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Comparison of second generation antipsychotics: are there any differences in efficacy?

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Since the re-introduction of clozapine in 1988, the so-called atypical or second generation antipsychotics (SGAs) have contributed considerably to the treatment of schizophrenia. The term "atypical" was at first given to clozapine because of its low propensity to cause extrapyramidal symptoms. This term has been applied uncritically to a series of drugs despite their striking differences in chemistry, pharmacology and specific clinical action profile. Their use also may be limited because of various existing controversies. At first, there is the question whether SGAs have to be preferred over the older, conventional first generation antipsychotics (FGAs). Secondly, there has been an ongoing debate to differentiate between them in terms of efficacy and safety.

The initial enthusiasm that most of the second generation antipsychotics (SGAs) showed a better efficacy and tolerability profile over the FGAs was subsided over the publication of a series of meta-analyses, the most recent being the first results of the CATIE study. These showed that there was no clear evidence of the advantage of SGAs compared to the FGAs. Treatment guidelines from various institutions issued analogous and equivocating recommendations between the two antipsychotic groups. Therefore, the clinician has remained free to make his own choice.

There have been many publications comparing SGAs with FGAs, in the regulatory process of the drugs. For example, a meta-analysis comparing SGAs over FGAs found reduced dropout and treatment failure rates with risperidone in comparison with haloperidol. Other efficacy trials have tried to find differences in efficacy between the SGAs but with conflicting results. In one study, clozapine proved more effective than risperidone in treatment resistant schizophrenia but methodological flaws prompt for cautiouness for the interpretation of the results A big issue was raised with two studies comparing the efficacy of risperidone versus olanzapine. The first showed an advantage of olanzapine over risperidone and the second showed the opposite. Two studies comparing ziprasidone with olanzapine and ziprasidone with risperidone didn't disclose any advantage in efficacy of either agent over the other. A better tolerability profile was found with ziprasidone. Studies involving quetiapine showed that this agent had similar efficacy to risperidone and olanzapine. Switch studies showed that the use of aripiprazole maintained the clinical effect acquired by the previous agent. in another study, aripiprazole showed similar efficacy with risperidone. Amisulpride, an atypical antipsychotic with a different mechanism of action than the other SGAs, is an effective agent for the treatment of acute exacerbations as well as for the chronic treatment of positive and especially negative symptoms of schizophrenia. Compared with haloperidol in two studies, showed at least the same rate of improvement in positive symptoms and a clear advantage in long term over haloperidol in negative, suggested no efficacy differences between them, when the haloperidol equivalent didn't exceed 12 mg/day. In the light of most recent evidence comparing the relative efficacy of the SGAs, there are no clear-cut differences between them. It is up to the clinician to weigh the risks, the benefits and the cost of each drug and choose the most appropriate therapy for the individual patient.

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