Knowledge Update

BC Centre for Disease Control
Provincial Health Services Authority

Topic	Brain Injury Following Drug Toxicity Events in British Columbia
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Data source	Provincial Overdose Cohort
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Key messages

- People who experience drug poisoning events continue to disproportionately experience higher rates of encephalopathy (brain injury) (2.2%) compared to those who did not experience drug poisoning events (less than 0.001%).
- The number of people with an encephalopathy diagnosis increased significantly in 2020 and 2021 compared to the period between 2015 and 2019.
- People who experienced drug toxicity events were 19.5 times more likely to have encephalopathy compared to those who did not experience drug toxicity events. Specifically, people older than 30, males, and people with a mental disorder faced a higher risk.

Introduction

- People who experience non-fatal toxic drug poisoning (NFTDP) events may suffer partial or complete deprivation of oxygen. Even a few minutes of reduced oxygen supply can cause irreversible brain damage, leading to cognitive and neurological impairments as well as motor dysfunction.

- Encephalopathy is a broad term for brain damage. If it occurs due to oxygen deprivation, it is known as anoxic brain injury; if caused by exposure to harmful substances, it is referred as toxic encephalopathy.[1]

- There is a growing population in British Columbia who have survived toxic drug poisoning and have been diagnosed with encephalopathy as the unregulated drug supply becomes more potent. The rise in unregulated drugs adulterated with benzodiazepines and tranquilizers has amplified the risks of toxic drug poisoning for people who use drugs, making the issue even more complex.[2]

- The British Columbia Provincial Overdose Cohort (BC-ODC) is a collection of linked administrative health datasets, including records of contacts with health care via ambulance, emergency room, hospital, and physician visits, as well as data on death. Additionally, a 20 percent random sample of BC residents registered for the Medical Services Plan (MSP) is linked to the BC ODC data.[3]

- Xavier et al. (2023) investigated the prevalence of encephalopathy among the 20 percent population sample and examined the association between toxic drug poisoning events and encephalopathy using this sample between January 1,2015, and December 31, 2019.[4]

- This analysis updates the work of Xavier et al. (2023) with more recent data from the BC-ODC's 20 percent Reference Cohort, spanning January 1, 2015, to December 31, 2021. We first identify the number of people diagnosed with encephalopathy and compare the characteristics of this group to those without an encephalopathy diagnosis. Next, we estimate the association between toxic drug poisoning events and encephalopathy. Finally, we compare our findings with those of the 2019 reference group.

Study Design and Methods

- Encephalopathy was identified in this study as *Anoxic brain injury, toxic encephalopathy, and encephalopathy unspecified,* as defined by Morrow et al. (2019), using the International Statistical Classification of Diseases (ICD) codes.[5,6] Diagnostic records from the Discharge Abstract Database (DAD), National Ambulatory Care Records System (NACRS), and Medical Services Plan (MSP) were used for this identification. To examine diagnostic codes in MSP, the ICD-10 codes were converted to ICD-9 codes (Table 1).

- This analysis follows the definition of mental disorder and substance use disorder (SUD) as outlined by Xavier et al. (2023), where SUD is defined as either two outpatient records (MSP) within one year or one hospitalization record (DAD) between January 1, 2015, and December 31, 2021, using ICD-9 and ICD-10 codes (Table 2).

- This study excludes people who had an encephalopathy diagnosis before their first toxic drug poisoning event or who had encephalopathy before January 1, 2015, and those who do not have complete sex and age information in the Client Roster data.

- As in Xavier et al. (2023), the log-binomial regression model was used to estimate the association between toxic drug poisoning events and encephalopathy, both unadjusted and adjusted models. The models included age, sex, and mental disorder (Table 2) (excluding substance use disorder) variables.

Findings

- There were 881,091 people in the study sample between 2015 and 2021. Among those with encephalopathy (N = 950), 23.7% (N = 225) experienced toxic drug poisoning events; 61.2% were 50 years or older; 65.4% were males; 58.0% had a mental disorder or substance use disorder; and 14.1% died from a toxic drug poisoning event. In contrast, among those without encephalopathy, 1.2% experienced toxic drug poisoning events; 40.4% were 50 years or older; 49.9% were males; 21.4% had a mental disorder or substance use disorder; and 0.2% died from a toxic drug poisoning event (Table 3).

