Outcomes After Toxic Alcohol Poisoning: a Systematic Review and Meta-Analysis

uOttawa
Faculté de médecine
Faculty of Medicine

Carol Wang[1], Daniel Samaha[1], Swapnil Hiremath[1], Lindsey Sikora[2], Manish M Sood[1], Salmaan Kanji[3], Edward G. Clark[1]
1=Department of Medicine, University of Ottawa; 2=Health Sciences Library, University of Ottawa; 3=Ottawa Hospital Research Institute, University of Ottawa.

Ottawa Hospital Research Institute
OHRI IRHO
Institut de recherche de l'Hôpital d'Ottawa

Background

•Poisonings by toxic alcohols (including methanol, ethylene glycol (EG), diethylene glycol (DEG), propylene glycol, and isopropanol) are associated with significant morbidity and mortality (Gallagher and Edwards, 2019).

•Accidental or intentional toxic alcohol poisonings are challenging to diagnose due to their non-specific presentations and patient inebriation (Hovda et al, 2005).

•While EXTRIP Workgroup and American Academy of Clinical Toxicology provide guidance to clinicians in the management of methanol and EG intoxications (Barceloux et al, 1999; Barceloux et al, 2002; Roberts et al, 2015), ambiguities pertaining to their treatments remain. Furthermore, there are no standardized treatments for isopropyl alcohol, propylene glycol and DEG ingestions.

•We know little about the short and long term outcomes of patient with toxic alcohol poisonings.

Objectives

This study aims to comprehensively synthesize existing evidence regarding short term and long term outcomes of adult patients following toxic alcohol poisoning.

Eligibility Criteria

Types of study	Both interventional and observational studies Case reports/series with ≤5 cases were excluded
Patients	Adults patients ≥18yo
Exposures	Toxic alcohol poisonings diagnosed per serum toxic alcohol level or other criteria included if clearly defined
Interventions	Groups of interest: a) Treated with dialysis b) Treated with antidotes fomepizole+/-ethanol c) Treated with both dialysis and antidotes d) Treated with supportive therapies only
Outcomes	Primary outcome: mortality at any time point reported Secondary outcomes: a) Renal outcomes: renal recovery, dialysis dependence b) Toxin mediated complicated

Study Selection

MEDLINE:
EMBASE:
CENTRAL:
TOTAL: 2019

→ 899 duplicates removed

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1120 Abstract and title screening

→ 972 irrelevant studies excluded

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147 Full text assessment for eligibility

→ 82 studies excluded:
Cases reports of ≤5 patients: 25
Lack report of mortality: 17
Lack of patient outcomes described: 8
No interventions specified: 4
Not original research (narrative reviews): 3
Mixed toxin poisoning with ≤5 patients due to toxic alcohols: 2
No toxic alcohol poisoning: 3
Wrong patient population: 2
Irrelevant outcomes: 1
Duplicate studies: 11
Unable to obtain full text articles: 5
Other: 1 (Abstract of an article that has been included)

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65 Studies met inclusion criteria
Observational studies: 14
Case reports/series: 52

Subsequent addition of 1 case report/series for total 66

Quality Assessment
Newcastle-Ottawa Quality Assessment scale was used to provide quality assessment of observational studies

Results

Studies: 13 retrospective, 1 prospective observational studies, 52 case reports/series.
Participants: Total participants across all included studies was 2347 with n=561 participants in the observational studies.

Baseline characteristics of observational studies on toxic alcohol poisonings.

