Risperidone: researchers report good news, bad news

New studies support evidence that the drug risperidone (brand name Risperdal) is safer and more effective than other drugs commonly used to treat autistic individuals. At the same time, however, researchers are reporting that the drug can have dangerous side effects. Among recent findings:

Horrigan and Barnhill: "substantial improvement" seen

In an open-label study of risperidone's effects on explosive aggression, Joseph Horrigan and L. Jarret Barnhill administered the drug to 11 autistic males ranging in age from 6 to 34. Study subjects, 10 of whom were also retarded, had extensive histories of treatment with other drugs which the researchers say "either failed completely to control... explosive aggression or provided only partial efficacy." Five patients received risperidone alone, while six others received the drug in addition to other medications they were already taking.

The researchers say that when risperidone therapy was instituted, "substantial clinical improvement was noted almost immediately," with all but one of the subjects showing significant gains within 24 hours. The most dramatic reductions were seen in aggression, self-injury, explosivity (sudden, intense tantrums), overactivity, and poor sleep patterns. "However," the researchers say, "a number of caretakers also reported that the patients were better able to tolerate transition as well as frustration, and they also appeared 'more calm' and 'more focused.'" They add that "five of the patients' parents or caretakers stated explicitly that the positive changes from the risperidone spared the child from being placed in an alternative setting."

The primary side effect seen in this study, as in several others, was significant weight gain caused by increased appetite. Interestingly, Horrigan and Barnhill note that "there appeared to be a general correlation between the magnitude of increase in the patients' appetite and the robustness of their response to the risperidone." Additional side effects included temporary sedation, possible seizures in one subject, and one case of suspected chemical hepatitis.

Horrigan and Barnhill note that the average optimal dose of risperidone for their autistic subjects was 0.5 mg twice a day, which they note is far lower than the standard dose used in schizophrenia and other disorders. "This is congruent," they say, "with the general tendency towards elevated potency of psychotropic medications when used with autistic individuals."

Findling et al: positive results

In a separate open-label study, R. L. Findling and colleagues administered risperidone to six autistic children between the ages of five and nine. After eight weeks of treatment, at an average dose of 1.1 mg per day, the children showed significant improvement as evidenced by improved scores on the Children's Psychiatric Rating Scale and the Clinical Global Impressions Scale. Side effects included weight gain and sedation.

Horrigan and Barnhill say that all but one of their subjects showed substantial improvement within 24 hours.

"This study," the researchers say, "provides preliminary evidence that risperidone monotherapy may be safe and effective in ameliorating dysfunctional behaviors in children with autistic disorder."

Khan: DD subjects improved markedly

A non-controlled study by Barkat Khan found that all of 13 developmentally disabled patients treated for more than a year "sharply improved" on risperidone, becoming less aggressive and self-injurious. Seven of eight patients treated for less than a year also improved.

Khan notes that in patients with pre-existing tardive dyskinesia (TD), a neurological disorder frequently caused by psychotropic drugs or drug withdrawal, risperidone often reduced TD symptoms. Other researchers have also reported that risperidone can ameliorate TD symptoms.

All of Khan's subjects had previously taken other psychotropic drugs which had failed to control their symptoms. Khan says that unlike these drugs, which tend to sedate individuals, "risperidone seemed to leave these patients more responsive to their surroundings and better able to relate to staff and focus on activities." No significant side effects were reported in the study.

Side effects: few but potentially serious

Unlike Haldol and similar drugs, risperidone rarely causes extrapyramidal symptoms such as Parkinson-like movement disorders. A recent study by G. M. Simpson and J. P. Lindenmayer, evaluating side effects experienced by subjects taking risperidone, Haldol, and a placebo, found that "low doses of risperidone cause few or no extrapyramidal symptoms," and that "at the clinically most effective risperidone dose [which was 6 mg/day for this group of schizophrenic patients] the mean Extrapyramidal Symptom Rating Scale change score was not significantly different from that of the placebo group."

Because of the risk of liver damage, Kumra et al. recommend liver function tests and careful monitoring.

As risperidone becomes more popular, however, researchers are reporting other side effects, some dangerous. Among them:

—**Cardiac arrest.** D. S. Ravin and J. W. Levenson report that a 34-year-old schizophrenic woman with no history of cardiac disease went into cardiac arrest and died after five days of risperidone treatment (at a dosage of 2 mg twice a day). The researchers say that "adverse cardiac events are rarely associated with risperidone therapy," but note that eight of 380 patients in a double-blind study by the drug's manufacturer experienced cardiac abnormalities.

—**Liver abnormalities.** S. Kumra and colleagues report that long-term risperidone use can cause adverse liver changes. The researchers examined the charts of all patients admitted to the National Institute of Mental Health between December 1993 and April 1996 who received risperidone treatment. "From the medical records of 13 psychotic children," they say, "two children (both male) who presented with obesity, liver enzyme abnormalities, and confirmatory evidence of fatty liver were identified." In each case, the researchers say, the liver damage was reversed after the drug was discontinued and/or the subjects lost weight. Kumra et al. conclude that pediatric patients treated with risperidone should have baseline liver function tests, and be carefully monitored during treatment.

—**Neuroleptic malignant syndrome.** P. P. Gleason and R. L. Conigliaro report a case of neuroleptic malignant syndrome in a 73-year-old patient taking risperidone. The disorder, which causes the body to "overheat"—sometimes fatally—has been reported earlier in a 43-year-old schizophrenic patient (see

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