- People who experienced drug poisoning events (N = 10,413) continue to disproportionately experience higher rates of encephalopathy (brain injury) (2.2%, N = 225) compared to those who did not experience a drug poisoning event (N=870,678) (less than 0.001%, N = 725).

- Table 4 shows the results of the association study between drug toxicity and encephalopathy. Once sex, age, and mental disorder were controlled for, people who experienced drug toxicity events were 19.5 times (95% CI: 16.6, 22.9) more likely to have encephalopathy compared to people who did not experience drug toxicity events. This estimate is higher than previously identified at 15.3 (Xavier et al. (2023).

- People older than 30 faced a higher risk of encephalopathy compared to those under 30. Specifically, individuals over 49 were 4.0 times (95% CI: 3.3, 4.9) more likely to have encephalopathy than those under 30. Risk of encephalopathy for males was 1.8 times (95% CI: 1.6, 2.1) higher than females, and people with a mental disorder faced 2.8 times (95% CI: 2.5, 3.2) higher risk of encephalopathy.

Interpretation

Comparisons to the characteristics of the 2019 reference group (Table 5)

- People in different demographic groups were affected differently by encephalopathy when comparing these data (2015-21) to analyses previously conducted (2015-19). A greater proportion of people aged less than 40 years had encephalopathy in the 2021 study sample, with an increase from 19.5% to 24.4 % between the two study samples. Encephalopathy also became more prevalent among males (63.4% to 65.4%), individuals who experienced one or more toxic drug events (14.6% to 23.7%), and individuals with substance use disorder (6.0% to 9.5%).

- The number of people who had experienced toxic drug poisoning had doubled in the 2021 study sample (N=10,413) compared to the 2019 reference group (N=5,357), reflecting the rise in the potency of the unregulated drug supply. It is a sharp increase, especially considering that the additional two years of the data since 2019 resulted in 5,056 more cases of drug toxicity events. This rise in toxic drug poisoning events aligns with trends in other overdose indicators, such as paramedic-attended opioid overdose events and unregulated drug deaths in BC, which rapidly increased during the Covid-19 pandemic in 2020.[7] This trend is more pronounced in people with encephalopathy: 23.7% of people with encephalopathy experienced drug toxicity events in the 2021 sample (N=225), compared to 14.6% in the 2019 sample (N=54). This indicates that 2020 and 2021 alone saw 171 encephalopathy diagnoses.

- The significant increase in the percentage of people who experienced toxic drug poisoning events and had encephalopathy diagnoses in the final two years of the study may reflect a growing awareness within the healthcare system of how overdose can lead to encephalopathy. This could mean that individuals who experienced overdose are now more frequently being screened for potential brain injury, such as anoxic or toxic brain injury, after drug poisoning. Alternatively, as the toxicity of unregulated drugs increased during the COVID pandemic—especially with the rise of benzodiazepines—those affected may have shown more noticeable or severe symptoms of encephalopathy, making it easier to detect.

Limitations

- The use of health administrative data imposed a few limitations on the study, leading to an underestimation of the true number of people with a history of toxic drug poisoning events and encephalopathy diagnosis for the following reasons:

    - The data only include people who sought healthcare for toxic drug poisoning events during the study period. For instance, if overdoses were reversed in community or if a person experiencing an overdose left before the ambulance arrived at the scene, this information would not be captured in the data.

    - It is unclear whether all encephalopathy diagnoses identified in the study sample were related to toxic drug poisoning, as some of the ICD codes are more specific in identifying encephalopathy caused by drug poisoning than others.

    - Health administrative data most likely reflect only severe cases of encephalopathy, rather than mild or moderate cases.

  - Symptoms of encephalopathy may take several weeks to show up after toxic drug poisoning events, while people who experience an overdose are typically discharged from the hospital within 24 to 48 hours. Without further examination or follow-up care, encephalopathy may go undetected.

  - People who use drugs often face barriers to accessing the care they need, due to the stigma and discrimination associated with dug use. These barriers contribute to the underestimation of the true number of encephalopathy and toxic drug poisoning events.