Author	Year of Publication	Country of Publication	Study Type	N	Serum toxin level (mg/dL)	Time from ingestion to medical presentation (hr)	Non-renal Interventions				Coingestions
							Antidote Ethanol (%)	Antidote Fomepizole (%)	Elimination Enhancement (%)	Supportive Therapies (%)	
Methanol studies											
Rulisek	2017	Czech republic	R	106 (short term), 54(post-discharge)	500.9	12hr for 11%, 48hr for 35%, >48hrs for 37%, NR for 18%	67.9	22.6	None	None	E 17
Lee	2014	Taiwan	R	32	121.9	22.1	59.4	0	AC 87.5 GL 87.5	Fo 50	E
Hunderi	2006	Norway	R	17	612.6	NR	17.6	82.4	None	B 100	None
Hantson	2005	Belgium	R	18	175	NR	88	12	None	None	None
Megarbane	2001	France	R	14	50	13 (ICU admission)	21.4	100	AC 21.4 GL 7.1	B 14.3, Fo 50, T 57.1, Py 57.1	E 57.1 I 7.1
Liu	1998	USA	R	50	1001.8	NR	100	0	None	B 100	E
Ethylene glycol studies											
Iliuta	2017	Canada	R	27	882.9	NR	E 70.4% E+F 11.1%	14.8	None	None	E 14.8
Lung	2015	USA	R	121	202.2	NR	E 24%, E+F19.8%	53.7	None	None	None
Krenova	2006	Czech republic	R	33	180 (only known for 15)	3	91	0	None	None	E 27.3
Hylander	1996	Sweden	R	17	NR	6-24 (range only)	None	None	None	None	None
Sabeel	1995	Sweden	R	18	239.6	9.02	100	0	AC % NR	B 100, T 100, Py 100	None
Methanol and/or ethylene glycol studies											
Wedge	2012	Canada	R	49 (n=23 M, n=32 EG, n=2 both)	M 414.4, EG378.4	3	100	0	None	None	Illicit drugs 22.4 Household chemicals 12.2
Lister	2005	Canada	R	27	M 774.8, EG767.6	NR	100	0	None	None	E 18.5
Diethylene glycol studies											
Conklin	2014	USA	P	32	NR	NR	NR	NR	None	None	None

Renal Outcomes

Author	Ave Cr at admission (umol/L)	Indications for dialysis (as specified in study)	Dialysis during hospitalization			Renal recovery by hospital discharge		Dialysis dependence at hospital discharge (%)	Elevated Cr, non-dialysis dependence at discharge (%)	Renal Recovery after discharge (%)	Progression to ESRD (chronic dialysis dependence) (%)
			Hemodialysis (%)	Peritoneal dialysis (%)	Both HD+PD (%)	Renal recovery (%)	Duration of dialysis (hr)				
Methanol studies											
Rulisek	NR	Metabolic acidosis, toxic alcohol concentration, visual disturbances	33% IHD, 38.7% continuous modalities, 4.7% extended daily dialysis	0	NR	NR	NR	NR	NR	NR	NR
Lee	176.8	Metabolic acidosis, toxic alcohol concentration, impaired renal function	58.1	0	NR	NR	NR	NR	NR	NR	NR
Hunderi	NR	NR	100	0	NR	NR	NR	NR	NR	NR	NR
Hantson	NR	Metabolic acidosis, toxic alcohol concentration, visual disturbances	83.3	0	NR	NR	NR	NR	NR	NR	NR
Megarbane	79.1	NR	28.6	7.1	NR	NR	NR	NR	NR	NR	NR
Liu	NR	NR	100	0	NR	NR	NR	NR	NR	NR	NR
Ethylene glycol studies											
Iliuta	NR (55.6% kidney injury)	NR	96.3	0	NR	96.3	Up to 336: 88.9% >336: 7.4%	0	NR	NA	NA
Lung	123.8	NR	84.3	0	NR	NR	NR	NR	NR	NR	NR
Krenova	293.8(based on n=28)	Toxic alcohol concentration	63.6	0	NR	NR	2-26 (range provided)	NR	30.3	NA	NA
Hylander	168.5	NR	64.7	11.8	11.8	64.7	Up to 336	0	52.9	NA	NA
Sabeel	159.9	Metabolic acidosis	61.1	0	38.9	61.1	NR	0	5.6	NA	0
Methanol and/or ethylene glycol studies											
Wedge	NR (0% kidney injury)	NR	91.8	0	NR	NR	NR	6.1	NR	NR	2
Lister	NR (7.4% kidney injury)	NR	96.3	0	NR	3.7	9.2	3.7	NR	NR	3.7
Diethylene glycol studies											
Conklin	NR	NR	NR	0	0	NR	NR	25	NR	3.1 (n=1) 6-18mon post-d/c	28.1

