Economic Evaluation of Zuclopenthixol Acetate Compared with Injectable Haloperidol in Schizophrenic Patients with Acute Psychosis

Claudine Laurier, PhD,[1,2] Wendy Kennedy, LLB, MBA,[2] Jean Lachaine, MSc,[1] Line Gariepy, MSc,[3] and Geneviéve Tessier, MSc[4]

[1]Faculty of Pharmacy, [2]Groupe de Recherche Interdisciplinaire en Santé (GRIS), University of Montréal, [3]Conseil Québécois d'Evaluation des Technologies Médicales, and [4]Health Economics, Hoechst Marion Roussel Canada, Montreal, Canada

ABSTRACT

Zuclopenthixol acetate is a rapid-acting, injectable neuroleptic drug with a duration of action that allows for administration once every 2 to 3 days, in contrast to injectable haloperidol, which may require administration more than once daily. To assess the place of zuclopenthixol acetate in the treatment of acute episodes of schizophrenia, a cost-consequence analysis was performed comparing this new medication with short-acting, injectable haloperidol. The perspective of the Quebec health care system was adopted. The study population comprised patients diagnosed with schizophrenia who experienced an acute episode of psychosis and who were treated with intramuscular (IM) haloperidol. The study assessed patients for 9 days after the start of treatment. The literature was the principal source of comparative data about the clinical outcomes of the two treatments. The total cost associated with zuclopenthixol acetate IM or haloperidol IM was modeled using a decision tree built around the number of IM injections required to achieve stabilization. To establish costs, expert panels were consulted and patients' files were reviewed for a sample of schizophrenic patients who had been hospitalized in a large psychiatric or general hospital subsequent to a visit to the emergency department and had received a short-acting IM neuroleptic drug. Only direct medical costs were considered. Because zuclopenthixol acetate was not on the market at the time of the study, the file review did not allow for a direct estimate of its related costs but did provide an account of haloperidol use. The literature shows that zuclopenthixol acetate is similar to haloperidol with respect to the control of psychotic episodes; however, zuclopenthixol acetate is associated with increased sedation and a lower incidence of extrapyramidal symptoms. Using the base-case estimate for the number of injections required for stabilization, the incremental cost of zuclopenthixol ace-

0149-2918/97/$3.50

tate 50 mg over haloperidol was $25.00 (1995 Canadian dollars) per patient at the psychiatric hospital and $21.00 per patient at the general hospital. The results were sensitive to the estimate of the number of injections and the number of minutes of nursing care required by agitated patients. Zuclopenthixol acetate resulted in cost savings over haloperidol if it permits a reduction of 25% in minutes of nursing care or if 85% of patients require 2 injections or less (45% requiring 1 injection and 40% requiring 2). However, whichever drug is used, the cost of the injectable neuroleptic represents a small fraction of the cost of care for acutely psychotic patients. ***Key words:*** schizophrenia, economic evaluation, injectable zuclopenthixol acetate.

INTRODUCTION

Schizophrenia is a psychiatric disorder with an estimated lifetime prevalence of 1.0% to 1.9%.[1] Although oral neuroleptic drugs are preferred for the treatment of the chronic phase of the disease, injectable drugs with a rapid onset of action are sometimes necessary for the management of acute episodes, especially with agitated or aggressive patients. Haloperidol administered as an intramuscular (IM) injection has long been used as the preferred treatment for these acute episodes and is still recommended as a first choice.[2,3] Lorazepam has also been used successfully.[4]

Zuclopenthixol, a neuroleptic drug belonging to the thioxanthene class, has recently become available on the market in Canada. The acetic acid ester of zuclopenthixol* is available as an oil solution for IM administration to treat acute psychotic episodes. Due to its rapid onset of action (2 to 4 hours) and its 48- to 72-hour duration of action, zuclopenthixol acetate IM can be administered once every 2 to 3 days,[5] in contrast to haloperidol IM, which may need to be administered more than once daily.

Because the decision to adopt a new drug treatment should include consideration of costs as well as clinical outcomes, we undertook an economic analysis comparing zuclopenthixol acetate (short-acting, injectable) with haloperidol in patients who require a parenteral neuroleptic to treat an acute episode of schizophrenia.

