

# A Drug Use Evaluation of Bedtime Sedation in Geriatric Patients

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## ABSTRACT

A pilot study was designed to assess the feasibility of a shared regional drug use evaluation (DUE) program involving patients. A retrospective DUE on the use of benzodiazepines, chloral hydrate and neuroleptics for bedtime sedation was performed on geriatric patient populations from two hospitals. Regional program staff coordinated the DUE, including development of the criteria and chart review. The participating Pharmacy departments performed the internal administrative and Pharmacy and Therapeutics committee communications.

Forty patient charts from two sites were reviewed. The DUE results indicated different rates of drug use and discontinuation of therapy between the two geriatric patient populations. The overall rates of inappropriate drug use were similar. One undesirable clinical outcome occurred. Benzodiazepine use for more than 30 days was high in both groups. Identification of the justification for drug use, dosage reduction and drug discontinuation did not occur in the majority of patients. The pilot study identified areas where use of bedtime sedation could be improved, and allowed development of DUE criteria for future evaluation.

**Key Words:** bedtime sedation, benzodiazepines, drug use evaluation, geriatrics

## RÉSUMÉ

On a effectué un projet pilote pour voir si on pouvait implanter un programme régional d'évaluation de l'utilisation des médicaments par les patients âgés. On a procédé pour cela à une analyse rétrospective de l'utilisation des benzodiazépines, de l'hydrate de chloral et des neuroleptiques par des patients âgés de deux hôpitaux, au coucher, en guise d'hypnotique. Le personnel du programme régional a coordonné l'exercice, établi les critères d'évaluation et revu les dossiers. Les départements de pharmacie participants se sont occupés des communications entre l'administration et le Comité de pharmacologie.

Les dossiers de 40 patients ont été examinés aux deux endroits. Les résultats révèlent des taux différents d'utilisation des médicaments et d'abandon du traitement pour les deux populations de patients âgés. Le taux global d'utilisation inappropriée des médicaments était similaire dans les deux hôpitaux. Un seul dénouement clinique indésirable a été relevé. L'utilisation de benzodiazépine pendant plus de 30 jours était relativement élevée pour les deux groupes. On n'a pas justifié l'indication du médicament, la diminution de la posologie et l'abandon du traitement dans la majorité des cas. Le projet pilote a cerné dans quelles situations il conviendrait d'améliorer l'utilisation des hypnotiques au coucher et a permis l'établissement de critères en vue d'une évaluation ultérieure de l'utilisation des médicaments.

**Mots clés:** benzodiazépines, évaluation de l'utilisation des médicaments, gériatrie, hypnotique

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## INTRODUCTION

Quality assurance for pharmacy departments includes drug use evaluation (DUE). Since accreditation reviews for hospitals examine quality assurance activities, DUE is a significant responsibility of pharmacists, physicians, and hospital administrators. With the growth of the geriatric population has come the recognition of adverse drug reactions as a reason for hospital admission. Adverse drug reactions are also associated with

patient incidents in hospital. To facilitate DUE in geriatric patients, a pilot study was designed to assess the feasibility of a shared program between two hospitals. This was done as part of a larger regional formulary review and DUE project in which members of the program staff coordinated and assisted in the completion of DUE within the participating hospitals.

The reasons for selection of a DUE on bedtime sedation in the geriatric patient group stemmed

from the literature concerning adverse drug reactions and the prevalence of psychoactive drug use in geriatric patients. These concerns have led to national health care regulations in the United States (Omnibus Budget Reconciliation Act, 1990) which attempt to limit psychoactive drug use in geriatric nursing home patients. The use of benzodiazepines with long elimination half-lives has been associated with hip fractures.<sup>1</sup> The literature also includes documen-

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tation of adverse drug reactions (e.g., falls, confusion, and bizarre behaviour) related to triazolam use in geriatric patients.<sup>2</sup> Indeed, specific recommendations to limit the dosage and duration of use for triazolam were developed by the Health Protection Branch (Health and Welfare Canada) in 1991 and in 1992.<sup>3,4</sup> In the United Kingdom, the drug was withdrawn from the market. Avorn et al<sup>5</sup> reported a reduction in the use of benzodiazepines of 20% in the study group compared to 9% in the control group after implementation of an educational program targeted at physicians, nurses, and aides. They noted reduced psychoactive drug use without adverse effects on behaviour or level of functioning. Bedtime sedative use of selected psychoactive agents was chosen for the DUE. The prevalent agents in the participating hospitals were benzodiazepines, chloral hydrate, and neuroleptics.

