ADVANCES

Emergency department visits for acetaminophen overdose: a Canadian population-based epidemiologic study (1997–2002)

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ABSTRACT

Objective: We describe the epidemiology of emergency department (ED) visits for acetaminophen overdose in a large Canadian health region, with a focus on sociodemographic risk factors and temporal trends.

Methods: Patients presenting to an ED in the Calgary Health Region (population ~1.1 million) for acetaminophen overdose between 1997 and 2002 were identified using regional administrative data.

Results: A total of 2699 patients made 3015 ED visits for acetaminophen overdose between 1997 and 2002, corresponding to an age- and sex-adjusted incidence of 45.7 per 100 000 population. Alcohol-related disorders were common (19%) and overdose rates were higher in females, younger patients, Aboriginals and social assistance recipients. The incidence decreased from 52.6 per 100 000 in 1997 to 35.1 per 100 000 in 2002 (34% relative reduction; $p < 0.0005$). When classified according to suicidal intent, the rates of intentional and unintentional overdose (69% and 25% of all overdoses, respectively) showed similar temporal trends. A marked seasonality was observed, with a peak in spring and early summer.

Conclusions: ED visit rates for acetaminophen overdose fell between 1997 and 2002. High-risk groups, including young females and marginalized populations, may benefit from preventive and educational initiatives.

Key words: acetaminophen, database, epidemiology, paracetamol, self-injurious behaviour

RÉSUMÉ

Objectif : Nous décrivons l'épidémiologie des visites à l'urgence pour surdose d'acétaminophène dans une grande administration régionale de la santé, au Canada, en insistant sur les tendances temporelles et les facteurs de risque sociodémographiques.

Méthodes : Les patients qui se sont présentés à l'urgence dans l'administration régionale de la santé de Calgary (population ~1,1 million) pour surdose d'acétaminophène entre 1997 et 2002 ont été repérés à l'aide des données administratives régionales.

Résultats : Au total, 2699 patients ont fait 3015 visites à l'urgence pour surdose d'acétaminophène entre 1997 et 2002, ce qui correspond à une incidence comparative selon l'âge et le sexe de 45,7 par 100 000 habitants. Les troubles liés à l'alcool étaient fréquents (19 %) et les

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taux de surdose étaient plus élevés chez les femmes, les patients plus jeunes, les Autochtones et les bénéficiaires de l'aide sociale. L'incidence est passée de 52,6 à 35,1 par 100 000 habitants entre 1997 et 2002 (diminution relative de 34 %, p < 0,0005). Classés selon l'intention suicidaire, les taux de surdose intentionnelle et non intentionnelle (69 % et 25 % de toutes les surdoses respectivement) affichaient des tendances temporelles semblables. Une fluctuation saisonnière marquée a été observée, le nombre maximal étant atteint au printemps et au début de l'été.
Conclusions : Le nombre de visites à l'urgence pour surdose d'acétaminophène a diminué entre 1997 et 2002. Des initiatives de prévention et d'information pourraient avantager les groupes à risque élevé, y compris les jeunes femmes et les populations marginalisées.

Introduction

Acetaminophen is the most commonly used over-the-counter analgesic and antipyretic in many countries, including Canada, and it has emerged as the leading cause of deliberate self-poisoning.[1,2] The major toxicity in cases of acetaminophen overdose is severe hepatic necrosis. While the recommended maximal dosage is 4 g daily, supratherapeutic ingestions exceeding 10 g are sufficient to cause acute liver failure (ALF).[3–6] Moreover, even lower doses have been reported to cause hepatotoxicity in patients with risk factors that include fasting and alcohol abuse.[3,7–9] Recent data from the US ALF Study Group identified acetaminophen as the etiology of ALF in approximately 50% of cases.[3,10] Although the prognosis of acetaminophen-related ALF is better than for other causes, mortality is approximately 30% and 8% of patients require liver transplantation.[3,4,10] The direct cost of acetaminophen overdose has been estimated at more than $87 million annually in the United States.[11]