Because the clinical impact of the alternatives studied cannot be summarized easily by a single measurement of effectiveness, a cost-consequence analysis was performed.[6] Indeed, although the control of psychotic symptoms, as reflected by scores on standard scales, can be viewed as the main measure of effectiveness, it fails to capture effects such as extrapyramidal symptoms, sedation, and uneasiness caused by repeated injections. A cost-consequence model provides a more appropriate means of accounting for these effects.

The perspective of the analysis was that of the Canadian health care system, as characterized by the situation in Quebec Province, the second most populous province in Canada.

PATIENTS AND METHODS

Patients

The target patient population comprised patients diagnosed with schizophrenia (*International Classification of Diseases, 9th*

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Revision, Clinical Modification code 295) who experienced an acute episode of psychosis and who required a short-acting, IM neuroleptic drug. Because clinical practices and, therefore, costs and outcomes are likely to differ in psychiatric hospitals when compared with general hospitals, two population subgroups were considered: patients treated in a psychiatric hospital and patients treated in a general hospital.

Zuclopenthixol acetate (50 or 100 mg IM, repeated if necessary) was compared with short-acting haloperidol (5 to 10 mg IM, repeated if necessary). Haloperidol was the comparator in clinical trials involving zuclopenthixol acetate and represents the less costly alternative.[7–10]

The study assessed patients for 9 days beginning with the time of their arrival at the emergency department and the prescription of a short-acting parenteral neuroleptic drug. A 9-day period was selected, as it represents the maximum follow-up period in clinical trials of zuclopenthixol acetate and it allows for the treatment of the acute phase of the episode.[5,7,10–16]

Clinical Outcomes

The published literature was the principal source of comparative data with respect to clinical outcomes. Clinical trials that compared zuclopenthixol acetate with short-acting haloperidol IM in the treatment of acute psychosis served as the primary information source. Studies looking at either one of the medications were also reviewed. Results pertaining to other formulations (eg, long-acting, injectable drugs) of zuclopenthixol or haloperidol were not included. Outcomes of interest were the control of psychotic symptoms, sedation, and the occurrence of extrapyramidal effects.

The studies were identified through MEDLINE™ using combinations of the following expressions as key words or text words: schizophrenia, acute psychosis, intramuscular, haloperidol, and zuclopenthixol. Only papers written in English or French were reviewed. Care was taken to avoid double-counting when a study considered a subgroup of patients included in a larger trial.

Model and Categories of Costs

The total costs (in 1995 Canadian dollars) associated with either zuclopenthixol acetate IM or haloperidol IM were modeled using the decision tree shown in the figure. It includes a 9-day treatment period and is built around the number of IM injections required to achieve stabilization. After an injection, control of symptoms may be achieved and the patient would be switched to oral therapy for the rest of the period. In some cases in which a single injection may be insufficient to achieve control, a supplementary injection may be administered or the IM treatment may be stopped because of the patients' intolerance or refusal.

In keeping with the chosen perspective, only direct medical costs were considered in this study. Resources considered were those used for the treatment of the schizophrenic patients during the 9-day period, both in the emergency department and after admission to the hospital.

The following categories of costs were included: basic hospital stay, neuroleptic drugs (zuclopenthixol acetate or haloperidol), hypnotic drugs, oral neuroleptic drugs, antiparkinsonian drugs, physicians' visits, diagnostic tests pertaining to the psychotic episode, and nursing care required to handle agitated patients.

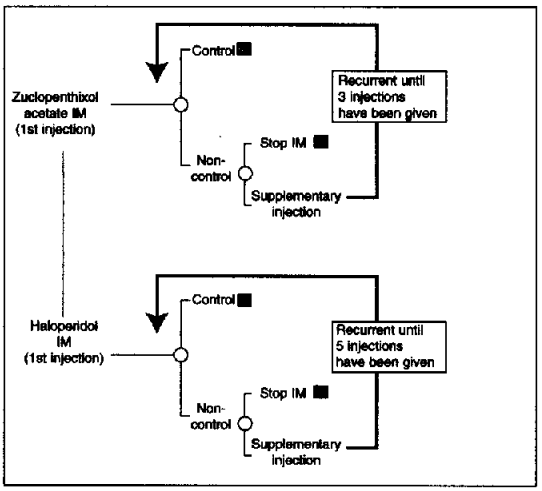

Figure. Decision tree for modeling total costs of therapy with zuclopenthixol acetate or intramuscular (IM) haloperidol for the treatment of an acute episode of schizophrenia.