DUE criteria for appropriate use of any drug for bedtime sedation have not been published. Benzodiazepines are first line drugs for bedtime sedation.<sup>6</sup> However, neuroleptics and chloral hydrate remain in use in geriatrics. When a neuroleptic is used for bedtime sedation, haloperidol has historically been chosen.<sup>7</sup> The choice of drug may be considered somewhat controversial. Dosing recommendations for geriatric patients are also problematic. Typical geriatric drug dosing references suggest the reduction of drug doses by 50%.<sup>7</sup> Some recommend use of 25% to 50% of the standard dose of hypnotics and anxiolytics for patients over 80 years of age because of altered pharmacokinetics and pharmacodynamics.<sup>8</sup> Despite these general recommendations, specific dosing guidelines for many drugs do not exist. A 1984 consensus conference on drugs and insomnia suggested a

number of measures to encourage appropriate drug use.<sup>6</sup> First, treatment of underlying medical or psychiatric disorders should occur since insomnia is a common symptom of many conditions. Second, insomnia should be classified as transient, short-term or long-term. Transient or short-term insomnia may require drug use of several days or three weeks duration, respectively. Drug use for long-term insomnia is controversial since the drugs are not considered effective for long-term use. Third, drug selection, when indicated, should consider the elimination half-life and presence of active metabolites of the benzodiazepine chosen. Fourth, duration of use should be related to the degree to which the patient is troubled by the insomnia, and patient education and non-drug measures should accompany intermittent benzodiazepine use. Fifth, the risks of drug use are not insignificant (e.g., decreased daytime performance, drug dependence, rebound exacerbation of sleep disturbance upon withdrawal). The population at increased risk for adverse effects is geriatric patients.

Hence, benzodiazepine, neuroleptic, and chloral hydrate use for bedtime sedation was chosen as a regional DUE pilot study to describe the characteristics of drug use in an attempt to improve geriatric patient care.

## **METHODS**

A retrospective DUE was carried out in two hospitals. Consent was required from Pharmacy, hospital administration, and medical staff for participation in the program to ensure access to patient charts and to address the issue of patient confidentiality. The DUE criteria were developed by the program staff and reviewed by a pharmacy advisory group, a psychogeriatric physician, and the Pharmacy departments of both hospitals.

Patient identification occurred early in 1993. This was done by the Pharmacy contact in each hospital (Director of Pharmacy). The criteria were submitted by the Directors to the hospitals' Pharmacy and Therapeutics (P & T) committees in April - June, 1993. The forms used for data collection were tested and revised by the program staff during the summer of 1993. Data collection for the DUE occurred between August 23 and September 23, 1993. All data collection was performed by one program staff member. A report of each hospital's results was prepared by the program staff and discussed with the Director of Pharmacy in October, 1993. The report was discussed with the participating hospitals' medical staff and/or P & T committee by the Directors of Pharmacy.

Patients eligible for inclusion in the DUE were identified. Geriatric patients were defined as over the age of 60 years. Hospital A was a 202-bed long-term care facility with a pharmacy staff of 3.0 full-time equivalents (FTE). For Hospital A, patients admitted to the chronic or rehabilitation beds, for whom a benzodiazepine, neuroleptic or chloral hydrate for bedtime sedation was prescribed, were eligible. Patient admissions, over a six-month period from October 1991 to March 1992, were used to identify potential charts for review. Hospital B was a 200-bed psychiatric facility with pharmacy staff of 5.0 FTE. For Hospital B, patients admitted to the acute psychogeriatric ward, for whom one of the above drugs for bedtime sedation was prescribed, were eligible. Patient admissions, over a six-month period from September 1992 to February 1993, were used. Patients for whom the reason for drug use was unclear (e.g., twice daily and bedtime use of a neuroleptic) were excluded. A random sample of 20 patient charts from each hospital was selected with

the use of a random numbers table. The choice of sample size was arbitrary but was made in an attempt to review at least 50% of the patient admissions. Description of the results was limited to the number of patients with drug use for bedtime sedation, discontinuation of therapy by the end of the review, inappropriate drug use and outcome of drug use, and benzodiazepine use for greater than 30 days.

