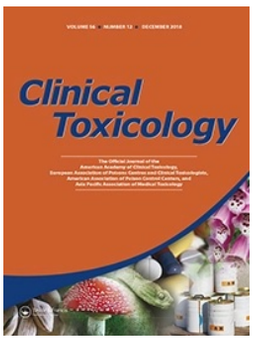

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REVIEW

Consensus statements on the approach to patients in a methanol poisoning outbreak

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ABSTRACT

Background: Methanol poisoning is an important cause of mortality and morbidity worldwide. Although it often occurs as smaller sporadic events, epidemic outbreaks are not uncommon due to the illicit manufacture and sale of alcoholic beverages.

Objective: We aimed to define methanol poisoning outbreak (MPO), outline an approach to triaging an MPO, and define criteria for prioritizing antidotes, extracorporeal elimination treatments (i.e., dialysis), and indications for transferring patients in the context of an MPO.

Methods: We convened a group of experts from across the world to explore geographical, socio-cultural and clinical considerations in the management of an MPO. The experts answered specific open-ended questions based on themes aligned to the goals of this project. This project used a modified Delphi process. The discussion continued until there was condensation of themes.

Results: We defined MPO as a sudden increase in the number of cases of methanol poisoning during a short period of time above what is normally expected in the population in that specific geographic area. Prompt initiation of an antidote is necessary in MPOs. Scarce hemodialysis resources require triage to identify patients most likely to benefit from this treatment. The sickest patients should not be transferred unless the time for transfer is very short. Transporting extracorporeal treatment equipment and antidotes may be more efficient.

Conclusion: We have developed consensus statements on the response to a methanol poisoning outbreak. These can be used in any country and will be most effective when they are discussed by health authorities and clinicians prior to an outbreak.

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Supplemental data for this article can be accessed here.

Introduction

Methanol poisoning is an important cause of mortality and morbidity worldwide. Although it often occurs as smaller sporadic events, epidemic outbreaks are not uncommon in different parts of the world due to the illicit manufacture and sale of alcoholic beverages. Outbreaks have occurred in Cambodia, Czech Republic, Ecuador, Estonia, India, Indonesia, Kenya, Libya, Nicaragua, Norway, Pakistan, Romania, Sudan, Iran, Turkey, and Uganda [1–11]. Other outbreaks are mentioned in news reports, but many methanol poisoning outbreaks are unreported. The size of the reported outbreaks ranged from 20 to over 1000 victims. Alarmingly, case fatality rates exceed 30% in some instances, and morbidity is often significant in survivors. The high mortality and morbidity are mainly due to the significant delay in victims seeking or obtaining effective medical care, because the effect of medical treatment is markedly reduced in delayed presentations [2,3]. Furthermore, in the absence of an adequate assessment of clinical and laboratory findings, methanol poisoning may be misdiagnosed as ethanol intoxication in early stages.

A number of factors contribute to the delay in receiving appropriate care. In areas where alcohol consumption is not socially or religiously acceptable, presentations may be delayed due to fears of punishment [1,3], making active case finding a positive and practical approach in such situations [3]. Second, the nonspecific signs and symptoms of early methanol poisoning leads to delays in diagnosis [1]. Limited knowledge of methanol poisoning amongst the clinicians coupled with the episodic nature of the outbreaks further contributes to delays in treatment initiation. Strategies to reduce these delays may include improving medical education about methanol, improving communication among health care facilities about sentinel cases, improving warning strategies to the public during ongoing outbreaks, and improving access to diagnostic and treatment resources [12].

Large outbreaks typically overwhelm local health care facilities. Here, prompt triage is important but complicated [12,13]. For example, symptoms may be minimal at the time of assessment for early presentations, despite a high risk of severe toxicity. In contrast, other patients may present with such severe toxicity that very poor outcomes are anticipated regardless of the treatment received [13].

Methanol poisoning outbreaks require a systematic and coordinated response, but there are few resources to guide clinicians and government health authorities. This is particularly concerning given that methanol poisoning outbreaks typically occur in resource-poor regions which lack infrastructure for a rapid response and planning.

Therefore, we aimed to develop consensus statements for responding to methanol poisoning outbreaks for health professionals and Government health authorities regardless of the clinical or geographical setting. The main goals of the present project were to agree on a definition of a methanol poisoning outbreak (MPO), outline an approach to triaging an MPO, and to define criteria for prioritizing antidotes, extracorporeal elimination treatments (e.g., dialysis), and indications for transferring patients in the context of an MPO.