Estimate of Resource Consumption

Two complementary approaches were used to evaluate the amount of resources used. First, members of expert panels were asked to define typical resources used by an average schizophrenic patient experiencing an acute psychotic episode, according to various courses of the illness. Two panels were constituted, one to represent the practice patterns encountered in general hospitals and the other for psychiatric hospitals. They included health care specialists (1 general practitioner, 3 psychiatrists, 4 nurses, and 2 social workers) involved in treating patients with acute psychotic episodes. The panel members were consulted separately in a semi-structured interview format.

Resource consumption was also estimated based on a review of patients' files. Because zuclopenthixol acetate was not on the market at the time of the study, the review did not allow for a direct estimate of its related costs. However, it did allow for an evaluation of the costs associated with standard treatment.

Files were reviewed to identify a sample of schizophrenic patients hospitalized in 1992, 1993, or 1994 subsequent to a visit to the emergency department who received haloperidol IM within 2 days of their arrival. After approval from hospital authorities, one sample was drawn from a large psychiatric hospital and the other from a large university general hospital. At the general hospital, 240 admissions of schizophrenic patients subsequent to a visit to the emergency department were identified for the selected years. The files were randomly reviewed and 20 episodes of care that met the inclusion criteria were analyzed. At the psychiatric hospital, computerized pharmacy records allowed for a direct selection of patients who were prescribed haloperidol IM. From that list, 24 episodes of care that met the inclusion

criteria were identified. All patients were hospitalized for at least 9 days.

The file-selection process excluded patients who came to the emergency department but were not hospitalized. However, it was assumed that most patients who were sufficiently ill to receive medication IM were hospitalized, making the exclusion effect small.

Costing

Basic hospital stay was costed using a per diem for services that could not be allocated directly to the treatment (food, laundry, maintenance and cleaning, equipment operation, administration, equipment repair and maintenance, general nursing, pharmacy hours). The cost of one visit from a resident per patient-day was also included. Financial reports of the study hospitals for 1992 and 1993 were used to calculate the per diem. As all patients were expected to be hospitalized during the entire 9-day period, basic hospital costs were included only to reflect the absolute costs related to an episode of care.

The cost of either zuclopenthixol acetate or haloperidol was determined by the number of injections, as defined by the probabilities of the decision tree, and the unit cost of one injection. For zuclopenthixol acetate, one set of analyses assumed the use of a 50-mg injection (50 mg/mL) at $14.00 per injection (price provided by Marion Merrell Dow Canada, Laval, Quebec, Canada). Another set of analyses assumed the use of a 100-mg injection (100 mg/2 mL) at $26.00 per injection (price provided by Marion Merrell Dow Canada). The unit price of haloperidol ampules was the price of the generic drug used in the study hospitals. Antiparkinsonian, oral neuroleptic, and hypnotic drugs were costed according to the price of the generic drug used in both study hospitals, and their frequency of use was based on data in the patients' files.

The number of physician visits required was determined by the sequence of events experienced by patients. Patients whose symptoms were controlled by one or two injections of either haloperidol or zuclopenthixol acetate were assumed to have received one complete physical examination and one principal psychiatrist visit in the emergency department. For patients whose IM medication was stopped despite insufficient control, one control psychiatrist visit was added. For patients who required more than two injections, one control visit was also added. Visits were costed according to the 1995 fee schedule of the Régie de l'Assurance Maladie du Québec, which pays for physicians' services provided in Quebec on a fee-for-service basis.

The basic laboratory tests reported in the patients' files were taken to represent testing for all arms of the decision tree and for both drugs. These costs were based on the number of technical units multiplied by the per-unit costs from each hospital. Basic hospital costs associated with diagnostic tests were identical for patients treated with haloperidol or zuclopenthixol acetate and did not have an impact on the incremental cost of one treatment over the other; instead, they were used to provide an accurate picture of the absolute costs related to an episode of care.

