

Antipsychotics in schizophrenia: a message from CATIE

The results of the first two phases of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia study provide a useful insight into the effectiveness of antipsychotics.¹⁻³

Study design

This publicly funded, double-blind, US study included a broad population of patients (n=1493) with chronic schizophrenia. It had minimal exclusion criteria and allowed co-existing conditions and use of other medications. In phase 1, patients were randomly allocated to treatment with olanzapine, quetiapine, risperidone, ziprasidone (not available in the UK) or the typical antipsychotic, perphenazine for up to 18 months.¹ Doses were adjusted within a defined range according to clinical judgment. Those receiving an atypical antipsychotic who discontinued treatment could be randomised to an alternative atypical in phase 2. This had two arms: A: ziprasidone vs. olanzapine, quetiapine, or risperidone;² or B: clozapine (open-label) vs. olanzapine, quetiapine, or risperidone.³ The primary outcome in all phases was time to discontinuation for any reason, an important clinical endpoint that reflects both clinician and patient judgements about efficacy and tolerability.

Main results

Only 26% of patients (range 18–36%) completed the study on their first assigned antipsychotic in phase 1: 10–19% of patients discontinued treatment because of intolerable side effects, 15–28% for lack of efficacy, and 24–34% for other reasons. The time to discontinuation for any reason was significantly longer for olanzapine than for risperidone or quetiapine, but not for perphenazine or ziprasidone (see **Table**). Compared with other treatments, olanzapine was associated with the lowest rate of discontinuations for efficacy reasons (15% vs. 24–28%), but the highest rate due to side effects (19% vs. 10–16%), notably weight gain or metabolic effects (9% vs. 1–4%, $P<0.001$). More patients discontinued perphenazine due to extrapyramidal effects (8% vs. 2–4%, $P=0.002$), and more patients discontinued quetiapine for anticholinergic side effects (31% vs. 20–25%, $P<0.001$). In phase 2, many patients who discontinued their assigned atypical were able to successfully complete the study on an alternative (see **Table**). In phase 2A, the times to discontinuation for patients switched to risperidone or olanzapine were significantly longer than for those switched to quetiapine or ziprasidone. Clozapine appeared more effective

than the other atypical antipsychotics in phase 2B. However, the low number of patients in this phase questions the validity of this finding.

What does it mean in practice?

The CATIE study suggests that there is little to choose in terms of overall effectiveness between the antipsychotics studied, including the typical antipsychotic, perphenazine. All were associated with high rates of intolerable side effects and failure to control symptoms. Within the limited range of effectiveness, and excluding clozapine (which requires careful safety monitoring),⁴ olanzapine appeared the most effective of the other atypical agents, although its benefits were limited by unacceptable weight gain and metabolic effects. It should be noted that the olanzapine doses used in CATIE were high (see **Table**) relative to the UK licensed dose range of 5–20mg daily, which may limit the relevance of these findings to UK clinical practice.

The CATIE study clearly identifies the need for individualised antipsychotic treatment for patients with schizophrenia. Doctors and patients should carefully evaluate the trade-offs between efficacy and side effects, to choose the antipsychotic (atypical or typical) that is most likely to be acceptable. No one antipsychotic is suitable for everyone.



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Table: Primary outcomes of CATIE (phases I and 2)¹⁻³

Phase	Treatment	Mean modal dose: mg	No.*	Completers [†]	Median time to discontinuation (95%CI): months
1	Olanzapine	20.1	336	36%	9.2 (6.9–12.1) [‡]
	Perphenazine	20.8	261	25%	5.6 (4.5–6.3)
	Quetiapine	543.4	337	18%	4.6 (3.9–5.5)
	Risperidone	3.9	341	26%	4.8 (4.0–6.1)
	Ziprasidone	112.8	185	21%	3.5 (3.1–5.4)
2A	Olanzapine	20.5	68	33%	6.3 (3.5–9.7) ^{††}
	Quetiapine	565.2	63	16%	4.0 (3.1–4.8)
	Risperidone	4.1	70	36%	7.0 (4.1–10.0) ^{††}
	Ziprasidone	115.9	137	23%	2.8 (2.4–4.4)
2B	Clozapine	332.1	49	44%	10.5 (7.3–16.1) [‡]
	Olanzapine	23.4	19	29%	2.7 (1.9–11.9)
	Quetiapine	642.9	15	7%	3.3 (1.0–4.9)
	Risperidone	4.8	16	14%	2.8 (1.1–4.0)

*Patients who received at least one dose of randomised medication

[†]Proportion completing study on assigned drug

Statistically significant differences after adjustment for multiple comparisons:

[‡]vs. quetiapine or risperidone; ^{††}vs. quetiapine or ziprasidone; ^{‡‡}vs. quetiapine or risperidone

References

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Independent prescribing for pharmacists and nurses

What is independent prescribing?