- The data used in this study do not include harm reduction interventions, such as drug checking, overdose prevention and supervised consumption sites, or take-home naloxone, which could offer important context to the numbers.

Next Steps

- There have been significant efforts in British Columbia to build consensus around identifying the priorities and solutions needed for people at the intersection of brain injury, mental health, and addiction. Government-funded researchers, organizations, and individuals living with brain injury have come together to explore ways to improve the quality of life for those affected, as well as for their families and communities.[8,9] In addition to these efforts, this study emphasizes the importance of developing specific guidelines, tools, and assessments to advance screening and diagnosis of encephalopathy following non-fatal toxic drug poisoning.

- Further research is required to better understand the role of social determinants of health in this context. People in their 50s, males, and individuals with mental health disorders are disproportionately affected, making it crucial to investigate the reasons why this group is particularly vulnerable to encephalopathy following toxic drug poisoning.

- Expanding the scope to include broader healthcare services could offer valuable insights into how to best meet the needs of people with brain injury after overdose. This approach may help identify the most effective ways to engage with and provide care for this population.

Supporting Information

References

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Data steward(s) disclaimer

All inferences, opinions, and conclusions drawn in this Knowledge Update are those of the authors, and do not reflect the opinions or policies of the Data Steward(s).

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Tables and Figures

Table 1. ICD codes for identification of encephalopathy cases, any documented diagnosis codes

	Hospitalizations, emergency department visits (ICD-10)	Primary Care (ICD-9)
Encephalopathy, including anoxic brain damage Toxic encephalopathy Unspecified encephalopathy	G93.1 G92 G93.4	
Encephalopathy, including anoxic brain damage Toxic encephalopathy Toxic encephalitis and encephalomyelitis Toxic myelitis Unspecified encephalopathy		348.1 323.71 323.72 349.*82* 348.30

Table 2. ICD codes for mental disorder and substance use disorder diagnoses, any documented diagnosis codes

	Hospitalizations (ICD-10)	Primary Care (ICD-9)
Substance use disorder		
Opioid related disorders	F11	
Cannabis related disorders	F12	
Sedative, hypnotic, or anxiolytic-related disorders	F13	
Cocaine related disorders	F14	
Other stimulant related disorders	F15	
Hallucinogen related disorders	F16	
Nicotine dependence	F17	
Inhalant related disorders	F18	
Other psychoactive substance related disorders	F19	
Drug-induced mental disorders		292
Drug dependence		304
Nondependent abuse of drugs		305 [a]
Anxiety disorder		
Phobia anxiety disorders	F40	
Other anxiety disorders	F41	
Neurotic disorders		300[b]
Depression		
Major depressive disorder, single episode	F32	
Major depressive disorder, recurrent	F33	
Dysthymic disorder	F34.1	
Neurotic depression		300.4
Depressive disorder, not elsewhere classified		311
Schizophrenia		
Schizophrenia	F20	
Schizotypal disorder	F21	
Delusional disorders	F22	
Brief psychotic disorders	F23	
Shared psychotic disorder	F24	
Schizoaffective disorders	F25	
Other psychotic disorder	F28	
Unspecified psychosis	F29	
Schizophrenic psychoses		295
Paranoid states		297
Other nonorganic psychoses		298
Bipolar disorder		
Manic episode	F30	
Bipolar disorder	F31	
Persistent mood/affective disorders	F34[c]	
Unspecified mood/affective disorder	F39	
Affective psychoses		296
Stress and adjustment disorders		
Reaction to severe stress, and adjustment disorders	F43	
Acute reaction to stress		308
Adjustment reaction		309

[a] does not include 305.0; [b] does not include 300.4; [c] does not include F34.1

Table 3. Characteristics by encephalopathy diagnostic code, 2015-2021 (column %)

