and also appear to have more substantial short-term and long-term overall benefits. However, important advances may have downsides. In the case of the new antipsychotic agents, these include cost and questions of how to prescribe and monitor those agents, how to change from old to new and from new to newer agents, how to cope in some cases with improvement and, most importantly, how to choose among these agents. A number of these problems were addressed at the recent symposium "The Routine Use of Atypical Antipsychotic Agents" held in 1997 and are discussed in this supplement.

Dr. Zafar A. Sharif examines acute treatment and concludes that newer agents are indeed a significant advance in both side effects and efficacy. He asks an interesting question, In which patient type should we not use these drugs? and concludes that only patients for whom there is a clear indication for long-acting depot formulations should not receive the newer medications. I would agree, and I doubt if anyone in the field would preferentially treat a family member with a typical neuroleptic. I would also emphasize that long-acting agents continue to be underprescribed in the United States.

Dr. John R. DeQuardo reviews the literature on the toxicity of psychosis in his article on the treatment of first-episode schizophrenia and points out that although early treatment intervention can improve long-term outcome, there remain long delays in patients for whom active treatment is indicated. These delays could relate to age at onset and/or the type of onset, but no matter, it would seem that we are almost ready for a Schizophrenia Awareness Week coupled with early interventions in high-risk families.

Dr. Bruce J. Kinon reviews the maintenance treatment data, in particular those for clozapine, risperidone, and olanzapine. The suggestion again is that maintenance treatment might be easier and more successful with the newer agents.

Dr. Richard G. Petty reviews this same subject from 4 viewpoints: biological, social, psychological, and (unusually) spiritual. He briefly addresses these viewpoints with a heavy emphasis on the biological, including an extended discussion of hyperprolactinemia—a side effect often ignored by physicians. The majority of the newer agents do not elevate prolactin levels and therefore should not produce amenorrhea and infertility but, on the other hand, may contribute to unwanted pregnancies.

Dr. Peter J. Weiden and colleagues give an elaborate presentation on how to change from one drug to another and how to assess medication response, both acutely and over

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a longer time frame. Their article includes a discussion of affective symptoms that may ensue and the hormonal side effects mentioned above. Thus, if a female patient has not menstruated in a decade and suddenly begins, she may be perplexed, and the issue certainly needs to be discussed in advance. Dr. Weiden and colleagues also examine common psychological reactions to clinical improvement on treatment with newer medicines. These reactions include everything from patients' having productive time on their hands to being depressed at the realization of the toll the illness has taken on their lives.

Dr. Weiden and colleagues provide considerable detail about how to switch from one medication to another. It is my belief that the main problem in changing medications is switching from clozapine, which remains a unique drug. The abrupt discontinuation of clozapine produces withdrawal effects in a considerable number of patients. These effects include movement disorders, deliria, and a rapid return of psychosis. Attempts to change patients from clozapine to risperidone rapidly, particularly if the D₂ blocking effect of the risperidone is ignored, inevitably result in acute dystonic reactions and other extrapyramidal symptoms (EPS). Similar reactions take place in many subjects who are taking an atypical neuroleptic plus an anticholinergic. Withdrawal of both will produce an upsurge in EPS in a substantial number of patients, which will then be attributed to the introduction of a new drug. Clearly, if a subject is taking an anticholinergic, its use should be continued until the transition has been made, and then slowly withdrawn.

Dr. Sumer D. Verma and colleagues discuss the management of the agitated elderly. They give a practical review of the behavioral approaches that may be used in this patient group and also emphasize some of the situations in which antipsychotics do not seem to be helpful. It would appear that atypical drugs will have a role to play in lessening agitation in the elderly.

Finally, Dr. William M. Glazer discusses health economics and presents data suggesting that over the long haul, the use of atypical agents will decrease morbidity and hospitalization and that this will supersede the cost of the agents.

The sum total of these studies does suggest that the newer agents will indeed lead to improvement in these important areas. A question that we still cannot answer, however, is, Which atypical is for whom? In the old days, we chose the agent by the side effect most acceptable to our patients. However, further studies may help elucidate a sound clinical rationale for medication selection based on patient subtype.