On 1st May, regulations were changed to allow independent prescribing by pharmacists and nurses. The Department of Health (DH) defines independent prescribing as prescribing by a practitioner (e.g. doctor, dentist, nurse, pharmacist) responsible and accountable for the assessment of patients with undiagnosed or diagnosed conditions, and for decisions about the clinical management required, including prescribing.¹

Once qualified, Pharmacist Independent Prescribers will be able to prescribe any licensed medicine for any medical condition, with the exception of controlled drugs (until appropriate changes are made to the Misuse of Drugs regulations).¹ Independent prescribers must accept full professional, clinical and medico-legal responsibility for their prescribing decisions. They should, therefore, only prescribe within their own experience, in situations where they feel fully competent, using medicines that they feel are effective for the patient and the condition being treated.²

The Extended Nurse Prescribers Formulary has been discontinued,³ and qualified Extended Formulary Nurse Prescribers are now known as Nurse Independent Prescribers, and can prescribe any licensed medicine for any medical condition within their competence, including some controlled drugs.¹ Community Practitioner Nurse Prescribers will still only be entitled to prescribe from the Nurse Prescribers' Formulary for Community Practitioners.⁴

What about supplementary prescribing?

Pharmacists and nurses will continue to be able to train and act as supplementary prescribers.⁴ In some settings, this will be the best option because it enables nurses and pharmacists to prescribe the same medicines as an NHS doctor, including all controlled drugs and unlicensed medicines, provided they are stipulated in the patient's clinical management plan.² Many nurses already have a dual independent-supplementary prescribing qualification.⁴

What training will pharmacists need?

Training requirements for Pharmacist Independent Prescribers are being worked on,² and the outline curriculum is expected later this year. Employing organisations will select eligible pharmacists to train according to local service and patient needs. Central funding will be available for those working for the NHS, including community pharmacists who supply services to NHS organisations.¹ Non-NHS pharmacists will need a source of funding for their training, a medical supervisor to help with the 'supervision in practice' element of the course, and access to a prescribing budget once qualified.²

Further information

A DH guide for prescribers and their employers is now available from www.dh.gov.uk.¹ It sets out the steps needed to allow registered nurses and pharmacists to practise as independent prescribers and provides information and advice on good practice. Two useful articles on the DH website answer 'frequently asked questions' about nurse and pharmacist prescribing.^{2,3}

References

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3. Department of Health. Nurse prescribing FAQ. May 2006. Accessed from www.dh.gov.uk on 26/06/2006
4. Pharmaceutical Services Negotiating Committee. Pharmacist and nurse independent prescribing. Accessed from www.psn.org.uk on 19/05/2006

Are you suffering from information overload?

The sheer volume of information being continually generated about different interventions makes it very difficult for healthcare professionals to keep up to date. Trying to keep up to date by reading primary research in journals is impossible. You can miss key evidence relevant to your practice, and what you do manage to read may not be a true portrayal of the evidence base. Abstracts can contain information not consistent with the full article,¹ and meeting abstracts or posters from conferences are particularly problematic in not giving the full picture.² A better way to keep up to date is to read summaries of evidence from reputable sources. These include NICE, The Cochrane Library, Clinical Evidence, InfoPoems, MeReC, Drug and Therapeutics Bulletin and PRODIGY.

This topic is discussed in more detail in *MeReC Briefing* No. 30, Using evidence to guide practice (September 2005) and the related supplement (www.npc.co.uk/MeReC_Briefings/briefing2004.htm).

To complement *MeReC Bulletins* and *Extras*, we have recently introduced a new electronic publication, *MeReC Rapid Review*. In this, we quickly appraise key new trials or guidance and set them into the context of the current evidence base and healthcare practice. The first two editions are available on the NPC website at www.npc.co.uk/merec_rapid_review.htm.

To ensure you continue to be aware of all MeReC support available to you, please register to receive an email alert when a new MeReC resource is added to the NPC website. Register at www.npc.co.uk/merec.htm.

References

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