

What calls to the BC Poison Centre tell us about electronic cigarette exposures

Original Research

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Email: alexandra.h.choi@gmail.com

Target Journal: CMAJ

Keywords: Electronic Nicotine Delivery Systems, Nicotine, Poison Center

References: 36

Word count (Article excluding tables): 2487/2500

Word count (Abstract): 271

This research was completed through internal funding at the BC Centre for Disease Control.

No potential conflicts of interest, financial or otherwise.

ABSTRACT

Background: Although the prevalence of traditional cigarette smoking has been declining, e-cigarettes (ECs) have continued to gain popularity. Poison centres in the United States have reported increasing numbers of calls about exposure to EC devices and associated paraphernalia. While the majority of call subjects experienced only minor side effects, severe neurologic symptoms have been noted in case reports. The aim of this study was to describe epidemiological trends in Canadian EC exposures in a rapidly changing use environment.

Methods: We conducted an observational case series using records containing both coded fields and free-text narratives from the BC Drug and Poison Information Centre (DPIC) for all 186 exposures involving ECs from 2012 to 2017. All calls which were recorded as exposures by poison center staff were included. Non-human exposures and non-patient-related calls for information only were excluded. We described trends in exposures and exposed persons, as well as clinical effects.

Results: Calls related to ECs increased nearly six-fold between 2013 and 2014, and have not declined since. Exposures were most frequently documented in children under the age of 4 ($n=81$, 56%), with 33% of exposures in 2-year-olds ($n=47$). 92% ($n=76$) of exposures in children under the age of 5 were due to accidental ingestions, while adults most frequently called the poison centre following spills ($n=11$; 35%) and EC malfunctions ($n=11$; 35%). Nearly half of exposed individuals were noted to have no symptoms ($n=94$; 47%).

Interpretation: Regulatory approaches aimed at minimizing access to children and harms due to subsequent ingestion should be considered. Increased surveillance will be needed to characterize exposure trends, including more targeted data collection and improved poison centre follow-up protocols.

Trial registration: Not applicable

BACKGROUND

First introduced to North American markets in 2007, electronic nicotine delivery systems (ENDS), including electronic cigarettes (ECs), are designed to vaporize inhalable chemical combinations for an experience that mimics smoking.(1) Devices typically include an electronic heating and aerosolization system, batteries, electronic controls, and a cartridge of “e-juice” or “e-liquid” – a variable mixture of propylene glycol (a carrier compound), glycerol, nicotine, and flavouring.(2)

Although the overall prevalence of traditional cigarette smoking has been declining, EC use has been increasing in the US among middle and high school students in particular – the first increase in nicotine product utilization in decades.(3-8) This has prompted new safety concerns regarding both regular use and accidental exposures. US poison centres have reported dramatic increases in the frequency of EC-related exposure calls, primarily concerning children 5 years of age or younger.(9-12) Most have been associated with minimal toxicity.(11, 13) However, case reports have documented severe neurologic symptoms, anoxic brain injury, and death resulting from unintentional pediatric ingestions of e-juices.(14, 15)

The primary known hazard associated with EC exposure is nicotine. Although nicotine is most commonly associated with central nervous system excitation through nicotinic acetylcholine receptors, excessive or prolonged exposure can result in loss of receptor specificity and paradoxical inhibition, causing cholinergic toxicity and blockade at the neuromuscular junction. Absorbed through the skin, alveoli, oropharyngeal mucosa, and gastrointestinal mucosa, the lethal dose of nicotine is estimated at less than 1mg/kg in adults.(14) This is concerning given that many ECs (including “nicotine-free” options) contain nicotine in excess of their labelled concentrations.(16-19)

Several studies have examined EC-related poison centre calls in the United States; however, the Canadian regulatory environment differs in important ways. Despite widespread availability, until recently the sale of nicotine-containing ECs was illegal under the Food and Drugs Act, while “non-nicotine” e-cigarettes were available for legal purchase by minors.(7) Recently passed Bill S-5 will allow for regulation of the manufacture, sale, labelling, and marketing of ECs and vaping products.(20)

In order to describe epidemiological poison centre data within a rapidly changing use environment and the Canadian context, we examined all EC-related calls to British Columbia’s poison centre exploring trends in exposures, populations, causes of exposures, and clinical outcomes.