In light of these important public health implications, the epidemiology of acetaminophen overdose has been the focus of numerous investigations.[1,12–17] Many studies have originated in the United Kingdom, where an estimated 70 000 cases occur annually[12,18] and where rising overdose rates prompted legislation limiting over-the-counter acetaminophen sales in 1998.[19] These restrictions required blister packing of acetaminophen-containing preparations and restricted non-prescription sales to limited quantities. Although data are conflicting, most studies suggest a benefit to this legislation.[1,12,13,15,16,20] For example, Turvill and colleagues reported a 21% reduction in acetaminophen overdoses and a 64% decline in severe overdoses presenting to the Royal Free Hospital in London during the year following this legislation.[11] A Canadian study showed acetaminophen overdose hospitalization rates of 22–29 per 100 000 population in 2002, but this excludes cases that did not require inpatient management, hence it does not describe population-based risk factors for this condition.[1] Other studies have identified a higher risk in females and younger age groups,[13,14] but sociodemographic risk factors are incompletely described.

The primary objective of this study was to examine temporal trends in the incidence of emergency department (ED) visits for acetaminophen overdose in a Canadian health region. Our secondary objective was to describe population-based risk factors for acetaminophen overdose, including sociodemographic factors. A more complete understanding of the epidemiology of acetaminophen overdose may help target future preventive and educational strategies in Canada.

Patients and methods

Study population

The study population consisted of Calgary Health Region (CHR) residents visiting an ED for acetaminophen overdose between April 1, 1997, and March 31, 2002. The CHR provides virtually all medical and surgical care to the approximately 1.1 million residents of Calgary and surrounding communities in southern Alberta. Acetaminophen overdose cases were identified using data derived from the Ambulatory Care Classification System (ACCS) database,[21,22] which contains information on all ED services in the province of Alberta. Since the Canadian health care system is a public, single payer system, the ACCS database captures almost every medical event resulting in emergency treatment. Available data elements include up to 15 diagnosis and 10 procedure coding fields, demographic details, region of residence and disposition from the ED. Acetaminophen overdose cases were identified via a search of the 15 diagnosis coding fields for diagnostic code 965.4 according to the *International Classification of Disease, Ninth Revision, Clinical Modification* (ICD-9-CM)[23] in the 1997–2001 data, and T39.1 according to ICD-10[24] in the 2002 data. Trained health records nosologists code each ED encounter before submission of the data to Alberta Health and Wellness. Coding is based on the entire ED

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record but not the inpatient record for patients who are hospitalized. The first ED separation was assigned as the index visit for patients with repeated visits for acetaminophen overdose.

Definitions of variables

Individuals with acetaminophen overdose were linked with the Alberta Health Care Insurance Plan (AHCIP) Registry[21] using a unique personal identifier. The AHCIP is a government-administered universal plan providing health care for more than 99% of Albertans.[21] Age, Aboriginal status, sex and socioeconomic variables were extracted from the registry. Aboriginal status was ascertained using a field that identifies individuals with "Treaty status" based on treaties between their First Nations bands and the federal government, which entitle patients to comprehensive health care without insurance premiums.[25] Receipt of social assistance or an insurance premium subsidy from Alberta Health and Wellness were used as a proxy for low socioeconomic status. Due to the methods of coding in the Registry, receipt of a subsidy or social assistance could not be determined in status Aboriginals. Comorbid alcohol-related diagnoses were defined using a previously-validated ICD-9-CM diagnosis coding algorithm[26,27] for 1997–2001. We translated ICD-9-CM codes to corresponding ICD-10 diagnosis codes for 2002 data (details available from the authors upon request).

Overdoses were classified as unintentional (ICD-9-CM, E850.4, E935.4; ICD-10, X40, Y45.5), intentional (ICD-9-CM, E950.0; ICD-10, X60) or other (undetermined or homicidal [ICD-9-CM, E962; ICD-10, X85] intent). According to the ICD-9-CM[23] and ICD-10[24] coding systems, intentional overdoses reflect overdoses taken for the purpose of self-harm (e.g., attempted and completed suicides and lesser self-inflicted injuries). We also considered overdoses involving self-inflicted poisoning by another drug, medicinal or biological substance (i.e., a coingestant) (ICD-9-CM, E950.1-E952.9; ICD-10, X61-X69) to be intentional. Unintentional overdoses reflect accidental ingestions of excessive amounts of acetaminophen or adverse effects of therapeutic dosages.

