ethics

Translated from ***Rev Prescrire*** **December 2003; 23 (245): 863**

Clinical trials participants' right to know

Health scientists wanted to know whether trial investigators routinely told participants, at the end of trials, which treatment they had been given (1).

To find out, they interviewed 212 investigators of placebo-controlled clinical trials published in 2000 in international journals or recorded in the British register of clinical trials. Of the 139 investigators who replied, 32 did not complete the questionnaire in full. Of the 107 other investigators, 48 said they had informed all (40) or nearly all the participants in their trials. 53 investigators gave no information to participants; 6 informed only those participants who asked them directly.

The 53 investigators who had not informed the participants gave a number of reasons: it didn't occur to them (21), or publicising the results could, in their view, have prejudiced the trial follow-up (12); 14 investigators claimed it would entail additional expense or work; 6 thought that people didn't want to know.

In clinical research as in the doctor/patient relationship, health professionals are expected to provide information to participants in an honest, understandable and respectful way. The kind of information considered essential for fully informed consent at the start of a trial is stipulated in the Helsinki Declaration (Article 22), and the European Directive on the implementation of good clinical practice in the conduct of clinical trials (article 3 paragraph 2d) (2,3). But none of these texts specify what information should be given to participants at the end of the trials.

These legal texts already seem to be lagging behind changes in society including the public's demand for information.

Selected references from our literature search.

1- Di Blasi Z et al. "Informing participants of allocation to placebo at trial closure : postal survey" *BMJ* 2002; (**325**): 1329-1331.

2- "World Medical Association Declaration of Helsinski". Full text available World Medical Association website: http://www.wma.net

3- "Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use" *Official Journal of the European Communities* L 121, 01/05/2001 p. 0034 - 0044. Available from http://www.europa.eu.int/eur-lex/en/search/search-lif.html.

Forum

Translated from ***Rev Prescrire*** **February 2004; 24 (247): 155-156**

Acute mania: is olanzapine really advantageous?

As a subscriber to la revue Prescrire, I found your article on olanzapine in acute mania rather disappointing (see Prescrire International n° 70 p. 45).

Both sides of any argument have to be considered. Your overall judgement (Nothing New) is wrong. Indeed, it is no longer acceptable to treat a manic patient with a classical neuroleptic first (haloperidol for example) instead of an atypical neuroleptic (olanzapine). This is mainly because bipolar patients are reputedly more sensitive to the adverse effects of neuroleptics than are psychotic patients (schizophrenics for example).

The dose of olanzapine required in these patients is far lower than the dose known to induce neurological adverse effects, while the required dose of haloperidol is close to that capable of causing parkinsonism and late-onset dyskinesia.

The olanzapine dossier also contains data showing a beneficial effect on mood disturbances, including depression, while classical neuroleptics may induce depression.

If one of your readers prescribes first-line haloperidol to a manic patient who subsequently develops permanent dyskinesia (possible after three months of treatment) and claims damages, you might come round to the view that an atypical neuroleptic is worthy of first-line use in this setting! Medicolegal experts would no doubt agree, and your reader would have discovered the hard way that he/she was misinformed.

Finally, you quote the Commission de la transparence's report, which is simply a medico-administrative opinion on the state of the evaluation dossier. Otherwise the Commission would have had to admit that olanzapine, having proven effectiveness in acute mania, offered a new therapeutic option carrying a lesser risk of extrapyramidal effects, which is not a negligible advantage!

Jean-Pierre Olié
Psychiatrist
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Jean-Pierre Olié's letter gives us the opportunity to re-examine our assessment of the clinical evaluation dossier on olanzapine in acute mania.

No comparison with neuroleptics carrying a moderate risk of extrapyramidal effects. The only trial comparing olanzapine with another neuroleptic was one versus haloperidol; but haloperidol was used at a high dose, increasing the risk of extrapyramidal effects. As clearly stated in our article, olanzapine was no more effective than haloperidol in this trial. We also pointed out that olanzapine caused fewer extrapyramidal effects but that it had other noteworthy adverse effects, including more weight gain. Finally, we deplored the lack of trials comparing olanzapine with neuroleptics that carry only a moderate risk of neurological adverse effects. Why have no such trials been done?

In our brief reminder of guidelines on drug therapy for acute mania, we did not state that