Haloperidol — Its Use in Children

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ABSTRACT

Haloperidol is safe and effective in children for relieving psychotic symptoms associated with childhood autism, schizophrenia and mental retardation. It is the drug of choice for Tourette’s syndrome, and may be useful in nonpsychotic hyperactive or aggressive children to control acute episodes, or when the stimulants normally useful in hyperactive children are ineffective. Such children taking haloperidol not only become calmer, but are often better able to respond to other modalities of therapy and to school instruction. Dosage, initially low, is increased gradually to minimize drowsiness and extrapyramidal symptoms, the most common side effects. Haloperidol in children is usually well-tolerated.


Haloperidol, a neuroleptic much used in the treatment of psychoses in adults has also been demonstrated to be safe and effective for use in children. Haloperidol has been shown to be useful in children for the relief of psychotic symptoms associated with a number of disorders, including childhood schizophrenia,1-4 infantile autism,1-3 other psychoses,3,4,6 and psychotic symptoms associated with mental retardation.1,2-6 It is demonstrably often useful for the control of the symptoms of Gilles de la Tourette’s syndrome.11,12 and is used to control acute episodes of hyperexcitability in nonpsychotic behavior disorders.5,6,13-15

TREATMENT OF NON-PSYCHOTIC SYMPTOMS

When children demonstrate hyperactive, hostile, aggressive, and/or withdrawn behavior they are unable to concentrate adequately to learn even the simplest tasks. No only are they untrainable, but they may be so disruptive that they interfere with the care and training of other children. The purpose of neuroleptic drug therapy in these children is to serve as one of a group of therapeutic measures.5,10,14-16 No drug can cure mental retardation, nor can drugs alone cure the psychoses of childhood. A drug such as haloperidol may help to relieve such symptoms as hyperactivity, aggressiveness, self-mutilation, rage, explosive outbursts, withdrawal, and stereotypy in some disturbed children so that they become more manageable, educable, and amenable to such other therapies as individual, family and group psychotherapy, behavior modification, and remedial education.5-7,8,14

TREATMENT OF NON-PSYCHOTIC SYMPTOMS

Haloperidol has been used successfully in children with nonpsychotic hyperactivity.5,6,14-15 — children often diagnosed as having hyperkinetic syndrome or minimal brain dysfunction—however, it is usually reserved for short-term use in these children. In these circumstances, haloperidol may be useful to bring acute, severe episodes under control, or for management of difficult cases when stimulant drugs, such as methylphenidate and amphetamine, have been tried without success.

An important advantage of haloperidol in children is that it minimally affects alertness and cognition.1,2,8,15 Except for some initial drowsiness, which ordinarily appears to be dose-related,3 haloperidol at therapeutically useful doses, does not oversedate the young patient.8,14,15 Furthermore, haloperidol in therapeutic dosages appears to have little potential for such toxic effects as photosensitivity, blood dyscrasias, jaundice, or cardiovascular effects.14,18 Although it may possibly lower the convulsive threshold, it has been given without incident to children with seizure disorders who were taking anticonvulsant drugs.6 Children on concomitant therapy should be carefully monitored to ensure that adequate levels of anticonvulsant medication are maintained.

TREATMENT OF TOURETTE’S SYNDROME

Gilles de la Tourette’s syndrome11,12 is an uncommon disorder characterized by disabling and embarrassing vocal utterances and motor tics. It usually begins during childhood with facial tics that spread to involve the trunk and extremities. Soon after the onset of facial tics, vocal tics also begin, starting with inarticulate grunting or bark- ing, and progressing, commonly at puberty, to coprolalia and often to echolalia. The course of the disorder is marked by frequent exacerbations and partial remissions. The etiology is unknown; patients are not mentally retarded or psychotic, and show no signs of brain damage.11

Haloperidol has been found to be quite effective in...
reducing or even eliminating the manifestations of this disorder, which is often resistant to other forms of treatment. Symptoms usually regress within 24 to 48 hours after therapy begins, and often disappear completely with adjustment of haloperidol dosage.

