Objective: The objective of the study was to document the effectiveness of a Cholinesterase Inhibitor (ChE-I) Review Committee in a long-term care (LTC) institution in Montreal, Canada.

Design: Retrospective cohort study.

Setting: Maimonides Geriatric Centre (MGC), a 387-bed LTC facility in Montreal, Canada, in which 352 patients have dementia.

Participants: Fifty-two patients on ChE-I who were reviewed at least once by the ChE-I Review Committee between January and November 2005.

Measurements: Recommendations for discontinuation, actual discontinuation, and restarting of ChE-I, along with reasons underlying these decisions, were collected from the patients’ charts over a 4-month period following Review Committee assessment.

Results: The Review Committee recommended discontinuation of ChE-I in 17 (32.7%) of the 52 patients. After 1 patient died and therefore was excluded from the study, 13 (81.3%) of the remaining 16 were actually discontinued. The most common reasons for recommendation to discontinue ChE-I were insufficient benefit on cognition, activities of daily living (ADL), and behavior. Subsequently, ChE-I was resumed in 4 (30.8%) of the 13 patients discontinued, 2 because of ADL deterioration and 2 at the request of the family.

Conclusions: Through the review process, almost one third of ChE-I users were recommended for discontinuation because of insufficient benefit; the majority of these were discontinued. Fewer than one third were subsequently restarted. A ChE-I Review Committee seemed to be an effective and acceptable model for decision making regarding ChE-I use in LTC.

Keywords: Cholinesterase inhibitors; long-term care; dementia; Alzheimer disease; discontinuation; review committee

Patients with mild to moderate Alzheimer Disease (AD) in the community are frequently treated with cholinesterase inhibitors (ChE-I) as per current guidelines.1–3 As their disease progresses over time with increasing functional disabilities, these patients often become institutionalized.4 Patients with dementia in long-term care (LTC) have been documented to generally have higher functional impairment, dementia severity, and frequency of behavioral problems.4–7

Because of these inherent differences, the effects of ChE-I demonstrated in community-based trials cannot necessarily be generalized to LTC patients. Unfortunately, there are few studies conducted on patients with dementia in the LTC setting.8 Only 2 randomized controlled trials (RCTs) of ChE-I in patients with dementia in LTC have been published.5,9 Although these trials have not shown conclusive evidence to support the effectiveness of ChE-I in the LTC setting, adverse effects have been documented. A recent multicenter observational study in Canada and in France has documented that over 25% of patients receiving ChE-I in the LTC setting met neither the official indication nor the professional guidelines for their use, and the clinical follow-up was incomplete for 40% of the patients.10

Treatment with ChE-I is costly. In Canada, these costs are generally assumed by provincial Medicare under specific criteria when the patients reside in the community or in private LTC facilities. On the other hand, when the patient is admitted to a public LTC facility in Canada, the costs are often covered by the institution’s budget.

Because of the lack of evidence for the effectiveness of ChE-I in LTC, the often suboptimal clinical follow-up, and high drug costs, clinicians in LTC are often confronted with...
the difficult questions of whether and when to discontinue these medications in advanced dementia. Unfortunately, there are no studies concerning discontinuation of ChE-I in the LTC setting in current literature. The lack of supportive evidence for discontinuation and the reports of "discontinuation syndromes" in the literature\textsuperscript{11–13} render it particularly difficult for physicians to make such decisions.

Therefore, we chose to study a particular model of decision making about ChE-I use in the LTC setting: a ChE-I Review Committee. To our knowledge, no such Review Committee has ever been documented in the literature. Specifically, we aimed to document the process and outcomes of the evaluations performed by the Review Committee.

**METHODS**

**Design**

A cohort of patients who were taking ChE-I between January and August 2005 was identified. A chart review was performed to collect information about the patients' evaluations by the ChE-I Review Committee from January 2005 to November 2005. Recommendations for discontinuation, actual discontinuation, and restarting of ChE-I, along with reasons underlying these decisions, were collected from the patients' charts over a 4-month period following the Review Committee assessment. The time frame of this study was chosen to accommodate the agenda of the principal investigator who was doing a 1-year fellowship in Health Care for the Elderly.

**Study Population**

The Maimonides Geriatric Centre (MGC) is a university-affiliated, publicly funded 387-bed LTC facility in Montreal, Canada. Patients require a minimum of 2.5 hours of nursing care per day for admission to this facility. There were 352 (91%) patients documented as having a diagnosis of dementia in 2005. Fifty-eight (16.5%) of these patients received a ChE-I between January and August 2005 and formed our study cohort.