The DUE criteria were approved by the participating hospitals' P & T committees. Appropriate drug use and outcome are outlined in brief as follows. Justification for use of bedtime sedation was appropriate if transient or short-term drug use of less than 21 days duration occurred, or if long-term insomnia was noted by the physician in the patient chart.<sup>6,9-12</sup> Poor documentation of the justification for use was anticipated, therefore, "cannot assess" was also present in the criteria for the purpose of describing the findings. Patient data collected were age, sex, concurrent medications, and past medical and psychiatric history. In order to maintain confidentiality, patient names and treating physician names were not included on the data collection forms. A coding form was maintained by the Director of Pharmacy which identified the applicable patients and physicians for future use within the hospital.

#### Assessment of Drug Use

Five elements were included in the assessment of drug use: a) The drug for bedtime sedation was considered appropriate if chloral hydrate, haloperidol, lorazepam, oxazepam or temazepam was used;<sup>7-9 11,13</sup> b) Contraindications to the drug used were noted if present;<sup>11,14</sup> c) For the purposes of defining the appropriate dose, approximate equivalent doses of benzodiazepines and neuroleptics were included as part of the DUE criteria;<sup>7,8,11,13,15-17</sup> For benzo-

diazepines, the appropriate dose for patients started on the drug was less than or equal to lorazepam 1 mg "qhs" equivalent. For patients already on the drug, the appropriate dose was not to exceed the equivalent of lorazepam 2 mg "qhs". The appropriate dose of neuroleptic was less than or equal to haloperidol 1 mg "qhs" equivalent. For chloral hydrate, the appropriate dose for patients started on it was 500 mg "qhs", and 1 g "qhs" for those already receiving it; d) Dosage titration toward discontinuation of the drug (not due to side effects) was considered appropriate if at least one attempt to titrate the dose down was made during the period of chart review. Titration of the dose implied that the physician changed the drug order; e) Duration of therapy was related to the justification for use. Transient or short-term drug use was up to 21 days duration. For chloral hydrate, appropriate duration was less than 14 days of continuous use.<sup>11</sup> When the justification for use could not be assessed, it was not possible to evaluate the duration of therapy. More specifically, the first drug used for bedtime sedation for each patient was assessed for selection and initial dose relative to the criteria. For patients admitted to Hospital A, only the first three months of each admission were reviewed. For patients admitted to Hospital B, the entire admission was reviewed since admissions were on average three months long. Overall, drug use was classified as appropriate or inappropriate based on the five elements described above.

#### Assessment of Outcome of Drug Use

Four elements were included for the DUE: a) If there was no significant drug interaction with the benzodiazepine, neuroleptic or chloral hydrate, then the outcome of drug use was considered appropriate;<sup>11</sup>

b) If there was no side effect resulting in dose reduction or drug discontinuation, then the outcome was considered appropriate; c) Dosage outcome was considered appropriate if drug use for bedtime sedation was absent at the end of the review or if still present, the dose was lower than at the beginning of the review. Dosage outcome was considered inappropriate if the dose was unchanged or higher at the end of the review. It could not be assessed if the drug used at the end of the review was of a different category than the initial drug (e.g., benzodiazepine followed by neuroleptic use) since the relative doses could not be compared; d) Clinical outcome was desirable if drug use for bedtime sedation was discontinued by the end of the review or if still present, no complications were noted. Clinical outcome was undesirable if complications occurred or if inadequate sedation was noted at the end of the review. Overall, outcome of drug use was classified as appropriate or inappropriate based on the four elements described above.

#### RESULTS

Forty patient charts were reviewed in this DUE on benzodiazepines, neuroleptics, and chloral hydrate for bedtime sedation. Twenty of the patients were geriatric admissions to Hospital A. The total number of admissions to this hospital during the applicable period was 83. Of these, 30 patients (36%) were prescribed one of the drugs for bedtime sedation and, therefore, were eligible for inclusion in the DUE. A sample of 20 of the eligible charts (67%) were reviewed. The other 20 patients were admissions to Hospital B. The usual number of admissions per month to this ward was 12 to 13. During a six-month period, a minimum of 72 admissions would be anticipated. Thirty-five patients were prescribed one of

the drugs for bedtime sedation and were eligible for inclusion in the DUE. A sample of 20 of the eligible charts (57%) were reviewed. Table I summarizes the numbers of male and female patients, and age distribution for the patients reviewed. Table II presents the DUE results for the two patient groups.