Data analysis

Descriptive statistics, including Fisher's exact, chi-squared and Mann–Whitney tests were used to describe demographic and clinical characteristics of patients. ED visit rates, herein referred to as incidence rates, were calculated by considering the entire end of fiscal year population of the CHR (as obtained from the AHCIP Registry) as at risk. Direct age- and sex-adjusted rates were calculated using the 2001 Canadian population as the standard. Temporal trends in incidence rates and risk factors for acetaminophen overdose were evaluated using Poisson log-linear regression.[28] The study protocol was approved by the Conjoint Health Research Ethics Board at the University of Calgary.

Results

Study population

During the study period, 2699 patients had 3015 ED visits for acetaminophen overdose (median 1; range 1–12), and 205 patients (7.6%) had 2 or more visits. Thirty-two percent of overdoses (n = 960) involved coingestions. Table 1 shows that 67% of patients were female and that median

Table 1. Characteristics of patients presenting to the emergency department with acetaminophen overdoes

Characteristic, *n* (%)*	All patients (*n* = 2699)	Single overdose (*n* = 2494)	Multiple overdoses (*n* = 205)	*P*†
Demographic				
Age, years, median (range)	22 (0–96)	22 (0–96)	24 (1–65)	0.16
Female sex	1808 (67.0%)	1661 (66.6%)	148 (72.2%)	0.11
Aboriginal status	197 (7.3%)	171 (6.9%)	26 (12.7%)	0.005
Social assistance	285 (10.6%)	266 (10.7%)	38 (18.5%)	0.001
Insurance premium subsidy	365 (13.5%)	332 (13.3%)	33 (16.1%)	0.29
Circumstances of overdose				
Intentional	2078 (68.9%)‡	1685 (67.5%)	161 (78.5%)	0.001
Unintentional	742 (24.6%)‡	658 (26.4%)	31 (15.1%)	
Other	195 (6.5%)‡	151 (6.1%)	13 (6.3%)	

*Unless otherwise specified, data are proportions (*n* [%]) and are presented as recorded at the first emergency department visit.
†For comparison of patients with single and multiple overdoses.
‡Percentages calculated based on total number of overdoses (*n* = 3015).

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age at first visit was 22 years (range 18 d–96 yr). Forty-one percent of patients (n = 1118) were less than 20 years old while 1.9% (n = 52) were aged 60 years or older. Seven percent were status Aboriginals, 11% were on social assistance and 14% received a subsidy for their insurance premiums. Table 1 also shows that patients with multiple overdoses were more likely to be on social assistance (p = 0.001) and Aboriginal (p = 0.005). Alcohol-related diagnoses were recorded in 19% (n = 513) of the patients.

Circumstances of the acetaminophen overdoses

The majority of overdoses (69%) were classified as intentional; 25% were unintentional (Table 1). Intentional overdoses were more common in younger patients (p = 0.0001; Fig. 1), in females (73% v. 60%), in non-Aboriginals (70% v. 56%) and in patients with alcohol-related diagnoses (77% v. 67%; $p < 0.0005$ for all comparisons). Patients with repeated visits were more likely to be classified as having an intentional overdose at their first visit than patients with single ED visits (79% v. 68%; p = 0.001; Table 1).

Incidence of acetaminophen overdose and risk factors

Between 1997 and 2002, the age- and sex-adjusted annual incidence of acetaminophen overdose was 45.7 per 100 000 population. Age-adjusted rates in females and males were 62.4 and 29.4 per 100 000 population, respectively (rate ratio [RR] = 2.07; 95% confidence interval [CI] 2.05–2.09). Figure 2 shows that the adjusted incidence of acetaminophen overdose decreased from 52.6 per 100 000 people in 1997 to 35.1 per 100 000 people in 2002 (34% relative reduction; $p < 0.0005$). Declines were observed in both males (41%; 95% CI 39%–42%) and females (30%; 95% CI 29%–32%). Figure 3 shows that intentional overdoses fell 44% (95% CI 43%–45%), while unintentional overdoses fell 26% (95% CI 24%–27%).