Methods

Review of literature and expert selection

The first author performed a literature review to find possible studies referring to the aim of the study and key people involved in MPOs. Recently published consensus recommendations for the use of extracorporeal elimination treatments (ECTRs) in methanol poisoning [14] did not provide guidance on patient triage in the context of an outbreak.

This project used a modified Delphi process. Twenty-five experts were identified, of whom 22 experts involved in MPOs and/or clinical toxicologists accepted the invitation to explore geographical, socio-cultural, and clinical considerations in the management of a methanol poisoning outbreak. The experts were from different parts of the world: 5 from United States of America, 4 from Iran, 2 from Australia, 2 from Norway, 2 from the UK, 2 from India, 2 from the Czech Republic, 1 from Estonia, 1 from France, and 1 from Belgium. Most experts are active members of any of the four main clinical toxicology associations and work in association with a poison control/information center.

Consensus statement development

The experts answered specific open-ended questions based on themes aligned to the goals of this project (Table 1). The primary author asked them to provide references to support their opinion, where possible. The lead and firewallem author developed these questions based on their experience with methanol poisoning outbreaks. In addition, the literature search identified experiences in poisoning outbreaks elsewhere and practices for responding to chemical and radiological emergencies.

The discussion continued until there was saturation of themes. The strength of the recommendation for each statement was determined according to Table 2, based on the GRADE system [15]. The quality of evidence was graded from A to D, whereby A (high quality) reflected well-conducted randomized controlled trials and D (very low quality) reflected data of lesser quality.

The panel considered laboratory tests useful in patients with methanol poisoning (Supporting Information Appendix, Table 1S). To initiate discussion regarding treatment prioritization on the individual level, we constructed 11 clinical scenarios (Supporting Information Appendix, Table 2S). The scope of the project was presented at the 2016 European Association of Poisons Centers and Clinical Toxicologists (EAPCCT) Congress in Spain to seek input from the international clinical toxicology community on the process.

Each expert responded to questions and provided justification using free text which was then returned to the lead (first) author. The lead and second authors then developed draft statements and submitted these to the expert panel to ascertain if they agreed ("agree", "disagree" or "neutral"). Each expert had the opportunity to make free text comments regarding specific concerns and/or suggestions to the draft text. The lead author reviewed all comments and, when appropriate, modified the draft to incorporate suggested

Table 1. Themes and examples of questions asked to expert participating in the project.

What is the definition of a methanol poisoning outbreak?
Notification of the public and health systems at the onset of an MPO, and active case finding
• Should an active case-finding strategy be undertaken?
• Who is responsible for case-finding and communication in this context?
• What methods should be used for case-finding?
• How to avoid overcrowding of healthcare facilities, for example the Emergency Department
The diagnosis of methanol poisoning
The use of triaging systems to prioritize patients
• How is methanol poisoning established in resource poor regions?
• Is it necessary or useful to triage patients in an MPO?
• Are there any existing triage systems (e.g., poisoning severity scores relevant to methanol)?
• Are there ethical implications of triaging patients in an MPO?
Administration of antidotes
• Are particular antidotes preferred in certain circumstances?
• How can stocks of antidotes be maximally utilized?
Administration of extracorporeal elimination treatments
• Are particular ECTRs preferred? Does this depend on the circumstance?
• How long should ECTR be performed for?
Transfer of patients to other centers
• If a healthcare facility is approaching capacity, which patients (if any) should be prioritized for transfer to another center?
• Should patients who are being transferred receive particular treatment?

Table 2. Determining the strength of recommendations for the expert consensus statements.

Level 1 _ Strong recommendation _ "We recommend … "
We used this recommendation if more than 95% ofexperts supported it with no major dissent. Here, the panel is confident that the desirable effects of adherence to the recommendation outweigh the undesirable effects of this course of action.
Level 2 _ Weak recommendation _ "We suggest … "
We used this recommendation if more than 90% ofexperts supported it, but some degree of dissent existed among the panelmembers. Here, the panel believes that the desirable effects of adherence to the recommendationprobably outweigh the undesirable effects of this course of action
Level 3 _ Neutral recommendation _ "It would be reasonable … "
We used this recommendation if more than 50% but less than 90% of experts supported it. Here, the panel believes that this course of action could be considered appropriate in the rightcontext
No recommendation
We could not reach any agreement.

changes. On each discussion round, comments were anonymized and copy-pasted directly into a table. The updated document and comments were then circulated back to each expert for reflection, voting ("agree", "disagree" or "neutral"), and further discussion.