### Drug Use

For the patient group from Hospital A, a benzodiazepine was used in 19 of the cases and chloral hydrate in one case. The benzodiazepine used was oxazepam in nine cases, lorazepam in six cases, and triazolam in four cases. The use of triazolam accounted for the cases of inappropriate drug used. Dosage titration was inappropriate in 14 cases as no attempt to reduce the dose was evident on chart review. Dosage titration led to discontinuation of the drug in five cases and

lower dose at the end of the review in one case. The initial dose used was inappropriate in one case. This patient received triazolam 0.375 mg "qhs". Duration of therapy was inappropriate in one case. A patient received chloral hydrate regularly for 81 days. No contraindications to drug use were noted. Overall, inappropriate drug use was noted in 14 cases. Justification for use was "cannot assess" in all 20 cases. There was no transient or short-term drug use, and no documentation of long-term insomnia in any patient chart. This resulted in poor assessment of duration of therapy. Fifteen of the 16 patients in hospital for more than 30 days who were treated with a benzodiazepine received the drug for more than 30 days.

For the patient group from Hospital B, a benzodiazepine was used for bedtime sedation in 16 cases. This included seven cases of

lorazepam use, six cases of oxazepam use, and three cases of temazepam use. Chloral hydrate was used in three cases and haloperidol in one case. No inappropriate drug was used. Dosage titration was inappropriate in 13 cases. Dosage titration led to discontinuation of the drug in two cases, lower dose at the end of the review in three cases, and unchanged dose at the end of the review despite attempts at dose reduction in two cases. Initial dose was inappropriate in three cases. These included the use of haloperidol 2 mg "qhs", temazepam 30 mg "qhs", and oxazepam 30 mg "qhs". Duration of therapy was inappropriate in two cases: chloral hydrate was given regularly to one patient for 18 days and lorazepam was given to another patient continuously for 37 days for documented long-term insomnia. One case of contraindicated drug use occurred: chloral hydrate was used for a patient with estimated creatinine clearance of less than 50 mL/min. Overall, inappropriate drug use was noted in 15 cases. Justification for use was "cannot assess" in 18 cases. Again the data on duration of therapy were incomplete. Benzodiazepine use for more than 30 days occurred in 10 of 11 cases.

TABLE I: Patient gender and age characteristics for the DUE

	Hospital A	Hospital B
No. of Patients Studied	20	20
Number of males/females	5/15	5/15
Age distribution		
60 - 70 years	4	2
71 - 80 years	7	12
> 80 years	9	6

TABLE II: Results of the DUE

		Hospital A	Hospital B
No. of Patients Studied		20	20
No. of patients not receiving drug at end of review		9	2
Inappropriate drug use	Drug used	14	15
	Contraindication	4	0
	Initial dose	0	1
	Duration	1	3
	Dosage titration	1	2
Inappropriate outcome	Dosage titration	14	13
	Drug interaction	9	14
	Side effects	0	0
	Dosage outcome	0	1
Benzodiazepine use for more than 30 days	Dosage outcome	9	13
	Clinical outcome	0	1
		15 of 16 cases	10 of 11 cases

### Outcome of Drug Use

For the patient group from Hospital A, no significant drug interactions, side effects or undesirable clinical outcome were noted. Outcome was not assessed in one case since the relative doses could not be evaluated when a change from a benzodiazepine to chloral hydrate was made. Inappropriate dosage outcome occurred in nine cases. Drug use for bedtime sedation was present at a lower dose in one case, and was absent at the end of the review in another nine cases. Four of these patients had active "prn" drug orders at the end of the review, but were

not receiving any drug. On the judgement of the nursing staff, the drug was not required. For the remaining five cases, the drug was discontinued by physician order.

For the patient group from Hospital B, outcome was inappropriate in 14 cases. Outcome was not assessed in one case where a change from a benzodiazepine to chloral hydrate occurred. Inappropriate dosage outcome accounted for 13 of the cases. In the last case, the dose was reduced after the patient sustained a fall in hospital. The initial dose used was inappropriate as defined by the criteria and the patient had a history of difficulty with mobility. Therefore, the patient may have experienced side effects and experienced a complication resulting in an undesirable clinical outcome. Drug use for bedtime sedation was present at a lower dose in three cases and was absent at the end of the review in two cases.