To account for the nursing time required to treat agitated patients, the cost of the minutes of nursing care was added to the basic per diem based on the average number of hours patients were in isolation with or without restraints (surveillance). The data on the number of hours of isolation were retrieved from the files of patients

hospitalized in the psychiatric hospital only, as this information was not reported in the files of patients in the general hospital. The average number of hours of isolation was computed for two subgroups of patients: those who received 1 or 2 injections of haloperidol and those who received 3 or more injections. Fifteen minutes of nursing time per hour of isolation was added. Because of the difficulty of administering a drug to an agitated patient, the cost of 15 minutes of nursing time per injection was also added to the basic nursing costs for these patients. The number of minutes added to normal nursing time when an agitated patient requires surveillance or an injection was based on a discussion with nurses and did not represent observational data. The unit price for nursing time was retrieved from the financial reports of both study hospitals.

Sensitivity Analysis

Sensitivity analyses were carried out for major variables of the analysis, as revealed by the literature and the file review.

RESULTS

Clinical Outcomes

Only two clinical trials comparing haloperidol IM with zuclopenthixol acetate in acutely psychotic patients were found.[7,8] Because of the classification of cases used in these studies, it was not possible to completely isolate the results obtained for nonschizophrenic patients from those obtained for schizophrenic patients.

Bobon and De Bleeker[7,8] reported the results of an open-label, randomized, controlled trial of 92 acutely psychotic patients that compared zuclopenthixol acetate 50 to 150 mg every 72 hours with haloperidol IM, with a switch to oral haloperidol when cooperation from the patient was obtained. The clinical effects on psychotic symptoms were measured by the Clinical Global Impression (CGI) scale and the Brief Psychiatric Rating Scale (BPRS) or by the Bech-Rafaelsen Mania Scale (BRMAS). A subgroup (n = 33) was also assessed using the AMDP scales.[9] Patients were assessed at baseline; at 24, 72, and 144 hours; and at the end point. Improvement of symptoms, as measured by the CGI, was observed in both treatment groups with no significant differences seen between treatments. Similar results were obtained on the BPRS; analysis of BPRS factor scores did not reveal qualitative differences between zuclopenthixol acetate and haloperidol. Using the BRMAS, the scores of patients treated with zuclopenthixol acetate were significantly ($P < 0.05$) lower than scores of patients treated with haloperidol at 24 and 72 hours, whereas no significant differences were noted at 6 days. Analysis of variance did not show significant differences between treatments. Sedation assessed on a four-point scale was significantly ($P < 0.05$) higher with zuclopenthixol acetate than haloperidol at 8, 24, and 48 hours. Twenty-nine percent of patients treated with zuclopenthixol acetate received a hypnotic drug compared with 46% of patients treated with haloperidol. Less than 20% of the patients in both groups experienced bothersome side effects. The maximum possible number of extrapyramidal side effects was computed and the distribution of observed versus possible side effects for both treatments was compared. At 72 and 144 hours, there was a significant difference favoring zuclopenthixol acetate ($P < 0.001$). Antiparkinsonian medications

were given to 22% of the patients treated with zuclopenthixol acetate and 46% of the patients treated with haloperidol.

Another open-label, randomized study comparing zuclopenthixol acetate (50 to 200 mg), haloperidol IM (5 to 10 mg), and zuclopenthixol short-term injectable (10 to 20 mg) was undertaken at 14 Nordic centers.[10] Patients for whom a parenteral neuroleptic drug was indicated were randomized with twice as many patients randomized to the zuclopenthixol acetate group. Patients were switched to oral therapy as soon as possible. Clinical outcomes were assessed with the CGI, BPRS, or BRMAS scale. Patients were assessed at baseline; at 24, 72, and 144 hours; and at the end point. The analysis did not reveal any significant differences in relative reductions of scores between treatments. The proportion of patients who showed a reduction of at least 50% of their BPRS or BRMAS scores was similar in all groups. The authors reported that sedation was somewhat weaker for patients who received haloperidol but did not perform a statistical analysis on these results. Less than 20% of the patients in all treatment groups experienced more than mild side effects. During the first 24 hours, the frequency of hypokinesia was significantly ($P < 0.05$) higher in patients in the haloperidol group than in patients in the zuclopenthixol acetate group; there was also a tendency to a higher incidence of rigidity in patients who received haloperidol ($P = 0.07$). Later in the trial, no differences in the frequency of side effects were noted, possibly due to the administration of antiparkinsonian drugs.

Other trials of zuclopenthixol acetate confirm its efficacy in the treatment of psychotic symptoms.[5,11–18] Most studies report a sedative effect after injections, although Chouinard et al[13] did not find this effect to be different from that seen with liquid haloperidol.

