Choice of medication

As mentioned in the discussion of General Principles, the choice of medication will be determined by the drugs available on the formulary, stage of illness (acute, stable), history of response and compliance, efficacy and tolerability of the available medications, and cost-effectiveness. An integration of all these elements is required to make the right choice for a given patient.

Ideally, the full range of atypical antipsychotic drugs will be available to the clinician. These include amisulpride, aripiprazole, clozapine olanzapine, quetiapine, risperidone and ziprasidone. The parenteral forms of olanzapine and ziprasidone are useful in management of the non-compliant, acutely agitated or violent patients (Brook et al, 2000; Breier et al , 2002) . They have a lower likelihood of causing EPS which can be very distressing and lead to long term aversion to compliance with antipsychotic drug treatment. They are, however, much more costly. Further studies are need to determined their cost-effectiveness and appropriate role in management of such patients. They may prove most useful in first episode patients compared to more chronic patients who have extensive experience with both typical and atypical antipsychotic drugs.

The choice of an oral antipsychotic drug must consider two main issues. Should it be an atypical or a typical is the first question. In many parts of the world, there is simply no choice as the atypical antipsychotic drugs are not available because of cost issues. In such cases, the lowest dose of a high potency antipsychotic drug is usually the best choice. Thus, haloperidol 2-10 mg/day or its equivalent will be effective and reasonably well tolerated in most patients. The lowest dose is usually not effective in more chronic patients but may suffice in some first episode patients. Occasional patients may need more than 10 mg but there is no benefit to the mega doses of 20 100 mg/day that were still in use in the 1990's in the US. These high doses are likely to cause severe EPS. The main disadvantage to the typical antipsychotic drugs, besides EPS and the risk of tardive dyskinesia, is their lack of effect on cognition and negative symptoms. This is discussed elsewhere.

If atypical antipsychotic drugs are available, these will be preferred over the typicals because of their greater tolerability, lower risk of non-compliance and relapse, and most importantly, their ability to improve cognition. Clozapine should generally be reserved for patients who have failed at least one adequate trial of the other atypical antipsychotic drugs. Some will argue for two trials. The more important issue is to determine when a patient is treatment resistant which means to consider all aspects of psychopathology and function. Choices among the other atypical agents can be made on a variety of dimensions: galenic formulations, cost, need for titration, effect on weight gain, lipids and risk for

diabetes, EPS liability, prolactin elevations, mechanism of action, full side effect profile, to name the most important. Cost will vary from country to country. In the US, risperidone and ziprasidone are the least costly for an average dose while clozapine, olanzapine and quetiapine are more costly. Aripiprazole is intermediate. Cost should always be considered in relation to benefits and possible offsets or liabilities (e.g future medical costs) (Liu et al., 2004)

To select the optimal antipsychotic drug for the individual patient, it is useful to know the patient's attitude toward possible side effects, e.g. weight gain, sedation, EPS. Only risperidone produces sustained elevation of serum prolactin levels. It has the greatest liability to cause EPS but this need not be a problem if the dose if titrated — in most patients a dose of 5 mg/day or lower is unlikely to cause EPS. Clozapine and olanzapine have the greatest risk of causing aspects of the metabolic syndrome, especially weight gain and lipid increases. The risk of type 2 diabetes mellitus may also be greater with these two agents but this has not been established definitively (American Diabetes Association, 2004). The increases in lipids produced by clozapine, olanzapine and quetiapine are indicative of greater insulin resistance.

References

American Diabetes Association. American Psychiatric Association. American Association of Clinical Endocrinologists. North American Association for the Study of Obesity. Consensus development conference on antipsychotic drugs and obesity and diabetes. Journal of Clinical Psychiatry. 65(2):267-72, 2004

Breier A. Meehan K. Birkett M. David S. Ferchland I. Sutton V. Taylor CC. Palmer R. Dossenbach M. Kiesler G. Brook S. Wright P. A double-blind, placebo-controlled dose-response comparison of intramuscular olanzapine and haloperidol in the treatment of acute agitation in schizophreniaArchives of General Psychiatry. 59(5):441-8, 2002

Brook S. Lucey JV. Gunn KP. Intramuscular ziprasidone compared with intramuscular haloperidol in the treatment of acute psychosis. Ziprasidone I.M. Study Group. Journal of Clinical Psychiatry. 61:933-41, 2000

Leucht S. Barnes TR. Kissling W. Engel RR. Correll C. Kane JM. Relapse prevention in schizophrenia with new-generation antipsychotics: a systematic review and exploratory meta-analysis of randomized, controlled trials American Journal of Psychiatry. 160(7):1209-22, 2003

Liu GG. Sun SX. Christensen DB. Luo X. Cost comparisons of olanzapine and risperidone in treating schizophrenia. Annals of Pharmacotherapy. 38(1):134-41, 2004