**DOSEAGE**

In general, it is best to begin therapy for children with a low, even ineffective, dose of haloperidol and to increase the dose gradually, in order to minimize the appearance of extrapyramidal symptoms and drowsiness. At times as in severely agitated children this gradual incremental regimen may not be desirable, and the occurrence of extrapyramidal symptoms may have to be accepted for the sake of prompt control of symptoms. These unwanted effects, if they occur, can then be controlled by lowering the dose or by use of an antiparkinsonian agent, such as benztropine mesylate, biperiden, trihexyphenidyl or procyclidine.

A suggested starting dose for children with psychotic symptoms or Tourette’s is 0.025 to 0.05 mg/kg body weight per day. The daily amount is usually divided and given as two or three equal doses. The starting dose is gradually increased (e.g., over a period of two or three weeks), until target symptoms are controlled. Dosage is then adjusted to the lowest level that will maintain this control. (Patients who have shown adverse reactions to other neuroleptic drugs may be controlled with lower doses of haloperidol. Dosage adjustment in such patients should proceed cautiously and by small increments.)

Patients vary considerably in the amount of medication they require, and the dosages reported in the literature reflect this. Maintenance amounts have ranged from 0.04 to 0.07 mg/kg/day. Because side effects are often dose-related, one should use the lowest maintenance dosage that will give the desired results.

The duration of therapy depends on the patient’s condition and his response to other modes of treatment, such as behavior modification and special education programs. Short-term therapy of four to six weeks may suffice for an acute psychotic episode, for example, while children with chronic conditions or with intrinsic disorders (e.g., organic brain syndrome) may need therapy for long periods. When children require long-term therapy, it may be advisable to gradually lower the dosage periodically in order to keep the maintenance dose as low as possible.

Haloperidol therapy should be stopped when the drug is no longer needed. Several investigators have suggested interrupting long-term therapy for a week or two after every three or four months of treatment. Such “drug holidays” allow an assessment of the child’s clinical status. If the child’s newly learned patterns of acceptable behavior hold up without neuroleptic therapy, the use of haloperidol can be stopped.

Recent studies of blood levels of haloperidol in children suffering psychotic episodes or tics have shown a lack of correlation between plasma levels and therapeutic response. Careful clinical assessment of dosage adjustment is, therefore, recommended.

**SIDE EFFECTS AND SAFETY**

Many published reports attest to the safety of haloperidol in children. There have been no reports of photosensitivity, and few, if any, blood dyscrasias have been reported in cases where haloperidol was the sole therapy. The most commonly seen side effects are an initial drowsiness and extrapyramidal symptoms (EPS). The drowsiness appears to be dose-related, and when it occurs it usually disappears within a few days with continued administration of the drug. If drowsiness does not disappear, it usually improves with downward dosage adjustment. The EPS are similar to those seen with the piperazine phenothiazines in children. They tend to occur early in the course of therapy, and with larger initial doses. The procedure of starting with a very low dose and increasing it gradually should help to reduce their incidence and severity.

Extrapyramidal symptoms include: 1) parkinsonian reactions (drooling, cogwheel rigidity, or tremor); 2) acute dystonic reactions (torticollis; grimacing; protrusion of the tongue; spasms that can affect speech, swallowing, and even breathing; oculogyric crises; or the arched back of opisthotonos); and 3) akathisia or a more general motor restlessness. EPS can be frightening to those unfamiliar with them, and so parents and comprehending patients should be forewarned. Dystonic reactions can be controlled fairly readily: parkinsonianism and akathisia less so.

EPS can often be relieved by a reduction in dosage; if this is unsuccessful, they can be treated with antiparkinsonian agents (benztropine mesylate, biperiden, trihexyphenidyl, or procyclidine) or with diphenhydramine. Once the EPS have been controlled, it is usually possible to discontinue antiparkinsonian medication.