Omerov et al[18] studied the number of aggressive incidents reported by closed-ward staff before and after zuclopenthixol acetate was introduced and routinely used. The mean number of aggressive events decreased from 76 in 1987, when standard neuroleptic drugs were used, to 31 per year in both 1988 and 1989, when zuclopenthixol acetate became the routine treatment. However, insufficient information is available to adequately interpret these results in terms of a difference between zuclopenthixol acetate and haloperidol.

The preceding trials lead to the conclusion that zuclopenthixol acetate and haloperidol IM are similar in terms of control of psychotic symptoms, as assessed on the usual scales (CGI, BPRS). Sedation appeared to be more pronounced with zuclopenthixol acetate. This finding may be a clinical advantage in a particular setting or for a particular patient population. A difference in the frequency of extrapyramidal symptoms was noted in favor of zuclopenthixol acetate. This might lead to a lower use of antiparkinsonian drugs and, in consequence, a decreased exposure to the risk of side effects from those drugs. To the extent that the decrease in aggressive events is related to the introduction of zuclopenthixol acetate, this finding might be advantageous for the health care team and might foster a climate more conducive to treatment.

Costs

Probabilities of Events

The proportion of patients who required different numbers of injections to be stabilized is a central variable in the model.

For zuclopenthixol acetate, the literature review gave some indications concerning the number of injections required.[5,11,15–18] Table I shows the number of injections required in studies that provided that data and in which the number of injections was not largely predetermined by the protocol.

An average of the proportion of patients with 1, 2, or 3 or more injections was computed. The results presented in one study[17] were then excluded because they were outside the interval created by the mean ± 1 SD for each category. This exclusion tended to be conservative with regard to the advantages of zuclopenthixol acetate. A weighted average was computed with weights being defined by the number of patients in each study.

The weighted average rounded to the nearest integer was used as the base-case estimate for the number of zuclopenthixol acetate injections. Because few patients needed more than three injections, we assumed that the maximum number of injections was three. Conservative and optimistic estimates for the number of injections were considered in sensitivity analyses. According to the conservative scenario, 20% would need 1 injection, 45% 2 injections, and 35% 3 injections. The proportions for the optimistic scenario were 45%, 40%, and 15%, respectively. The conservative scenario was based on results provided by Balant et al[11] and the optimistic estimate was based on results provided by Omerov et al.[18]

The files reviewed in the two hospitals were used to estimate the number of haloperidol injections considered in the analysis. In the psychiatric setting, 58% of patients required 1 injection, 17% 2 injections, 8% 3 injections, 4% 4 injections, and 13% 5 injections (n = 24). In the general setting, the proportions were 55%, 20%, 5%, 5%, and 15%, respectively (n = 20). The proportions were similar in both settings.

The literature did not provide detailed information about the probabilities of discontinuing the treatment because of patient intolerance or refusal after the first

Table I. Proportions of patients according to number of injections of zuclopenthixol acetate received.

Study	Year	N	1 Injection (% patients)	2 Injections (% patients)	≥3 Injections (% patients)
Amdisen et al[5]	1987	83	19	71	9
Balant et al[11]	1989	21	19	48	33
Hebenstreit[15]	1989	117	12	34	54
Lowert et al[17]	1989	67	39	27	34
Matar et al[16]	1990	15	93	7	0
Omerov et al[18]	1990	108	51	34	15
		100	48	41	11
Average % (SD)		578	40.1% (27.9%)	37.4% (19.6%)	22.3% (18.8%)
Average % (SD)*		563	31.3% (16.7%)	42.5% (15.7%)	26.0% (17.5%)
Weighted average†		563	32.9%	41.3%	25.7%

*Excluding results of Matar et al.[16]

†Weighted by N and excluding results of Matar et al.[16]

injection. In the absence of quantitative data in this regard, assumptions have to be made. Therefore, it was assumed that 2% of patients would stop treatment after both the first and the second injection of zuclopenthixol acetate. For haloperidol, the probability of stopping after one injection was set at 2% and at 1% after each additional injection. A lower rate at the second and consecutive injections was considered to reflect a selection process (only tolerant patients are given a second dose) that might be more pronounced for haloperidol. These assumptions are conservative with respect to zuclopenthixol acetate.

