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Prescribing...

Antipsychotics

- This month's bulletin looks at two new studies which add to our understanding regarding the safe and cost effective use of this drug group.
- The first is a UK case controlled study which reported in the past few months and which suggested that there is an increased risk of venous thromboembolism or VTE with the use of antipsychotics.
- The increased risk equates to about four extra cases per 10,000 people of all ages treated, and ten extra cases for people aged 65 years or over.
- The risk may be greater among new users and those prescribed second generation (atypical) antipsychotics.
- The second is an American study has found that long-acting injectable risperidone was no better than oral antipsychotics in achieving a range of patient oriented outcomes in people with unstable schizophrenia.

A. VTE and Antipsychotics

What is the background to this?
In 2009 the MHRA carried out a review of UK Yellow Card reports and worldwide studies on antipsychotics and VTE and concluded that an increased risk "could not be excluded". It advised that all possible risk factors should be identified before and during antipsychotic treatment and that appropriate preventative measures be taken. At that point there was not sufficient information to determine any difference in risk between first and second generation antipsychotics or between individual drugs.

What were the findings of the latest study?
This nested case-control study used a cohort of more that 7 million patients from 453 UK GP practices. People who were prescribed an antipsychotic in the previous 24 months were found to have had a 32% greater relative risk of VTE than non-users, despite adjustment for potential risk factors. The risk was higher for those prescribed second generation antipsychotics than those prescribed second generation antipsychotics.

The 2009 MHRA assessment of the risk of VTE with antipsychotics reported thatall of the studies reviewed concluded that there was an increased risk of VTE associated with exposure to antipsychotics.

So what?
Antipsychotic drugs are associated with a wide range of adverse effects e.g. extraparamidal side effects , dry mouth, blurred vision and constipation, feeling of dizziness and lightheadedness and weight gain. They can also cause more serious adverse effects such as diabetes or metabolic syndrome, neuroleptic malignant syndrome and cardiac arrhythmia.

There is a clear increased risk of stroke and a small increased risk of death when antipychotics, either first generation or second generation, are used in elderly patients with dementia.

B. Long-acting risperidone

What is the background to this?
Three randomised controlled trials, discussed at our NPC Schizophrenia Workshop in April, have shown no advantage of long-acting risperidone over oral treatment in patients with clinically stable schizophrenia. This latest study tested the hypothesis that long-acting risperidone would be superior in reducing the risk of hospitalisation for up to two years , compared with a psychiatrist's choice of an oral antipsychotic, in patients with unstable disease. It included 369 patients in the US Veterans Affairs systems were given either 25 – 50mg LA risperidone every two weeks or an oral therapy. All of the participants had been hospitalised within the previous two years or were at risk of being hospitalised and were followed up for just under one year.

What does this study claim?
The rate of hospitalisation after randomisation was not significantly lower among patients who received the LA preparation than among those who received oral antipsychotics. Psychiatric symptoms, adherence to the prescribed treatment, service use, quality of life and scores on scales of global functioning were also not significantly improved with the injected preparation. Patients who received the injected formulation reported more injection site reactions, headache, and extra-paramidal signs and symptoms.

So what ?
There were some limitations to the study in terms of doses used and the fact that some decisions regarding hospitalisations were unblinded. The trial included older primarily male veterans so the results may not be generalisable to other populations. However it's main strength are that it used important patient oriented outcomes and involved recently hospitalised people with unstable schizophrenia. This is the patient group that in practice we may often consider for depot therapy.

Its findings are also consistent with those of the other three RCTs which showed no difference between LA and oral risperidone in patients with stable schizophrenia.

Results of all four studies support NICE guidance, which advises that long-acting preparations should only be used in limited circumstances i.e. in patients who would prefer such treatment after an acute episode, or where avoidance of covert non-adherence either intentional or non intentional to antipsychotic medication is a clinical priority within the patient's clinical management plan.

Thirty Risperidone 3mg tablets, prescribed generically, cost £1 compared with £159 for two Risperidone 25 mg Injections per month.

Information on the uses and adverse effects of antipsychotics can be found on the MRHA website and on the NPCi sections for schizophrenia, bipolar disorder and dementia. More information on VTE can be found on the VTE section of the NPCi. This includes Patient Decision Aids, Data Focused Commentaries, Quizzes, Short Presentations, Case Studies and links to NICE guidance.

Please contact me if you would like any more information.
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