The effect of age on the incidence of acetaminophen overdose is illustrated in Figure 4. The highest adjusted rates were observed in the 10–19 and 20–29 year age groups (102.7 and 85.5 per 100 000 population, respectively). These groups were approximately 3-times more likely to have an overdose, compared with patients aged 30 years and older (RR = 3.14; 95% CI 3.12–3.17). Figure 4 shows that, females between the ages of 10 and 50 years were at significantly higher risk, with the greatest disparities in the 10–19 year and 20–29 year age groups, where the crude overdose rates were 167.9 and 116.8 per 100 000 in females versus 34.9 and 52.9 per 100 000 in males, respectively.

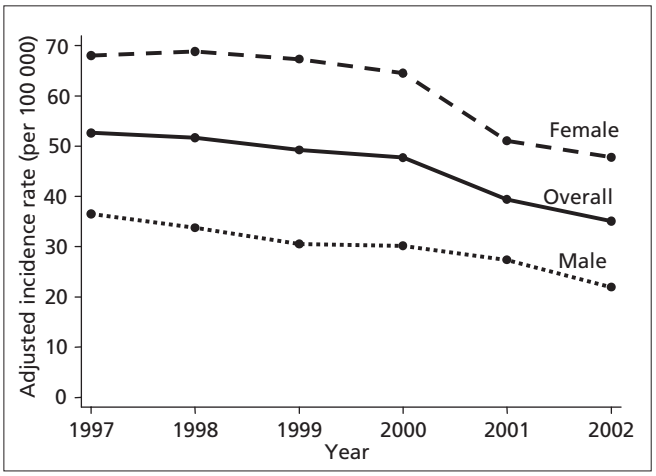

Fig. 2. Annual age-adjusted incidence rates for acetaminophen overdose by sex (1997–2002).

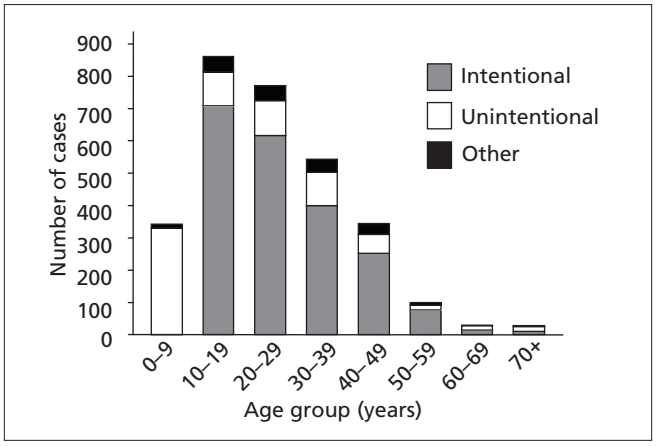

Fig. 1. Number of emergency department visits for acetaminophen overdose in the Calgary Health Region by age and suicidal intent (1997–2002). "Other" indicates overdoses of indeterminate or homicidal intent.

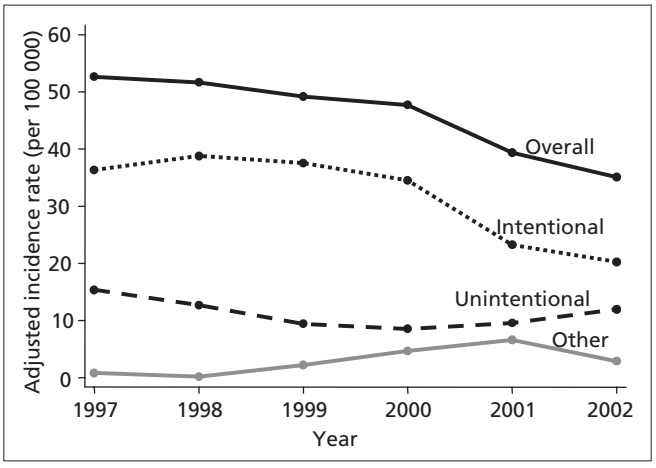

Fig. 3. Annual age- and sex-adjusted incidence rates for acetaminophen overdose by suicidal intent and year (1997–2002).