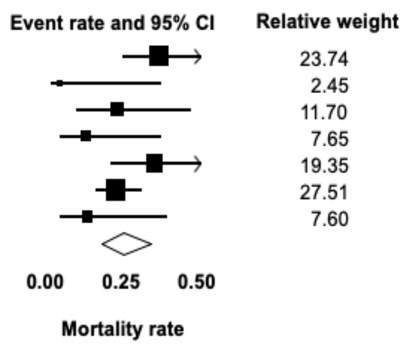
Mortality

Pooled in-hospital mortality: methanol 24% (17-33%, p<0.001), EG 11% (5-21%, p<0.001)

Methanol

Study	Year	Event rate	p-Value	Total	Relative weight
Liu	1998	0.36	0.05	18 / 50	23.74
Megarbane	2001	0.03	0.02	0 / 14	2.45
Hantson	2005	0.22	0.03	4 / 18	11.70
Hunderi	2006	0.12	0.01	2 / 17	7.65
Lee	2014	0.34	0.08	11 / 32	19.35
Rulisek	2017	0.22	0.00	23 / 106	27.51
Lister	2005	0.13	0.01	2 / 16	7.60
Summary		0.24	0.00		

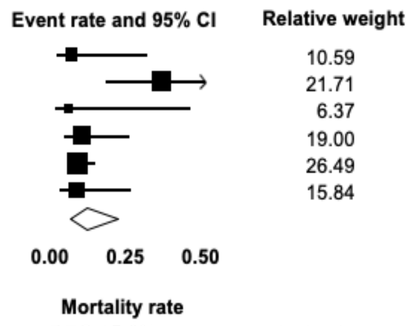
Heterogeneity Cochran Q= 10.5 I^2= 43 p=0.11



Ethylene glycol

Study name	Year	Event rate	p-Value	Total	Relative weight
Sabeel	1995	0.06	0.01	1 / 18	10.59
Hylander	1996	0.35	0.23	6 / 17	21.71
Lister	2005	0.05	0.04	0 / 10	6.37
Krenova	2006	0.09	0.00	3 / 33	19.00
Lung	2015	0.07	0.00	9 / 121	26.49
Iliuta	2017	0.07	0.00	2 / 27	15.84
Summary		0.11	0.00		

Heterogeneity Cochran Q= 11.5 I^2= 57 p= 0.04



Longterm mortality: Not reported in M, EG and M+/-EG studies. DEG 15.6% based on a single study.

Toxin Related Outcomes

- Methanol: 5.9-28.6% patients experienced short term visual deficits.
- EG: 48.8-70.6% patients required ventilatory support and 5.8-22.2% experienced short term neurologic deficits.
- DEG: 12.5% patients had cardiovascular complications while 87.5% experienced long term neurologic deficits.
- Long term visual, neurologic and cardiovascular outcomes after methanol and EG poisonings were lacking.

Conclusion

-This review summarized existing evidence of short and long term outcomes of toxic alcohol poisonings amongst adults, including mortality, renal recovery and toxin mediated complications.

-Small sample sizes, low quality and significant heterogeneity.

-Lack of standardization in reporting clinical presentations and outcomes for all types of toxic alcohol poisonings.

-Significant deficiencies in reporting of long term outcomes.

-This study may serve as a catalyst for studies on the optimal management and long term follow up of toxic alcohol poisonings.

References

•Gallagher N, Edwards FJ. The diagnosis and management of toxic alcohol poisoning in the emergency department: a review article. 2019. Adv J Emerg Med;3(3):e28.
•Hovda KE, Hunderi OH, Tafjord AB, Dunlop O, Rudberg N, Jacobsen D. Methanol outbreak in Norway 2002-2004- epidemiology, clinical features and prognostic signs. J Intern Med 2005;258:181-90.
•Barceloux DG, Krezelok EP, Olson K, Watson W. American Academy of Clinical Toxicology practice guidelines on the treatment of ethylene glycol poisoning. J Toxicol Clin Toxicol. 1999;37:537-60.
•Barceloux DG, Bond GR, Krenzelok EP, Cooper H, Vale JA. American Academy of Clinical Toxicology practice guidelines on the treatment of methanol poisoning. J Toxicol Clin Toxicol. 2002;40:415-46.
•Roberts DM, Yates C, Megarbane B, Winchester JF, Maclaren R, Gosselin S, et al. Recommendations for the role of extracorporeal treatments in the management of acute methanol poisoning: a systematic review and consensus statement. Crit Care Med. 2015; Feb;43(2):461-72.