Subsequent rounds of discussion were supplemented by additional information and evidence. For example, expert opinions on triaging and the prioritization of treatments were guided by aggregated data published in two separate publications (representing 304 patients from five countries [2,16]) which summarizes clinical outcomes on the basis of admission clinical features, Figure 1. These data reveal six different levels of risk (Risk groups A to F) which were collapsed into four clinical risk categories based on outcomes:

- Category 1 (Risk group A): pH $\geq$ 7 and alert: mortality 5%
- Category 2 (Risk group B): pH 6.74-6.99 and alert: mortality 14%
- Category 3 (Risk groups C + D + E): pH $<$ 6.74 and alert or pH 6-74-6.99 and coma: mortality 52%
- Category 4 (Risk group F): pH $<$ 6.74 and coma: mortality 83%

At the point of near-finalization of the consensus statements, the lead author identified the panel to each other and invited them to attend a face-to-face meeting for further discussion at the 2017 Asia Pacific Association of Medical Toxicology (APAMT) Annual Scientific Congress in Sri Lanka. The two lead authors collected the feedback and incorporated that into the current manuscript.

The proposed consensus statements were then distributed to key clinical/medical toxicology associations for external review. The final recommendations were presented at the 2019 EAPCCT Congress in Italy.

Results

Definition of a methanol poisoning outbreak

We recommend (Level 1D) that a methanol poisoning outbreak is defined as a sudden increase in the number of cases of methanol poisoning during a short period of time (days to weeks) above what is normally expected in the population in that specific geographic area [17]. Local Poison Control Centers (PCCs) or Government health authorities should define the "normally expected number" on the basis of their annual statistics or local conditions.

In the absence of such baseline data, we recommend (Level 1D) that three victims in a community or geographical area (e.g., village, town, or city) within a limited time (e.g., $<$48–72 h) should be considered an MPO.

Where MPOs occur frequently, for example Indonesia, they should be considered an endemic problem. However, in these circumstances temporal increases in cases, usually on a large scale, are still reported and each should still be considered an MPO according to the definition recommended.

Although time and resources are important for the management of an MPO, their availability should not be used in defining an outbreak.

Notification of the public and health systems at the onset of an MPO, and active case finding

We suggest (Level 2D) that local health authorities actively search for cases when an MPO occurs. Here, case-finding refers to activities that alert the public and health professionals to an MPO and facilitates presentation to a healthcare facility.

We suggest (Level 2D) that Government health authorities should be responsible for the active case-finding of poisoned individuals who have not yet presented to hospital. An expert who did not agree with this recommendation stated that this was due to unawareness of who could do this, and how it could be done, in his/her country or region.