## DISCUSSION

All facets of this DUE should be evaluated in light of its preliminary nature. For simplicity, dimenhydrinate, zopiclone, trazodone and other alternative agents for bedtime sedation were excluded. Their exclusion is not meant to comment on their place in therapy.

Discussion of the reports of the two participating hospitals' results with the Directors of Pharmacy took place in October, 1993.

Several areas of similarity in the results of the DUE on the two patient groups were noted. Lack of transient or short-term drug use (up to 21 days), and lack of documentation of long-term insomnia was common to both hospital groups. Subsequent to this, lack of dosage titration and long duration of therapy would not be unexpected due to an apparent lack of definition of the endpoint of therapy. Benzodiazepine use for more than 30 days was common to both hospital groups. The overall

inappropriate drug use was high in both groups with the main reason being the lack of dosage titration down toward discontinuation of the drug. There was an apparent lack of definition of a treatment plan with attention to justification, dosage titration, and duration of therapy. Specific recommendations on drug use in long-term care facilities by the Coroner's Committee of the Ontario Medical Association suggest documentation of the reasons for drug use.<sup>18</sup>

There were also some differences between the results of the two groups. There appeared to be a difference in the rate of use of drug therapy for bedtime sedation, with Hospital A exhibiting use in 36% of admissions while the rate of usage in the Hospital B patients was estimated to be higher (approximately 50%). The DUE results also showed differences in the rates of inappropriate initial dose used and inappropriate drug used. For the three patients from Hospital B, initial drug doses were higher than defined in the criteria. It is interesting to speculate on the reasons for this. It may have been due to an increased comfort level by the physicians with higher sedative dosing in the patient population or the presence of underlying psychiatric disorders more resistant to therapy. However, one of the patients treated with an inappropriate dose experienced a fall which may have been associated with drug therapy. For the patient group from Hospital A, triazolam use resulted in the four cases of inappropriate drug used. Since the time of these patient admissions triazolam use has declined, however the drug was present on the hospital formulary (Fall, 1993). The overall rate of inappropriate outcome was quite high due to unchanged or higher doses at the end of the review. For nine of the Hospital A patients and 13 of the Hospital B patients,

the dosage outcome was inappropriate. However, approximately half of the appropriate dosage outcome cases in the Hospital A patients were due to nursing assessment with no drug therapy for bedtime sedation in patients with "prn" orders.

Upon discussion of the results with the Directors of Pharmacy, some areas of concern became apparent. The difficulties in the withdrawal of a drug for which physical and/or psychological dependence has evolved is much more complex than can be defined in DUE criteria. Related to the DUE criteria, the areas of concern were the lack of identification of the justification for use (transient, short-term or long-term insomnia), long duration of therapy, lack of dosage titration, triazolam use and chloral hydrate use. The definition of justification for use, though difficult, would facilitate the involvement of both nursing and pharmacy staff in encouraging appropriate dosage titration and duration of therapy. The use of automatic stop orders (ASO) as a policy initiated by the P & T committee is one option to limit the duration of use, however, it may not lead to the development of a treatment plan for the patient. Increased attention to drug use for bedtime sedation by all members of the health care team may be more effective in promoting patient care objectives. Termination of long-term drug use presents a difficult dilemma for physicians. The attending physician may not have initiated the drug and may hesitate to change it. However, it is easy to see how inappropriate use of drugs for bedtime sedation may be perpetuated in this manner. The concerns over triazolam have been widely publicized to physicians in newsletters.<sup>3,4</sup> The patients in this DUE who received triazolam were treated before publication of the newsletters, however, these

newsletters followed published reports in the literature at least as early as 1987.<sup>2</sup> Concerns about chloral hydrate use have not been as widely publicized, however, its use has apparently declined. It should not be included as an appropriate drug if the criteria were revised. Chloral hydrate is metabolized primarily to trichloroethanol which is pharmacologically active. Though chloral hydrate itself undergoes very little renal elimination, the main route of elimination of the metabolites is renal. Bennett et al<sup>14</sup> recommend against the use of chloral hydrate in patients with creatinine clearance < 50 mL/min. Estimation of creatinine clearance by the Cockcroft and Gault method for patients over the age of 80 years with serum creatinine in the normal range (80 - 120 µmol/L) is often < 50 mL/min. In addition, tolerance and dependence may occur within two weeks of therapy and resemble alcoholism.<sup>11</sup> Withdrawal of chloral hydrate from patients who are physically dependent can result in hallucinations and delirium tremens.<sup>11</sup> The appropriateness of chloral hydrate or triazolam use in the geriatric population is questionable.