Slight weight gain is often seen in children receiving haloperidol. This effect has been reported with other neuroleptics as well.

As is well known, in adults, long-term neuroleptic therapy can cause the symptom complex of tardive dyskinesia (“tardive” because symptoms are delayed: they may not appear until after drug has been reduced or stopped). Characteristic are stereotyped, involuntary choreoathetotic movements, usually facial, such as lip-smacking and protrusion of the tongue. In some patients the condition appears to be irreversible. A similar, but apparently reversible, condition occurs in some children after withdrawal of some neuroleptic drugs, particularly those that are prone to cause extrapyramidal symptoms during treatment. The condition, known as “withdrawal emergent symptoms” (WES), differs from tardive dyskinesia in several important ways. First, WES appears ordinarily to be reversible, and to disappear spontaneously. Tardive dyskinesia is usually irreversible or of very long duration. Secondly, tardive dyskinesia usually affects facial muscles, and does not cause ataxia; WES primarily affects the extremities and trunk, with ataxia and symptoms that resemble Huntington’s chorea. Also, WES can occur following relatively brief therapy (although there appear to be no reports of such symptoms in children who have dropped out of short-term clinical trials of haloperidol). The dosage used, and the speed of withdrawing the drug, do not affect the incidence of WES. Like tardive dyskinesia, WES does not respond to antiparkinsonian drugs.

There has been one report of prolonged severe dystonia and opisthotonos that followed haloperidol therapy in a child with Sydenham’s chorea. Numerous drugs
were tried to no avail, and the dystonia had persisted for five months at the time of the report.50

Slightly elevated SGOT, SGPT, or alkaline phosphatase levels with no clinical evidence of hepatotoxicity: have been reported in some clinical trials of haloperidol in children;54 levels returned to normal shortly after the clinical trials were ended.7

Aman and Werry51 have studied the cardiovascular effects of single doses of haloperidol in hyperactive children. A dose of 0.035 mg/kg caused only minimal changes in heart rate and blood pressure, effects that were less than the increased heart rate induced by food ingestion.

In the few reports of acute accidental overdosage of haloperidol, the children recovered without sequelae.52,53 Most of these children showed extrapyramidal symptoms, and most were somnolent. Nine had impaired consciousness, four had convulsions, and two had hypotension; one child apparently showed no ill effects at all.55

In three reported cases,56 biperiden 3 mg was administered and symptoms disappeared within a few hours. In another report57 two children, 11 and 29 months old, were reported to have sinus arrhythmia, bradycardia, hypothermia, and hypotension after accidental ingestion of unknown quantities of haloperidol. Although such effects can be considered to be potentially life-threatening, both children recovered completely within four to seven days. It is of interest that all of the clinical laboratory, hematological, and urinary tests done in both these children were normal.58

In summary, haloperidol has been found to be a very useful therapeutic agent to control psychotic symptoms of Tourette’s syndrome in children. It has also been safe and effective in the acute treatment of hyperactivity and aggressiveness associated with mental retardation. With appropriate dosage adjustment, sedation is minimized and children are more manageable, more alert and able to respond to the other therapeutic measures. The suggested starting doses for psychotic symptoms and for Tourette’s syndrome, are 0.025 to 0.05 mg/kg/day given in two or three divided doses daily. The required maintenance dose varies considerably from patient to patient and also for a given patient over time. Side effect problems are readily managed. Transient initial drowsiness may occur, and the patient may require concomitant antiparkinsonian therapy for extrapyramidal symptoms, which are the most commonly reported adverse effects. Overall, haloperidol appears to have a highly acceptable safety record in the pediatric population.

REFERENCES


11. Shapiro AK, Shapiro E and Wayne H: Treatment of Tourette’s Syndrome with haloperidol, review of 34 cases. Arch Gen Psychiatry 28:92-97, 1973