METHODS

Provincial Poison Data System

The BC Drug and Poison Information Centre (DPIC) provides poison information services to 4.8 million British Columbians.(21, 22) It is staffed 24-hours a day by trained pharmacists, nurses, and physicians who receive approximately 26,000 phone calls per year.(23) Product information is entered using American Association of Poison Control Centers (AAPCC) generic codes, AAPCC product IDs, and Posindex descriptors. All data is maintained in an electronic database. We retrospectively reviewed all EC and ENDS-related calls from January 1, 2012, until December 31, 2017. All calls recorded as exposures were included in our dataset, regardless of toxicity, clinical symptoms, or outcomes. Exposures involving multiple, co-ingested substances were analyzed for all variables except those describing symptoms and clinical care pathways since symptoms attributable to ECs could not be reliably disaggregated. Non-human exposures and callers purely seeking information were excluded.

We obtained case records containing coded fields and free-text narratives for all EC-related calls during our study period. Two co-authors reviewed the free-text and verified all coded fields. Coded fields which were assessed included the age and gender of the exposed person, relationship to the caller, route of exposure, location of exposure, and timing of both the call and the exposure. Additional data were abstracted from the free-text into predetermined standardized fields. The free-text was reviewed to assess the vehicle of exposure (e.g. EC device, EC cartridge, e-juice or e-liquid), cause of exposure (accidental access, device malfunction, usual use, misuse, etc.), and clinical symptoms. Clinical symptoms were categorized as (a) stimulatory effects typical for low-level nicotine exposure (including nausea, vomiting, headache, dizziness, anxiety, and tachycardia), (b) depressive effects typical for high-level nicotine exposure (including coma and respiratory failure), and (c) effects not typical for nicotine exposure. In cases where nicotine concentration and/or dose appeared in either coded fields or the free-text, they were recorded.

In order to examine the relationship between rates of EC-related calls and numbers of retail units, we allocated callers to BC's 16 Health Service Delivery Areas (HSDAs).(24) Current lists and counts of EC retailers, (which were up to date as of April 2018,) were obtained from tobacco regulation enforcement teams for 13 of 16 HSDAs. In order to determine if population density affected the incidence of EC-related calls, we categorized subjects' place of residence (which is routinely recorded) as metropolitan, mixed urban/rural, and remote using the BC Ministry of Health's geographic service area definitions.(25)

Statistical Analysis

Characteristics of EC exposures and exposed persons were described using frequencies and proportions. Age, gender, and geographic area were compared to the BC population using the Chi-square test. The characteristics of exposures and exposed persons were stratified by age, route of exposure, and nicotine concentration. For each HSDA, we calculated the number of EC-related calls and retail units per 100,000 population. We used the Pearson correlation to determine the relationship between the number of EC retail outlets, and the rate of EC-related poison centre calls within each HSDA.

RESULTS

Characteristics of E-Cigarette exposures and exposed persons.

From 2012 to 2017 calls were recorded for 186 unique exposures to ECs, e-juices, EC cartridges, and other associated paraphernalia (3.86 per 100,000 population). The characteristics of EC-related exposures and exposed persons are presented in Table 1. Calls related to ECs were infrequent in 2012 and 2013; a nearly six-fold increase occurred in 2014, which has not abated. (Table 1) From 2014-2017, there was a mean of 43 calls per year (range 39-47).

Males were overrepresented, and the median age was 3 years (range: 1 to 75). Exposures were most frequently reported in 2 year olds (n=47; 33%), followed by 1 year olds (n=22; 15%), 3 year olds (n=9; 6%), and 16 year olds (n=6; 4%). (Figure 2) During all time periods, children aged 0-4 years were disproportionately exposed, and the increase in EC calls over the study period was driven by young children. (Figure 1)

Almost all (n=174; 94%) exposures occurred at the exposed person's own place of residence; 6 occurred in a public area, 1 occurred in a school, and 2 occurred at workplaces. 94% (n=68) of exposed children under the age of 5 accessed ECs or EC paraphernalia in their own households.