	Total (N=881,091)		Encephalopathy diagnosis (N=950)		No encephalopathy diagnosis (N=880,141)		
	N	%	N	%	N	%	p-value
Drug toxicity event (overdose), fatal or non-fatal							
Yes	10,413	1.2%	225	23.7%	10,188	1.2%	p<0.01
No	870,678	98.8%	725	76.3%	869,953	98.8%	
Age[a]							
<30 years	218,898	24.8%	114	12.0%	218,784	24.9%	p<0.01
30-39 years	158,652	18.0%	118	12.4%	158,534	18.0%	
40-49 years	147,510	16.7%	137	14.4%	147,373	16.7%	
>= 50 years	356,031	40.4%	581	61.2%	355,450	40.4%	
Sex							
Female	441,102	50.1%	329	34.6%	440,773	50.1%	p<0.01
Male	439,989	49.9%	621	65.4%	439,368	49.9%	
Mental disorder (MD) or substance use disorder (SUD)[b]							
No SUD or MD	691,944	78.5%	399	42.0%	691,545	78.6%	p<0.01
SUD	8,489	1.0%	90	9.5%	8,399	1.0%	
MD	164,341	18.7%	278	29.3%	164,063	18.6%	
SUD and MD	16,317	1.9%	183	19.3%	16,134	1.8%	
Number of drug toxicity events							
One toxic drug event	6,516	0.7%	124	13.1%	6,392	0.7%	p<0.01
Two or more toxic drug events	3,897	0.4%	101	10.6%	3,796	0.4%	
none	870,678	98.8%	725	76.3%	869,953	98.8%	
Fatal drug toxicity event							
yes	2,117	0.2%	134	14.1%	1,983	0.2%	p<0.01
no	878,974	99.8%	816	85.9%	878,158	99.8%	

[a] Age on January 1st, 2015; [b] Diagnosed 2015-2021; SUD: substance use disorder

Table 4. Association of drug toxicity and encephalopathy

	Unadjusted, PR (95% CI)	Adjusted, PR (95% CI)
Drug toxicity event (overdose)		
No	*Reference*	*Reference*
Yes	25.9 (22.4-30.1)	19.5 (16.6-22.9)
Age		
<30 years	*Reference*	*Reference*
30-39 years	1.4 (1.1-1.8)	1.4 (1.1-1.8)
40-49 years	1.8 (1.4-2.3)	1.9 (1.5-2.4)
>= 50 years	3.1 (2.6-3.8)	4.0 (3.3-4.9)
Sex		
Female	*Reference*	*Reference*
Male	1.9 (1.7-2.2)	1.8 (1.6-2.1)
Mental Disorder (MD) [a]		
No MD diagnosis	*Reference*	*Reference*
MD diagnosis	3.7 (3.2-4.2)	2.8 (2.5-3.2)

[a]Mental disorder does not include substance use disorder

PR: Prevalence ratio, CI: confidence interval

Table 5. Characteristics by encephalopathy diagnostic code, 2015-2019 (column %)[3]

	Total (N=824,165)		Encephalopathy diagnosis (N=369)		No encephalopathy diagnosis (N=823,796)		
	N	%	N	%	N	%	p-value
Drug toxicity event (overdose), fatal or non-fatal							
Yes	5,357	0.6	54	14.6	5,303	0.6	p<0.01
No	818,808	99.4	315	85.4	818,493	99.4	
Age[a]							
<30 years	197,378	23.9	41	11.1	197,337	24.0	p<0.01
30-39 years	149,377	18.1	31	8.4	149,346	18.1	
40-49 years	141,428	17.2	63	17.1	141,356	17.2	
>= 50 years	335,991	40.8	234	63.4	335,757	40.8	
Sex							
Female	414,959	50.3	135	36.6	414,824	50.4	p<0.01
Male	409,206	49.7	234	63.4	408,972	49.6	
Mental disorder (MD) or substance use disorder (SUD)[b]							
No SUD or MD	677,154	82.2	144	39.0	677,010	82.2	p<0.01
SUD	7,145	0.9	22	6.0	7,123	0.9	
MD	128,312	15.6	132	35.8	128,180	15.6	
SUD and MD	11,554	1.4	71	19.2	11,483	1.4	
Number of drug toxicity events							
One toxic drug event	3,623	0.4	35	9.5	3,588	0.4	p<0.01
Two or more toxic drug events	1,734	0.2	19	5.2	1,715	0.2	
none	818,808	99.4	315	85.4	818,493	99.4	
Fatal drug toxicity							
yes	229	0.0	8	2.2	221	0.0	p<0.01
no	823,939	100.0	361	97.8	823,575	100.0	

[a] Age on January 1st, 2015; [b] Diagnosed 2015-2019; SUD: substance use disorder