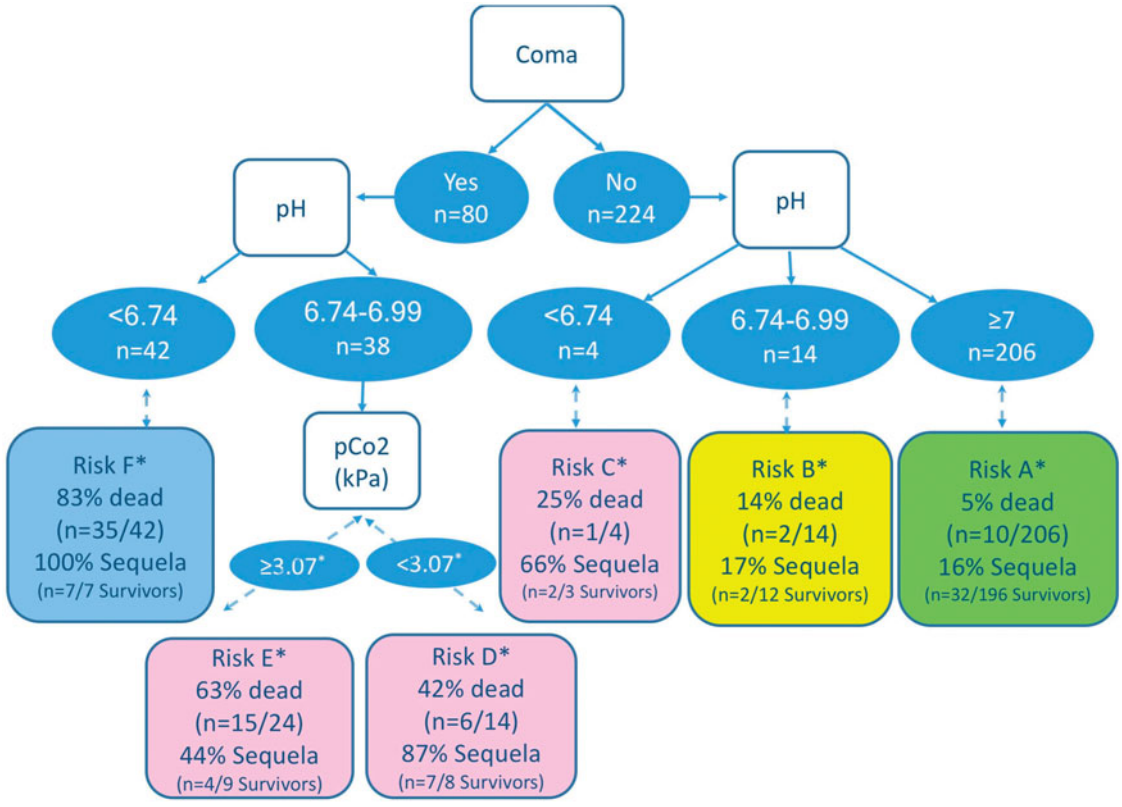

Figure 1. Overview of outcomes on the basis of admission conscious level, blood pH and pCO_2, based on aggregated data from Paasma et al. [16] and Zakharov et al. [2]*. Version 1 (color): * 3.07 kPa = 23 mmHg. Version 2: B&W: * 3.07 kPa = 23 mmHg.

The use of triaging systems to prioritize patients

We believe it is reasonable (Level 3D) to use a triage system in the context of an MPO in both developed and developing countries. However, the triage process is potentially complicated in an MPO given that it requires a number of clinical and biochemical variables, and their severity, to be considered relative to the time of exposure and presence of ethanol; the age of the patient is of limited relevance. When a triaging system is used, we recommend (Level 1C) triage using level of consciousness, pH, and pCO_2 when and where these are available (Figure 1).

Administration of antidotes

We recommend (Level 1C) that patients with a high probability of methanol poisoning during an MPO are promptly administered an antidote while further assessment is undertaken.

We recommend (Level 1B) that antidote administration should occur in the pre-hospital setting where possible, because early antidote initiation improves clinical outcomes [18–20]. We believe that potential misuse of oral ethanol is uncommon in MPOs and that the need for early antidotal treatment of poisoned patients overrides this potential concern. This is especially so when there is high suspicion of methanol poisoning and a long transporting time.

We recommend (Level 1D) that in the event both fomepizole and ethanol are available, patients with more severe poisoning receive fomepizole and that lesser poisoned patients receive ethanol [21]. We recommend (Level 1D) that patients who are pregnant or <14 years old are prioritized to receive fomepizole [21].

We recognize that ethanol dosing is often difficult [19], but we also recognize that fomepizole may be scarce or unavailable in settings where MPOs may arise. Considering the variable availability and expense of fomepizole, we recommend (Level 1B) a "use what you have" approach [22] to the selection of ethanol or fomepizole.

We did not achieve consensus on using lower doses of fomepizole to allow more patients to be treated with this antidote. We recommend (Level 1D) the published loading dose of fomepizole (15 mg kg^{-1}) to the patients with most severe poisonings (acidosis, visual disturbance, or coma).

We recommend (Level 1D) that if sufficient fomepizole is available, patients at high risk of toxicity but no current acidosis or end organ damage receive fomepizole. For example, this includes patients with a high osmol gap (>20–30 mOsm after accounting for the effect of ethanol, if any) or methanol concentration >50 mg dL^{-1} (15.6 mmol L^{-1}). This will allow admission to a non-high dependency unit (HDU)/intensive care unit (ICU) environment, thereby prioritizing such facilities for patients in more need. It is important to emphasize that osmolality must be measured by a freezing-point depression method, and not a vapor-pressure method: The latter will not detect the increased osmolality caused by the volatile alcohols, and thus give a false negative result. Thus, this excludes the osmolality measurements by some blood gas machines [23]. We recommend (Level 1D) that patients requiring antidote treatment also receive optimal treatment

with bicarbonate, folic/folinic acid, and supportive treatment as necessary.