Quantity and Cost of Resources

As observed in their files, patients received a mean total of 21 mg of haloperidol IM at the general hospital and 14 mg at the psychiatric hospital, for an average dose per injection of 11.7 mg and 7 mg, respectively. Benztropine IM was prescribed in conjunction with haloperidol IM for 9 (45%) of 20 patients at the general hospital and for 4 (17%) of 24 in the psychiatric hospital. For these patients, the cost of benztropine IM was added to the cost of haloperidol IM. In the base-case analysis, it was assumed that benztropine would be prescribed in conjunction with zuclopenthixol acetate at the same rates as those observed with haloperidol.

Most patients received oral antiparkinsonian and neuroleptic drugs, and about 50% received an oral benzodiazepine. Because the small number of patients does not allow a precise estimate of the consumption of these oral drugs according to the number of haloperidol injections received, and because there was no reason to anticipate a significant difference in this regard, the overall estimate of use was applied to every arm of the decision tree. In the base-case analysis, consumption of neuroleptic and hypnotic drugs was assumed to be identical for zuclopenthixol acetate and haloperidol.

The patients' files revealed that during the 9-day study period, biochemistry blood tests were performed in 84% of the study patients, complete blood count in 82%, and urinalysis in 65%. The percentages were similar in both hospitals.

In the psychiatric hospital, 62.5% of patients were placed in isolation and restraints for a mean of 49 minutes (median, 30 minutes).

Total Costs

The total treatment costs for a 9-day episode in which haloperidol IM or zuclopenthixol acetate (50 mg per injection) was used are reported in Table II. Total treatment costs for zuclopenthixol acetate 100 mg are shown in Table III. Costs are rounded to the nearest dollar in all cases.

Using the base-case estimate for the number of injections required, the total cost associated with haloperidol was $2722.00 in the psychiatric hospital and $2857.00 in the general hospital. For zuclopenthixol acetate 50 mg, the modeled total costs were $2747.00 and $2878.00, respectively. These costs represent an incremental cost of zuclopenthixol acetate over haloperidol of $25.00 per patient in the psychiatric hospital and $21.00 per patient in the general hospital.

Basic hospital stay was the major component of the total cost for both hospital settings and both treatments, representing 87% of the total treatment costs when haloperidol IM was used and 86% when zuclopenthixol acetate was used. Nursing care was the second most costly

Table II. Total treatment costs and incremental costs in 1995 Canadian dollars with zuclopenthixol acetate 50 mg or haloperidol 50 mg.

	Psychiatric Hospital			General Hospital		
Scenario	Zuclopenthixol Acetate	Haloperidol	Difference*	Zuclopenthixol Acetate	Haloperidol	Difference*
Base-case scenario†	$2747.00	$2722.00	$25.00	$2878.00	$2857.00	$21.00
Conservative‡ estimate of the no. of zuclopenthixol acetate injections	$2777.00	$2722.00	$55.00	$2909.00	$2857.00	$52.00
Optimistic§ estimate of the no. of zuclopenthixol acetate injections	$2713.00	$2722.00	($9.00)	$2843.00	$2857.00	($14.00)
25% Reduction in nursing care to treat agitated patients with zuclopenthixol acetate†	$2685.00	$2722.00	($37.00)	$2814.00	$2857.00	($43.00)

*Incremental costs of zuclopenthixol acetate over haloperidol. All costs are rounded to the nearest dollar.
†With base-case estimates for the number of injections.
‡Twenty percent of patients with 1 injection, 45% with 2, and 35% with 3.
§Forty-five percent of patients with 1 injection, 40% with 2, and 15% with 3.

Table III. Total treatment costs and incremental costs in 1995 Canadian dollars with zuclopenthixol acetate 100 mg or haloperidol 50 mg.

Scenario	Psychiatric Hospital			General Hospital		
	Zuclopenthixol Acetate	Haloperidol	Difference*	Zuclopenthixol Acetate	Haloperidol	Difference*
Base-case scenario†	$2770.00	$2722.00	$48.00	$2901.00	$2857.00	$44.00
Conservative‡ estimate of the no. of zuclopenthixol acetate injections	$2803.00	$2722.00	$81.00	$2935.00	$2857.00	$78.00
Optimistic§ estimate of the no. of zuclopenthixol acetate injections	$2733.00	$2722.00	$11.00	$2863.00	$2857.00	$6.00
25% Reduction in nursing care to treat agitated patients with zuclopenthixol acetate†	$2708.00	$2722.00	($14.00)	$2837.00	$2857.00	($20.00)

*Incremental costs of zuclopenthixol acetate over haloperidol. All costs are rounded to the nearest dollar.
†With base-case estimates for the number of injections.
‡Twenty percent of patients with 1 injection, 45% with 2, and 35% with 3.
§Forty-five percent of patients with 1 injection, 40% with 2, and 15% with 3.

element, representing 9% of the total costs, whereas physicians' visits accounted for 2%. When zuclopenthixol acetate was the chosen treatment, it represented 1% of the total cost, whereas haloperidol accounted for 0.1% to 0.3% of the total cost.

