Well-being and co-morbidity in recent onset schizophrenia
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Chapter 1.3

Early withdrawal in a double-blind randomized clinical trial with olanzapine and risperidone performed in adolescents with first psychosis

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Halfway a randomized double-blind study comparing olanzapine and risperidone in adolescents with first psychosis, we found that 19 (24%) of the 78 included patients terminated the double-blind phase before the end of the determined 6 weeks. There was no difference in dropout rates between sexes; the total group consisted of 65 males (83%) and 13 females (17%), and the dropout group comprised 16 men (84%) and 3 (16%) women. The mean age of the total group was 25.4 years (24.1 years for men and 31.5 for women). The mean age of the dropouts was 25.3 years (25.2 for men and 25.9 for women).

Reasons for dropout were: medication was not effective enough (n = 5); side effects (n = 6); withdrawal of consent (n = 4) and a combination of reasons (n = 4). Some patients told us that early withdrawal from the study was related to tension they experienced from ingesting the capsules not knowing their content, though we closely informed them that it was either olanzapine or risperidone. Three discontinuations were from patients with paranoid delusions. They had received the same neuroleptic trial medication, in an equal dose but not in a double-blind manner, one year before. This suggests that the double-blind aspect of a trial can lead to higher dropout rates, especially in patients with paranoid delusions. The most frequent reasons for dropout in clinical trials performed in patients with schizophrenia are severe extrapyramidal effects (Ahlfors et al 1990), clinical ineffectiveness (Ahlfors et al 1990, Azorin et al 1990) and refusal of medication administration (Azorin et al 1990). In drug trials with bulimic subjects, dropouts tended to have higher scores on the Paranoid Ideation Subscale of the SCL-90, compared to completers (Margittai et al 1986). It was also suggested that personality traits involving novelty seeking and impulsivity might contribute to early discontinuation from clinical trials, independent of anxiety (Wingerter et al 1993). Paranoia, impulsivity and anxiety are frequently encountered in patients with schizophrenia. The fact that many of the subjects in our study were using cannabis or other drugs might also have been a factor in the dropout rate (Bergman et al 1988, Kranzler et al 1996, Silva da Lima et al 2002, Vendetti et al 2002). The combination of adolescence and tobacco and alcohol use predicted loss to follow-up in trials (Morrison et al 1997).

In summary, the specific characteristics of adolescents with first psychosis might be related to high dropout rates in double blind clinical trials. Refusal of participation and premature discontinuation is a threat to the external validity of these studies, as it will decline the generalizability to the aimed population. An intent-to-treat design with last observation carried forward might reduce this problem. Many trials do not report reasons for dropout (Jokstad et al 2002); however, reporting the dropout rate and reasons for dropout is very important (Meinert 1998).
Early withdrawal in a double-blind randomized clinical trial

References