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Aboriginal status (RR = 4.78; 95% CI 4.24–5.39) and receipt of social assistance (RR = 5.05; 95% CI 4.60–5.56) were strong risk factors for acetaminophen overdose, while receipt of an insurance premium subsidy was not significant (RR = 0.92; 95% CI 0.84–1.01).

Temporal variations in acetaminophen overdose

ED visits for acetaminophen overdose rose steadily from December to a peak in June (Fig. 5), with the lowest incidence during July, August and December. The curves for intentional and unintentional overdoses fluctuated in parallel, while overdoses of other intents were not associated with the months. ED visit rates were relatively stable throughout the week (Fig. 6), but highest in the late evening and early hours of the morning (Fig. 7).

Disposition from the ED

Overall, 33% (n = 986/3015) of patients required hospital admission, 4.1% (n = 40) were admitted to an intensive care unit and 0.06% (n = 2) died on route to the ED. The majority of patients (67%) were discharged, while 1.2% (n = 37) left against medical advice or without being seen by a physician. The proportion of patients admitted to hospital increased from 28% in 1997 to 39% in 2002 (p = 0.0005).

Discussion

Acetaminophen is the most commonly used antipyretic and analgesic; excluding combination preparations, approximately 1.5 billion tablets are sold annually in Canada.[1] Between 1997 and 2002, the adjusted incidence

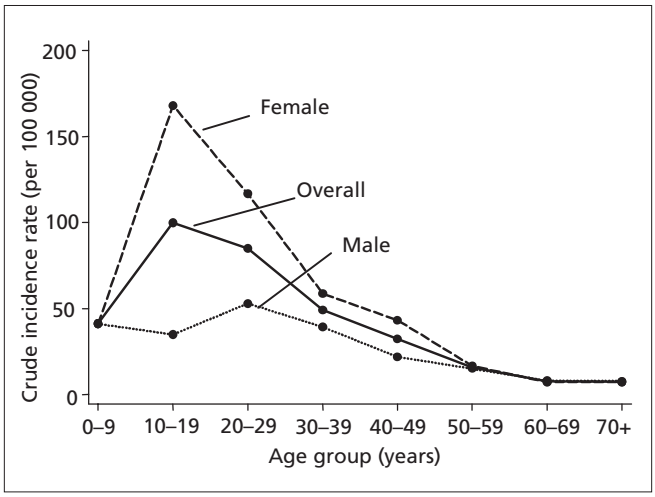

Fig. 4. Crude incidence rates of acetaminophen overdose by age group and sex (1997–2002).

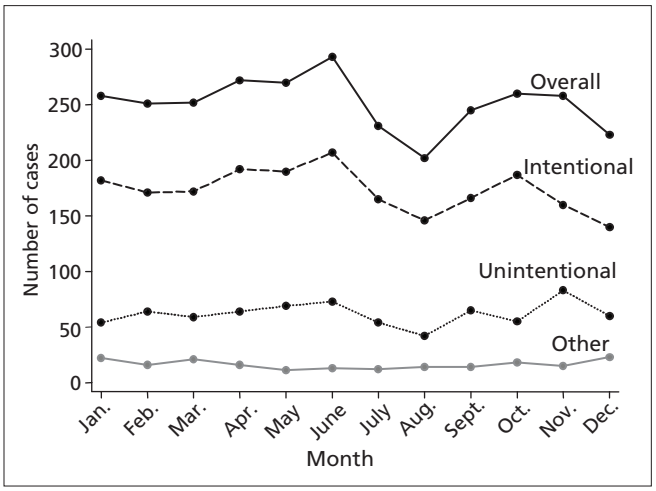

Fig. 5. Temporal variations in number of ED visits for acetaminophen overdose (1997–2002) according to suicidal intent and month.