**The Cholinesterase Inhibitor Review Committee**

The Review Committee was formed in November 2001 in response to the availability of donepezil as a limited-use medication covered by provincial Medicare (Régie de l’assurance maladie du Québec, or RAMQ). A limited-use medication is one that is covered by Medicare only if certain specified criteria are fulfilled. The Review Committee consisted of a physician (geriatrician), pharmacist, and occupational therapists who assessed all patients receiving ChE-I. These disciplines were chosen to ensure a comprehensive medical, pharmacological, and functional evaluation of the patients. The Committee's objectives were to ensure that ChE-I was prescribed appropriately. The Committee based its criteria on those of provincial Medicare (RAMQ),\textsuperscript{14} but allowed clinical judgment for heterogeneity of response and potential benefits in each individual case. The RAMQ criteria are as follows (English translation from French):

- Cholinesterase inhibitors are indicated for the treatment of patients suffering from mild to moderate stage Alzheimer Disease. For initial request, the following elements must be present: Mini Mental State Exam (MMSE) score between 10 and 26 or on repeat testing, between 27 and 28 with pertinent justification; and medical confirmation of degree of impairment (intact, mild, moderate, or severely affected) in the following domains: intellectual function (including memory), mood, behavior, independence in activities of daily living (ADL) and activities of domestic life, and social interaction, including the capacity for social conversation. The initial authorization is for 6 months.
- Subsequent requests for continuation require evidence of beneficial effect in each of the following elements: MMSE score of 10 or more, if less than 10, with pertinent justification; decrease in MMSE score by 3 points or less over 6 months, if higher than 3, with pertinent justification; stabilization or improvement of symptoms in one or more of the following domains: intellectual function (including memory), mood, behavior, independence in activities of daily living (ADL) and activities of domestic life, and social interaction, including the capacity for social conversation.

The occupational therapists evaluated each patient using the Mini Mental State Exam (MMSE)\textsuperscript{15} for cognition, the Bedford Alzheimer Nursing Severity scale (BANS-scale)\textsuperscript{16} for activities of daily living, and the Empirical Behavioral Pathology in Alzheimer’s Disease Rating Scale (E-BEHAVE-AD)\textsuperscript{17} for behavioral disturbance. The geriatrician also saw the patient for clinical assessment. Whereas the occupational therapists and pharmacist on the Committee were regular staff at MGC and were involved in the patients' care, the geriatrician was not directly involved in the care of the patients reviewed, beyond performing assessments for the reviews.

Based on the evaluations, the Committee members reached a consensus to recommend continuation or discontinuation of the ChE-I. In the case of uncertainty or disagreement among Committee members, the general approach was to continue the ChE-I with reevaluation in 3 to 6 months. The recommendations and the reasons justifying them were filed in the patient's chart to inform the attending physician. If the attending physician accepted the recommendation and started tapering the ChE-I, the families were informed of the decision. The pharmacist enforced a tapering schedule when ChE-I was discontinued.

The Committee met every 6 to 8 weeks. Each ChE-I user was reviewed every 6 to 9 months. For patients who were already on a ChE-I upon admission to MGC, the medication was continued and supplied by the pharmacy until the Committee evaluated the case.

**Data Collection**

From the patients' charts, the dates of Committee reviews, types of dementia, and current and previous MMSE scores were documented. The following information was also collected for each patient: the Committee's recommendation at
each review, tapering of ChE-I within 4 weeks of recommended discontinuation, actual discontinuation, and resumption within 4 months of the review. The reasons for the Committee’s decision to discontinue, continue, or restart the ChE-I were collected. Written approval to access the patients’ charts was obtained from the Director of Professional Services and from the Ethics Committee at MGC.

**Statistical Analysis**

Descriptive characteristics of the cohort were calculated. Numbers and proportions of those in the cohort recommended for discontinuation, tapering within 4 weeks of the review, actual discontinuation, and restarting were calculated. Reasons for these decisions were also summarized. Patients in the cohort who were not reviewed by the Committee were excluded from this analysis. Patients who died during follow-up were documented and excluded from subsequent calculations.

As some patients were reviewed more than once between January and November 2005, reported proportions were calculated on the basis of the initial reviews alone to ensure consistency across the cohort.

**RESULTS**

The characteristics of the cohort of 58 patients are displayed in Table 1. The cohort consisted of 18 (31%) male and 40 (69%) female, with the mean age being 87.7 (SD 7.1), and mean time since admission to the facility being 2.1 years (SD 1.4). The mean MMSE score of the cohort was 8.8 (SD 8.5, range 0–27). AD was the most common type of dementia in this cohort, and donepezil was the most commonly prescribed ChE-I. Only 3 patients in the cohort (5.2%) were initiated on ChE-I de novo after admission to the facility.

Six patients were not reviewed by the Committee and were excluded from analysis, leaving 52 patients to be followed for their reviews and outcomes.

Among the 52 reviews, the Review Committee recommended discontinuation in 17 (32.7%) patients. After 1 patient died and therefore was excluded from the study, 16 were eligible to assess tapering, discontinuation, and resumption of ChE-I over the 4-month period. The attending physicians started tapering the ChE-I in 13 (81.2%) patients within 4 weeks of the review. The ChE-I was then actually discontinued in all 13 (100%) patients. Of these patients, 4 (30.8%) were restarted on ChE-I within 4 months of the review (see Figure 1 for flow diagram).