For zuclopenthixol acetate 100 mg, the incremental costs in the base-case scenario were $48.00 per patient in the psychiatric hospital and $44.00 per patient in the general hospital.

Sensitivity Analysis

Tables II and III show the results of various sensitivity analyses. A set of analyses was carried out using variations of the probabilities associated with the number of injections of zuclopenthixol acetate needed. The conservative estimate (20% with 1 injection, 45% with 2, 35% with 3) led to an incremental cost of $55.00 and $52.00 per patient at the psychiatric hospital and the general hospital, respectively, for zuclopenthixol acetate 50 mg and $81.00 and $78.00 per patient, respectively, for zuclopenthixol acetate 100 mg. On the other hand, when the optimistic estimate (45% with 1 injection, 40% with 2, 15% with 3) was used, zuclopenthixol acetate 50 mg resulted in cost savings of $9.00 and $14.00 per patient, respectively, and the incremental cost for zuclopenthixol acetate 100 mg dropped to $6.00 and $11.00 per patient, respectively.

When zuclopenthixol acetate was used, a 25% reduction of nursing time was assumed in one sensitivity analysis. This led to cost savings of $37.00 and $43.00 per patient at the psychiatric hospital and the general hospital, respectively, for zuclopenthixol acetate 50 mg and $14.00 and $20.00 per patient, respectively, for the 100-mg dose.

Other changes in the basic assumptions included a reduction of neuroleptic, hypnotic, and antiparkinsonian drug use with zuclopenthixol acetate to reflect its greater sedative effect and somewhat lower incidence of extrapyramidal symptoms. These analyses were carried out only for the 50-mg dose. A 50% reduction in neuroleptic and hypnotic drugs led to a decrease of approximately $8.00 or $9.00 per patient in the incremental cost (data not shown). Assuming that no injectable antiparkinsonian drug would be used in conjunction with zuclopenthixol acetate had a marginal impact on the total cost differentials.

DISCUSSION AND CONCLUSIONS

With regard to clinical consequences, the literature review indicates that zuclopenthixol acetate and haloperidol IM have similar efficacy in controlling psychotic episodes. However, zuclopenthixol acetate was associated with increased sedation, which can present a clinical advantage in some situations. It was also associated with a lower incidence of extrapyramidal symptoms. These clinical advantages must be weighed against the incremental costs of zuclopenthixol acetate in most situations.

However, the estimate of incremental costs depends on the number of zuclopenthixol acetate injections that would be required in practice. The optimistic estimate was associated with cost savings when zuclopenthixol acetate 50 mg was used. This estimate was based on a retrospective analysis of actual use observed in Sweden.[18] The fact that the data were obtained outside the context of a trial could favor their validity as a measure of real use, although the validity in a Canadian context is unknown.

The costs were also sensitive to the additional number of minutes of nursing required to treat agitated patients. If zuclopenthixol acetate decreases the need for close surveillance, it could become a dominant alternative treatment. Because little documented evidence of this effect when compared with haloperidol was found in the literature, a further study of this effect would be warranted. Such a study should provide an estimate of nursing time that is based on observational data.

Whichever drug—zuclopenthixol acetate or haloperidol—is used, it must be remembered that this drug cost is a small fraction of the total costs of caring for an acutely psychotic patient.

ACKNOWLEDGMENTS

This study was partly funded by a grant from Marion Merrell Dow Canada. The authors thank the members of the expert panel, the archivists in the institutions involved in this study, and Mrs. Louise Rousseau for her participation in the data-collection process.

Address correspondence to: Claudine Laurier, PhD, Faculty of Pharmacy, University of Montreal, PO Box 6128, Station Centreville, Montreal, Quebec, Canada H3C 3J7.

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