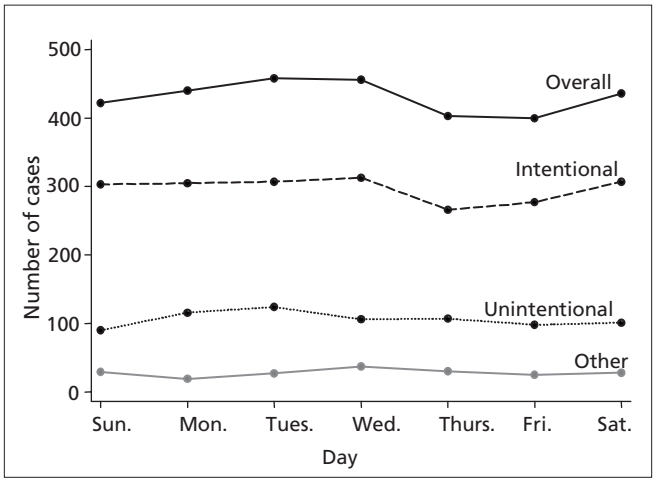

Fig. 6. Temporal variations in number of ED visits for acetaminophen overdose (1997–2002) according to suicidal intent and day.

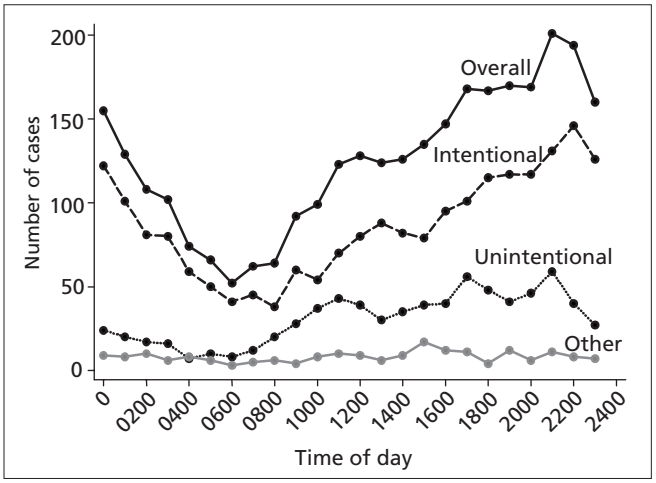

Fig. 7. Temporal variations in number of ED visits for acetaminophen overdose (1997–2002) according to suicidal intent and time of day.

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of acetaminophen overdose was 46 per 100 000 population (~1/2200). Although other Canadian incidence data are lacking, this figure is approximately double that reported in the United States. Using the National Hospital Ambulatory Medical Care Survey, Nourjah and colleagues estimated that 56 000 ED visits occur annually in the United States, corresponding to an incidence of approximately 20 per 100 000 population.[13] In a study from the state of Virginia,[17] an incidence of 21.4 per 100 000 was reported. Acetaminophen overdose is much more common in the United Kingdom where legislation was introduced in 1998 to limit over-the-counter sales due to rising rates of deliberate self-poisoning.[19] Despite this legislation, Bateman and colleagues reported an annual hospitalization rate for acetaminophen overdose in Scotland of 124.4 per 100 000 during the following year.[14] Although the explanation(s) for these discrepancies in incidence is beyond the scope of this study, differences in acetaminophen availability seem unlikely considering the liberal sale of acetaminophen in North America and the similarities between suicide rates across countries.[29,30]

Data from other countries show downward trends in the incidence of acetaminophen overdose. Using information from the Toxic Exposure Surveillance System, Nourjah and colleagues reported a 10% decline in acetaminophen-related "poison control calls" to US centres between 1997 and 2002.[13] Similarly, Turvill and colleagues reported a 21% decline in overdoses presenting to the Royal Free Hospital in London between 1995 and 2002.[12] In Scotland, hospitalizations increased from 1990 to 1997, but decreased by 20% between 1997 and 1999.[14] Reductions in the United Kingdom have been attributed to the aforementioned legislation; however, the 34% decline seen in our study occurred in the absence of legislative initiatives and despite a concurrent increase in Alberta emergency department visits for self-inflicted injuries.[31]