There was no apparent pattern in the number of EC-related calls by day of the week (p=0.47), or month of the year (p=0.48). Most calls were received between noon and midnight (n=143; 77%); few were made overnight (n=12; 6%).

Individuals from mixed urban/rural populations constituted 33% of the EC-related poison centre calls, but only 12% of the province's population. Three of the top five highest rates of regional EC exposure were geographically clustered in Vancouver Island's three HSDAs, one of which had the highest rate of reported exposures in the province (8.5 per 100,000 persons). (Figure 3)

Exposures and clinical sequelae

Exposure characteristics by age are presented in Table 2. Exposures in children under the age of 5 were generally the result of accidental acquisition ($n=79$; 95%), and subsequent ingestion ($n=76$; 92%) of bottled e-juice ($n=52$; 63%). The most frequently reported causes of exposure in adults were spills ($n=11$; 35%) and EC malfunctions ($n=11$; 35%), followed by mistaking e-juices for other substances such as eye drops ($n=4$; 13%).

While only 11% ($n=9$) of children under the age of 5 were documented to be symptomatic, 32% ($n=27$) were seen at health care facilities. In contrast, 93% ($n=14$) of 15 to 18-year-olds were symptomatic, but only 27% ($n=4$) were seen at health care facilities.

Four exposures were coded as chronic, defined as “continuous, repeated, or intermittent” exposures lasting greater than eight hours.(27) Excluding chronic exposures, the median time between the exposure and poison centre call was 10 minutes (range 0 minutes to 62 days). 53% ($n=98$) of callers phoned poison control within 10 minutes of the exposure, and 82% ($n=153$) of individuals phoned within 60 minutes of the exposure. 9 individuals identified a second exposure which could have contributed to the clinical picture. Of these, 2 were exposed to a second nicotine-containing substance, 2 had recently undergone a change in psychotropic medications, 1 was exposed to alcohol (and potentially gamma-Hydroxybutyric acid), 1 was exposed to THC, 1 was exposed to gun oil, and 1 was exposed to analgesics including possible opioids.

Nearly half of exposed individuals did not report symptoms ($n=94$; 47%). 97 (52%) of callers were able to report the labelled concentration of their EC products. Three of the four exposed to “no nicotine” solutions developed symptoms, compared to 39% ($n=7$) of those exposed to low nicotine solutions, 28% ($n=15$) of those exposed to medium nicotine solutions, 40% ($n=6$) of those exposed to high nicotine solutions, and 57% ($n=4$) of those exposed to very high nicotine solutions. (Table 4) The majority of symptoms reported were typical for low-level systemic nicotine exposure ($n=54$; 29%) (Table 3).

Relationship with EC retail units

Figure 3 shows the rate of e-cigarette exposures by the number of retail units in each region, frequently referred to as vape/vapor shops or lounges. There was no statistically significant association between the number of EC-related poison centre calls in an HSDA and the number of retail units ($R=-0.11$, $p=0.7181$).

Missing information and absent fields

119 records (64%) contained no mention of flavouring. Packaging attributes (e.g. child-proof packaging) were not recorded. 131 (70%) call records did not specify the volume of exposure, and 89 (48%) did not contain mention of the concentration of nicotine. Product names and product characteristics were infrequently recorded.

DISCUSSION

BC's poison centre has experienced a recent increase in EC-related calls, predominantly in young children accessing EC paraphernalia accidentally within their own households. However, nearly half of those exposed were asymptomatic, and only 8 required admission to a health care facility. As in other jurisdictions, the recent spike in EC-related exposures may reflect an increase in EC use, lack of

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familiarity with new products, and/or increased media reports highlighting adverse effects.(11, 13, 28)
In contrast to other jurisdictions, EC-related exposure calls in BC have not declined since 2017, and were consistent across days of the week and months of the year.(13)

Some of the exposures in toddlers might have been prevented through child-resistant packaging, which has been effective in preventing mortalities associated with other oral drugs.(29, 30) Since multi-use refill bottles were the most common vehicles of exposure, single-use products could decrease risks. As children most frequently found these products within their own homes, increased user education around product storage might be helpful. Products’ owners were infrequently documented in poison centre calls; further data could assist in targeting messaging.