The Committee often cited more than one reason or domain to justify its decision to discontinue or continue the ChE-I. The reasons for the recommendation to discontinue the ChE-I were, in order of frequency, insufficient benefit on cognition (15 patients), ADL (12 patients), behavior (5 patients), and mood (1 patient). The reasons for the Committee’s decision to continue the ChE-I were, in order of frequency, benefit on ADL (27 patients), cognition (13 patients), behavior (6 patients), social function (2 patients), and mood (1 patient). The mean MMSE score of the patients recommended for discontinuation of ChE-I was 0.9 (SD 2.4); the score of those recommended for continuation was 13.3 (SD 7.2).

The reasons for restarting ChE-I were ADL deterioration in 2 (50%) patients and request by the family in 2 (50%) patients. Eleven (84.6%) of the 13 patients discontinued did not have adverse outcomes during the 4-month follow-up period.

![Fig. 1. Flow diagram of outcomes of reviews.](image_url)
DISCUSSION

Through the Review Committee’s evaluation process, almost one third of the cohort was recommended for discontinuation of ChE-I, most commonly because of insufficient benefit on cognition, ADL, and behavior. Most of the patients recommended for discontinuation were subsequently tapered and discontinued. Among those discontinued, fewer than one third were restarted, and most were observed to have no adverse outcomes in the post-review follow-up period of 4 months.

Our results suggest that a relatively high proportion of patients on ChE-I in LTC may not be benefiting enough from these medications to warrant continuation. A ChE-I Review Committee could identify these patients through clinical evaluation. The recommendations made by the Review Committee in our study had a high acceptance rate by the attending physicians, resulting in over 80% actual discontinuation. Furthermore, only 2 patients were restarted at the request of the family, suggesting that decisions made by the Review Committee were accepted by the majority of patients’ families as well.

Compared to strict observation of criteria such as those defined by provincial Medicare (RAMQ), a Review Committee that considers the heterogeneity of patients’ response to ChE-I represents better medical practice and may be better suited to this population. The multidisciplinary approach to evaluation, with the expertise of a geriatrician, a pharmacist, and occupational therapists, ensures a comprehensive assessment. The pharmacist and occupational therapists on the Committee are involved in the patients’ regular care, and hence may present a conflict of interest in the review process. However, the use of objective evaluation tools and the inclusion of the geriatrician who is not otherwise involved in the patients’ care should ensure an objective decision. We believe a multidisciplinary Review Committee, such as that at MGC, may be an effective and highly accepted model to guide decision making regarding the use of ChE-I in the LTC setting.

The issue of discontinuation of ChE-I in severe dementia in LTC is an important one. Unfortunately, there are no trials in the current literature addressing this question. There are, however, reports of “discontinuation syndromes” or clinical deterioration in community patients upon abrupt withdrawal of ChE-I. These reports describe community-dwelling patients with mild to moderate dementia, and cannot be generalized to include patients with more severe dementia in LTC. Furthermore, pharmacological principles and good clinical practice dictate that, similar to other psychotropic medications such as benzodiazepines and selective serotonin reuptake inhibitors, ChE-I should be tapered gradually rather than withdrawn abruptly to avoid a withdrawal effect.

Contrary to the “discontinuation syndromes” described in the literature, the results from our study suggest that discontinuation of ChE-I through gradual tapering in severe dementia in LTC may not result in adverse clinical outcomes or sudden deterioration in most patients. Although ADL deterioration was quoted as the reason for restarting the ChE-I for 2 patients in our study, it is difficult to conclude, given the progressive nature of dementia, whether the functional deterioration occurred as a result of disease progression or medication discontinuation. Only an RCT on discontinuation of ChE-I in LTC with a longer observation period can objectively elucidate this issue.

This study was a pilot, descriptive study. It is limited by the lack of controlled data and a small cohort size. The prevalence of ChE-I use at MGC was 16.5%, which was higher than the 6% rate documented in a recent multicenter study. This suggests that there may be heterogeneity in therapeutic practices regarding dementia and ChE-I among different centers and countries; hence our findings may not be representative of all LTC settings. The university affiliation of MGC, its high prevalence of dementia, the advanced mean age of its patients, and its prevalence of severe dementia may also not be representative. This study, however, was the first investigation into the role of a ChE-I Review Committee as a model for decision making in LTC, and a first step in generating a hypothesis to address discontinuation of ChE-I in severe dementia in LTC.

CONCLUSION

Our study has shown that a multidisciplinary Review Committee is a feasible and acceptable model for decision making regarding the use of ChE-I in LTC. The Committee in our study identified a proportion of ChE-I users recommended for discontinuation due to insufficient benefit. Discontinuation of ChE-I with gradual tapering did not result in adverse outcomes in most patients in our study. These encouraging results support further research into the discontinuation of ChE-I in severe dementia in LTC; specifically, a large scale RCT would be useful in addressing this issue.

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REFERENCES