In keeping with other reports, we observed a high rate of acetaminophen overdose in young patients, particularly females,[13,14] and marginalized populations including Aboriginals and social assistance recipients. The latter groups had 5-fold higher rates of acetaminophen overdose and were more likely to have repeated ingestions. Increased risk of deliberate self-harm has been reported in Aboriginal communities worldwide,[32,33] emphasizing the necessity of preventive initiatives in this and other high-risk populations. The high rate of alcohol-related diagnoses in our cohort (19%; much higher than the 4% reported by Saitz and colleagues[27]) particularly among Aboriginals (37%), presumably contributed to this risk. Since alcohol abuse has been associated with a higher risk of acetaminophen-related hepatotoxicity,[3,7–9] this high prevalence is concerning.

One-third of our cohort was hospitalized for management of their acetaminophen overdose. We suspect that this reflects the mild nature of most acetaminophen overdoses and the effective use of the Rumack-Matthew nomogram[34] (or both) for identifying patients at risk of hepatotoxicity. An unexpected finding was that an increasing proportion of patients were hospitalized in later years of the study despite growing limitations on hospital bed availability. This may relate to changing trends in the severity of acetaminophen overdose or to associated suicidality. Temporal changes in the threshold for hospital admission should be considered when examining hospitalization rates for acetaminophen overdose as a measure of disease burden.

Like previous investigators,[13,35] we found that most ingestions (69%) were intentional, and that individuals with repeated overdoses were more likely to have intentional ingestions. Surprisingly, 15% of repeat visits were classified as unintentional, perhaps reflecting misclassification of intent in some cases. Unintentional overdoses, often termed "therapeutic misadventures," were more common in males, older patients and individuals without alcohol-related diagnoses. In one study,[36] older patients were more likely to be erroneously classified as having accidental overdoses, and our finding of a greater rate of unintentional overdoses among the elderly may reflect such misclassification. Nevertheless, other studies have suggested greater agreement between E-codes obtained from administrative data and medical record review for defining suicidal intent.[37,38] Since unintentional ingestions are associated with a greater risk of ALF,[6,39] these data emphasize the importance of clear labelling of acetaminophen-containing medications and educational initiatives regarding the potential toxicity of acetaminophen, particularly in these patient subgroups.

Numerous studies have examined temporal and seasonal effects on the incidence of self-harm. As in our study, most reports describe a peak of suicides in late spring and early summer when daily sunshine exposure is maximal.[40–43] This may relate in part to sunshine-induced alteration of central neurotransmitters including serotonin or melatonin.[43] We found no association with day of the week; however, other researchers have reported a peak on Mondays and nadir on weekends.[41] We did, however, find that ED visits were highest in the evening and early morning hours. These temporal trends should be interpreted in light of the fact that most patients with acetaminophen overdose present hours or even days following their ingestions.

Limitations

Our study has several limitations. Most importantly, by an-

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alyzing the ACCS database, we were only able to capture individuals with an acetaminophen overdose who sought medical attention in an ED; therefore, we have underestimated the true incidence of acetaminophen overdose, since a substantial proportion of parasuicide patients do not present for medical care.[44] The examination of additional data sources, including hospitalization databases, coroner's reports, and poison control centre data may provide a more accurate assessment of the incidence of acetaminophen overdose. The accuracy of the "external causes of injury or poisoning" codes (E-codes) used to define suicidal intent has been questioned, and in a Canadian validation study, Rhodes and colleagues reported that E-codes underestimated the prevalence of intentional self-poisoning by 63%.[36] Moreover, the accuracy of diagnostic coding used in our study requires validation.

Conclusions

In this Canadian population-based study, the annual rate of ED visits for acetaminophen overdose was approximately 46 per 100 000 population. The incidence of both intentional and unintentional ingestions decreased between 1997 and 2002. Several patient subgroups including young females, Aboriginals and recipients of social assistance, are at greatest risk and may benefit from educational and preventive initiatives.

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