In addition, given toddlers’ low body weight, limiting the availability of highly concentrated nicotine products might be prudent. The generally accepted lethal dose of nicotine in an adult is 30-60mg.(31) The extrapolation of the LD50 to children is debatable, but could be estimated as 0.8-1.0mg/kg. While further exploration of the toxicokinetics of e-juices is required, (particularly given the “free-base” nicotine used by manufacturers,) proposals to limit e-juices’ nicotine concentrations to 66mg/mL may be insufficient. The low prevalence of major effects to date could be due to lower nicotine concentrations in ingested products.(11)

Apart from toddlers, there was a weak signal that youth might more frequently be the subject of calls than young children or adults. In Canada, minors’ ability to legally purchase “non-nicotine” ECs and higher-risk, novel use patterns such as “dripping” (inhaling e-liquids dropped directly onto heated atomizers) could contribute to higher call volumes among youth.(32) Adults most frequently called regarding spills and device malfunctions. Improved packaging and manufacturing standards might help, although vendors frequently sell components that are assembled at home. As in other studies, a small but significant number of exposed persons mistook bottled e-juice for another solution (e.g. eyedrops).(10, 13) Users might benefit from clearer labelling or more distinctive packaging.

The collection and interpretation of poison centre data was complicated by a lack of regulation and product standardization. In most cases nicotine dose could not be calculated as concentrations of products and/or volumes of exposure were not recorded. Many of those exposed to “low” nicotine or “nicotine-free” solutions still developed symptoms, consistent with prior studies demonstrating that labelled concentrations poorly reflect nicotine content.(33, 34) Unregulated EC sales via web-based vendors could have complicated the relationship between the number of retail units and EC-related poison centre calls in each HSDA; the number of brick and mortar retail units might not be indicative of access.

LIMITATIONS

The availability of poison centre data presented a timely opportunity to study a rapidly changing, relatively novel exposure, using detailed exposure records taken within minutes to hours of their occurrence. However, there were a number of limitations. Case-identification was limited to exposures which were voluntarily self-reported, leading to possible case ascertainment bias, and underestimates of true exposures. The American National Academy of Medicine estimates that less than half of all poisonings lead to poison centre calls.(35) In addition, urban and rural populations use poison centres differently.(36)

All information was gathered from callers or relevant health care practitioners, and some records contained missing fields. There were also variations in coding, and free text case reports were not standardized. For other fields, there was a default, (e.g. the default for place of exposure was "own place of residence".) While we attempted to validate all fields using the available free text, there could be residual misclassification. Specific product names, characteristics (e.g. flavouring), and delivery systems (single use ECs, vape pens, e-pipes, etc.) were not recorded.

Lack of follow-up created significant limitations in the interpretation of clinical symptoms. The majority of callers phoned the poison centre within 10 minutes of the exposure, and follow up by the centre to callers even over 24 hours, was inconsistent. Full clinical trajectories were not recorded, and could not be discovered afterward as patient identifiers were inconsistently disclosed. It is possible that we underestimated calls with a significant health effect. This could be addressed through more rigorous poison centre follow up procedures or by data linkage.

CONCLUSION

BC has experienced a dramatic increase in EC-related calls to poison centres, driven by ingestions in young children. Worryingly, the six-fold call increase may still underestimate the true number of exposures. ECs are relatively novel, and it is important that both the public and health care providers are aware of potential health effects. Nicotine is the primary known hazard, and the amount of nicotine present in e-juices can exceed the labelled concentrations. High concentration products may present a unique hazard to young children given their low body weight. Moreover, there is little information available regarding other chemicals present. Given that e-juice bottles are sometimes mistaken for other substances, clear, standardized packaging and labelling could be helpful. Given that rates of exposure do not seem to be declining, increased surveillance (including surveillance across multiple provinces) may be beneficial in further elucidating the epidemiology of exposures.

