Long-acting injectable paliperidone compared with haloperidol for maintenance treatment of schizophrenia

A US randomised controlled trial in adults with schizophrenia or schizoaffective disorder reports that the long-acting injectable antipsychotics paliperidone palmitate and haloperidol decanoate have comparable efficacy and tolerability.

Overview: Schizophrenia is a psychiatric disorder that typically first presents in adolescence and young adulthood. It is characterised by psychotic symptoms (for example, hallucinations, delusions and thought disorders), negative symptoms (for example, emotional blunting, poor concentration and social withdrawal), and a lack of insight by the person into their condition. With treatment, psychotic symptoms may resolve fully, recur intermittently with periods of remission between, or persist (NICE 2014).

Schizoaffective disorder occurs when, during the same illness, the person experiences a major depressive, manic or mixed episode. This occurs along with the symptoms of schizophrenia. Treatment of schizoaffective disorder is based largely on the treatment of schizophrenia (patient.co.uk 2011).

Current advice: The NICE guideline on psychosis and schizophrenia in adults recommends that clinicians should consider offering depot or long-acting injectable antipsychotic medication to people with psychosis or schizophrenia who would prefer this type of treatment after an acute episode, or where avoiding covert non-adherence (either intentional or unintentional) to antipsychotic medication is a clinical priority within the treatment plan. When initiating depot or long-acting antipsychotics, the service user’s preferences and attitudes towards regular intramuscular injections and organisational procedures (for example, home visits or location of clinics) should be taken into account.

The choice of antipsychotic medication should be made by the service user and healthcare professional together, taking into account the views of the carer if the service user agrees. There should be a discussion about the likely benefits and possible side effects of each drug.

The NICE Clinical Knowledge Summary on psychosis and schizophrenia states that in general, second-generation antipsychotics are associated with fewer extrapyramidal symptoms than first-generation antipsychotics. However, second-generation antipsychotics are associated with several other important adverse effects. Choosing the most appropriate drug and formulation for an individual is more important than the drug group (first or second generation).

The NICE Pathway on psychosis and schizophrenia brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.

New evidence: The ACLAIMS study (McEvoy et al. 2014) was a US multisite, double-blind, randomised controlled trial that compared the effectiveness of the second-generation long-acting injectable antipsychotic paliperidone palmitate with the older long-acting injectable antipsychotic haloperidol decanoate. The study enrolled people aged 18–65 years with a diagnosis of...
schizophrenia or schizoaffective disorder who were clinically assessed to be at risk of relapse and likely to benefit from treatment with a long-acting injectable antipsychotic.

Eligible participants (n=311) were randomised to monthly intramuscular injections of either haloperidol decanoate 25–200 mg (n=154, mean monthly dose range after the first month 67–83 mg) or paliperidone palmitate 39–234 mg (equivalent to 25–150 mg of paliperidone [UK product]; n=157, mean monthly dose range after the first month 129–169 mg) for up to 24 months. Treatment was assessed by efficacy failure (that is, inadequate control of the psychopathology of schizophrenia or schizoaffective disorder), which was indicated by psychiatric hospitalisation, crisis stabilisation, increased frequency of outpatient visits, ongoing need for oral antipsychotic medication, or clinician decision to discontinue treatment because of inadequate therapeutic benefit. Common adverse effects – including changes in weight, lipids and prolactin, as well as the incidence of extrapyramidal symptoms – were also assessed.

There was no statistically significant difference in the rate of efficacy failure in the paliperidone palmitate group (33.8%) compared with the haloperidol decanoate group (32.4%; adjusted hazard ratio=0.98, 95% confidence interval 0.65 to 1.47, p=0.93). The most common reasons for efficacy failure were psychiatric hospitalisation and clinician discontinuation of study medication.

The paliperidone palmitate and haloperidol decanoate groups were similar with respect to treatment discontinuations due to any cause (70.7% compared with 68.7%) and due to unacceptable adverse effects (10.2% compared with 9.5%). The authors suggested that the modest dose of haloperidol decanoate used in the study may account for the better-than-expected comparative tolerability.

The authors concluded that although there was no statistically significant difference between paliperidone palmitate and haloperidol decanoate in efficacy failure, a clinically meaningful difference favouring 1 of the drugs over the other cannot be ruled out because the 95% confidence intervals for the event rates were quite wide. Other limitations included that the study was terminated early, so not all patients were followed up for the planned 24 months.

**Commentary:** “Treatment of schizophrenia should be individualised to support adherence, promote recovery and prevent relapse. This study provides some further evidence to assist with discussions with service users and carers on available treatment options, as recommended in the current NICE clinical guideline.

“The study confirms that long-acting injectable haloperidol and paliperidone are equally effective, with treatment failure reported in a third of patients in each group, and substantiates the differences in adverse effects. Paliperidone was more likely to cause weight gain and increases in serum prolactin. Haloperidol was associated with increased need to treat akathisia and parkinsonism with medicines.

“The haloperidol doses used were comparable to current recommendations (12.5–75 mg every 4 weeks; Maudsley Prescribing Guidelines in Psychiatry 2012) and caused lower than anticipated rates of abnormal movements, parkinsonism and tardive dyskinesia. However, outside of current recommendations in the UK summary of product characteristics, a second dose of haloperidol was given on day 8, and the first 2 doses were administered in the deltoid rather than the gluteal region.

“Because the study ended sooner than planned, limitations include fewer patients recruited than the 360 proposed and a shorter monitoring period, with some patients being followed up for 12 months rather than the full 2 years. Further studies like this one that compare long-acting antipsychotics would be helpful.” – Louise Jackson, Chief Pharmacist, North Staffordshire Combined Healthcare NHS Trust

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