Discussion of the DUE results by the Directors with the P & T committees will be necessary in order to define the follow-up actions appropriate for the two participating hospitals. Limiting the duration of bedtime sedation orders and removal of triazolam from the hospital formulary are two possibilities. Simplified follow-up activities to the DUE should be possible for hospitals with limited resources. Rather than repeating the DUE in its entirety, audits focusing on the overall rate of bedtime sedation use, selection of drug for bedtime

sedation, dose used, duration of benzodiazepine use, and duration of chloral hydrate use would be useful. Within the Pharmacy department, review of the results could lead to improvement in the drug order review process (e.g., evaluation of doses ordered for patients relative to their age and medical history). Pharmacy departments should consider their role in educating the patient, medical and nursing staff regarding the use of drugs for bedtime sedation and the risks of drug use in patients over the age of 60 years.

It is possible to overcome time constraints and to perform DUE activities through the use of shared programs between hospitals. In this way, the existing lines of communication within each hospital can be utilized by the Directors of Pharmacy to improve patient care. Physicians, pharmacists, and nurses should define their roles and collaborate in the use of DUE results and education programs, as suggested by Avorn et al<sup>5</sup>, to reduce psychoactive drug use and improve the quality of patient care. 

## REFERENCES

1. Ray WA, Griffin MR, Downey W. Benzodiazepines of long and short elimination half-life and the risk of hip fractures. *JAMA* 1989;262:3303-7.
2. Phillips MS. Quality assurance through adverse drug reaction reporting: Improving hypnotic prescribing. *Hosp Pharm* 1990;25:246-8.
3. Ontario Medical Association's Committee on Drugs and Pharmacotherapy. *The Drug Report* 1991 (Nov); 35.
4. Ontario Medical Association's Committee on Drugs and Pharmacotherapy. *The Drug Report* 1992. (June); 37.
5. Avorn J, Soumerai SB, Everitt DE, et al. A randomized trial of a program to

- reduce the use of psychoactive drugs in nursing homes. *New Engl J Med* 1992;327:168-73.
6. Consensus Conference: Drugs and insomnia - the use of medications to promote sleep. *JAMA* 1984;251:2410-4.
7. Kane RL, Ouslander JG, Abrass IB. Drug Therapy. In: Essentials of clinical geriatrics. New York: McGraw-Hill; 1989:341-71.
8. Lader M. The use of hypnotics and anxiolytics in the elderly. *Int Clin Psychopharmacol* 1986;1:273-83.
9. Jenike MA. Psychoactive drugs in the elderly: Antipsychotics and anxiolytics. *Geriatrics* 1988;43(9):53-65.
10. Reeves R. Comparison of triazolam, flurazepam and placebos as hypnotics in geriatric patients with insomnia. *Clin Pharm* 1977;17:319-23.
11. McEvoy GK, Litvak K, eds. AHFS Drug Information 92. Bethesda: American Society of Hospital Pharmacists, 1992.
12. Wincor MZ. Sleep disorders. In: DiPiro JT, Talbert RL, Hayes PE, et al, eds. Pharmacotherapy. A pathophysiologic approach. New York: Elsevier; 1989:782-9.
13. Walker JI, Covington TR. Psychiatric disorders. In: Covington TR, Walker JI. Current geriatric therapy. Philadelphia: W.B. Saunders Co.; 1984:75-103.
14. Bennett WM, Aronoff GR, Golper TA, et al. Drug prescribing in renal failure. 2nd ed. Philadelphia: American College of Physicians; 1991.
15. Harvey SC. Hypnotics and sedatives. In: Gilman AG, Goodman LS, Rall TW, et al, eds. The pharmacological basis of therapeutics 7th ed. New York: MacMillan Publishing Co.; 1985:339-71.
16. Central nervous system drugs. In: Olin BA, Hebel SK, Dombek CE, eds. Facts and comparisons. St. Louis: J.B. Lippincott Co.; 1990:265.
17. Reynolds JEF, Prasad AB, eds. Martindale: the extra pharmacopoeia, 28th ed. London: The Pharmaceutical Press, 1982.
18. Ontario Medical Association's Committee on Drugs and Pharmacotherapy. *The Drug Report* 1994, (Apr);46.