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Table 1. Characteristics of calls and exposed persons

	EC exposures reported to poison control		BC Population(25, 26)		P value
	N=186		N=4,648,060		
	Count	%	Count	%	
<i>Demographics of exposed persons</i>					
Gender					0.0086
Female	76	41.3	2,369,815	51.0	
Male	108	58.7	2,278,245	49.0	
Unknown*	2				
Age (years)					<0.0001
0-4	81	56.3	220,625	4.8	
5-14	7	4.9	470,670	10.1	
15-19	18	12.5	258,980	5.6	
20-24	7	4.9	287,560	6.2	
>25	31	21.5	3,410,130	73.4	
Not recorded*	42				
<i>Temporal and geographic characteristics of calls</i>					
Year					
2012	7	3.8	-		<0.0001
2013	7	3.8			
2014	39	21.0			
2015	47	25.3			
2016	40	21.5			
2017	46	24.7			
Time of day			-		<0.0001
Morning (06:00-11:59)	31	16.7			
Afternoon (12:00-17:59)	71	38.2			
Evening (18:00-23:59)	72	38.7			
Overnight (00:00-05:59)	12	6.5			
Geographic area(25)					<0.0001
Metropolitan	79	42.5	2,643,866	56.5	
Mixed Urban/Rural	62	33.3	1,485,317	11.8	
Rural and Remote	45	24.2	554,078	31.7	

*Persons with missing data not included in comparisons

Table 2. Characteristics of EC-related exposures, symptoms, and care trajectories by age

	Infant or Toddler (≤5 years) N=83		Child (6-14 years) N=5		Youth (15-18 years) N=16		Young Adult (19-24 years) N=9		Adult (≥25 years) N=31		Total* N=186	
	Count	%	Count	%	Count	%	Count	%	Count	%	Count	%
Cause of exposure												
Accidental access**	79	95.2	2	40.0	2	12.5	0	0.0	0	0.0	85	45.7
Handling device***	0	0.0	1	20.0	2	12.5	1	11.1	1	3.2	10	5.4
Intentional inappropriate use	0	0.0	1	20.0	1	6.3	1	11.1	2	6.5	7	3.8
Making e-juice	0	0.0	0	0.0	0	0.0	0	0.0	1	3.2	1	0.5
E-cigarette malfunction	1	1.2	0	0.0	2	12.5	1	11.1	7	22.6	17	9.1
Mistaken identity****	1	1.2	0	0.0	0	0.0	1	11.1	4	12.9	12	6.5
Spill	1	1.2	0	0.0	0	0.0	0	0.0	11	35.5	7	3.8
Usual e-cigarette use	0	0.0	0	0.0	7	43.8	1	11.1	1	3.2	25	13.4
Other or not recorded	1	1.2	1	20.0	2	12.5	4	44.4	4	12.9	22	11.8
Vehicle of exposure												
E-cigarette device	11	13.3	1	20.0	1	6.3	1	11.1	1	3.2	17	9.1
E-cigarette cartridge	19	22.9	0	0.0	11	68.8	4	44.4	19	61.3	74	39.8
Bottled e-juice	52	62.7	4	80.0	4	25.0	4	44.4	11	35.5	93	50.0
Other or not recorded	1	1.2	0	0.0	0	0.0	0	0.0	0	0.0	2	1.1
Route of exposure*****												
Dermal	15	18.1	2	40.0	1	6.3	4	44.4	4	12.9	34	18.3
Ingestion	76	91.6	4	80.0	7	43.8	5	55.6	15	48.4	126	67.7
Inhalation	2	2.4	0	0.0	8	50.0	1	11.1	10	32.3	28	15.1
Nasal	0	0.0	0	0.0	0	0.0	0	0.0	1	3.2	1	0.5
Ocular	1	1.2	0	0.0	1	6.3	0	0.0	2	6.5	14	7.5
Vaginal	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5
Symptoms present*****												
Symptoms	9	11.1	2	50.0	14	93.3	4	50.0	25	86.2	80	45.2
No symptoms	70	86.4	2	50.0	1	6.7	4	50.0	4	13.8	94	53.1
Not recorded	2	2.5	0	0.0	0	0.0	0	0.0	0	0.0	3	1.7
Care trajectory*****												
Managed outside of HCF*****	51	63.0	4	100.0	9	60.0	7	87.5	22	75.9	125	70.6
Treated/evaluated at HCF and released	21	25.9	0	0.0	2	13.3	0	0.0	5	17.2	31	17.5
Admitted to noncritical care unit	2	2.5	0	0.0	2	13.3	1	12.5	1	3.4	7	4.0
Admitted to critical care unit	1	1.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6
Lost to follow-up	6	7.4	0	0.0	2	13.3	0	0.0	1	3.4	13	7.6

* Total column includes individuals for whom age was not recorded (n=42).

** Accidental acquisition of e-cigarettes or associated paraphernalia by a person (usually a child) who is not the intended user, and subsequent use without the intention of causing harm.

*** Includes cleaning, refilling, or otherwise manipulating e-cigarette devices and cartridges.

**** E-juice mistaken for another substance frequently housed in a similar container (e.g. eye drops).

***** Cases with multiple routes of exposure were counted in all applicable categories.

***** Excludes co-ingestions as these substances could contribute to symptomatology.

***** Health Care Facility, includes EMS.

Table 3. Symptoms by route of exposure*

	Dermal**		Ingestion**		Inhalation**		Total***	
	N=19		N=110		N=27		N=177	
	Count	%	Count	%	Count	%	Count	%
Symptoms present								
Symptoms	10	52.6	37	33.6	24	88.9	80	45.2
No symptoms	9	47.4	70	63.6	3	11.1	94	53.1
Not recorded	0	0.0	3	2.7	0	0.0	3	1.7
Symptoms***								
Local								
Dermal	4	40.0	0	0.0	1	4.2	5	2.8
Oral/Pharyngeal	0	0.0	10	27.0	1	4.2	11	6.2
Respiratory	0	0.0	1	2.7	1	4.2	2	1.1
Ocular	0	0.0	0	0.0	0	0.0	12	6.8
Vaginal	0	0.0	0	0.0	0	0.0	1	0.6
Systemic								
Not typical for nicotine exposure	1	10.0	2	5.4	0	0.0	3	1.7
Typical for low nicotine exposure	6	60.0	24	64.9	20	83.3	48	27.1
Typical for high nicotine exposure	0	0.0	1	2.7	0	0.0	0	0.0

* Excludes individuals with co-ingestions as these substances could contribute to symptomatology.

** Excludes individuals with multiple routes of exposure.

** Includes individuals with nasal, ocular, and vaginal exposures as well as multiple routes of exposure.

*** Multiple symptoms may be experienced by a single individual.

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Table 4. Age, presence of symptoms, and care trajectories, by nicotine concentration of EC product*

		No nicotine (0 mL/mg) N = 4		Low (<6 mL/mg) N = 18		Medium (6-18mL/mg) N = 53		High (18-23 mL/mg) N = 15		Very High (>24 mL/mg) N = 7	
		Count	%	Count	%	Count	%	Count	%	Count	%
Age											
	Infant or Toddler (≤5 years)	0	0.0	10	55.6	33	62.2	9	60.0	4	57.1
	Child (6-14 years)	0	0.0	2	11.1	0	0.0	0	0.0	0	0.0
	Youth (15-18 years)	1	25.0	1	5.6	5	9.4	0	0.0	1	14.3
	Young Adult (19-24 years)	0	0.0	1	5.6	3	5.6	1	6.7	0	0.0
	Adult (≥25 years)	1	25.0	2	11.1	7	13.2	3	20.0	1	14.3
	Not recorded	2	50.0	2	11.1	28	9.4	2	13.3	1	14.3
Symptoms present											
	Symptoms	3	75.0	7	38.9	15	28.3	6	40.0	4	57.1
	No symptoms	0	0.0	11	61.1	29	54.7	7	46.7	1	14.29
	Not recorded	1	25.0	0	0.0	9	17.0	2	13.3	2	28.6
Care trajectory											
	Managed outside of HCF**	3	75.0	13	72.2	37	69.8	11	73.3	5	71.4
	Treated/evaluated at HCF and released	1	25.0	4	22.2	10	18.9	3	20.0	2	28.6
	Admitted to noncritical care unit	0	0.0	0	0.0	2	3.8	1	6.7	0	0.0
	Admitted to critical care unit	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Lost to follow-up	0	0.0	1	5.6	4	7.6	0	0.0	0	0.0

* Excludes cases where nicotine concentration was not recorded.

** Health Care Facility, includes EMS.

Figure 1. Annual EC-related exposure calls to the BC Drug and Poison Information Centre