Administration of extracorporeal elimination treatments

We recommend (Level 1D) the "use what you have" approach [22] to the selection of ECTR modality.

We recommend (Level 1D) prioritizing ECTR to those with visual disturbances, particularly when deciding between patients within the same risk category (Figure 1).

We recommend (Level 1D) that category 3 (Figure 1) has the highest priority for ECTR in the context of an MPO where the need for ECTR exceeds resources.

It is reasonable (Level 3D) that category 4 is the next priority (14 experts (64%) supported this) due to the severe clinical condition and lower chance of survival without ECTR. However, eight experts (36%) prioritized category 2 above category 4 because 17% (7/42) survivors in category 4 were likely to suffer marked/irreversible neurological sequelae, while category 2 had a reasonable chance of survival without sequelae (71% (10/14)) if ECTR was provided immediately. We recommend (Level 1D) that category 1 is the lowest priority, particularly in those without visual disturbance.

These decisions about ECTRs follow the requirement that all patients have received optimal treatment, notably antidote (discussed above), bicarbonate, folic/folinic acid, and supportive treatment as necessary. Furthermore, patients should be re-assessed at least every 30 minutes for the most severely ill, with a similar re-assessment at least every hour for the patients with lesser toxicity.

Transfer of patients to other centers

We recommend (Level 1D) that a preparedness plan is established for the transferring of poisoned patients to other hospitals in each region. Issues to consider include bed capacities, distance of transferring between the hospitals, ability to maintain optimal treatment during transfer, experience, availability of ECTR and antidotes, and expected outcome.

We recommend (Level 1D) that the most stable patients are transferred to other centers when patient numbers exceed local resources or capacity. Specifically, we recommend (Level 1D) that patients in risk category 1 and 2 in Figure 1 are the highest priority for transfer to another center, when feasible.

Discussion

We present expert consensus recommendations to guide processes and decision-making in a methanol poisoning outbreak. These are relevant to both clinicians and government health authorities and equally applicable in resource-limited and -sufficient environments, regardless of the facility (whether a primary, secondary or tertiary center). Past experience indicates that the majority of outbreaks occur in regions where resources and capacity are most limited [1,3]. During outbreaks, major challenges include limits in laboratory facilities, antidotes, ECTR facilities, ICU facilities, and experienced medical staff. This emphasizes the importance of training, as well as appropriate triaging so that resources are appropriately utilized in this context. The proposed categorization seems appropriate as it is based on clinical outcomes from case series in methanol outbreaks, ranging from 5% mortality when $pH \geq 7$ and alert (category 1) to 83% mortality in $pH < 6.74$ and coma (category 4), Figure 1. Therefore, during this project we sought to make recommendations that are as generalizable as possible.

Definition of a methanol poisoning outbreak

We adopted a definition that was similar to that used by the WHO, specifically that an outbreak as the occurrence of cases of a condition in excess of what would normally be expected in a defined community or geographical area [17]. However, by this definition, even one case of unintentional methanol exposure may be considered as a methanol poisoning outbreak. Because sporadic cases of methanol exposures which do not pose a risk to other individuals are frequently reported in many countries across the world, we decided that this definition was too liberal and may unnecessarily increase resource utilization. Therefore, the expert panel modified the WHO definition to a minimum number of three cases within a few days to a few weeks (Table 3).

Notification of the public and health systems at the onset of an MPO, and active case finding

These statements were considered necessary because the early management of the patients in a healthcare facility optimizes clinical outcomes. These statements are considered particularly important in countries where there may be legal issues regarding the use of alcohol because this is associated with significant delays in hospital presentation. Active case finding reduced severe outcomes in a large outbreak in Iran in 2014 by facilitating the clinical management of poisoned victims who had not developed symptoms, those with symptoms not yet attributed to methanol (e.g., misdiagnosis), and those reluctant to seek help due to local, cultural, and religious barriers.

The use of triaging systems to prioritize patients

Diagnosing methanol poisoning was not a key goal of this project because specific criteria can vary depending on the history and resources available, see Supporting Information Table 1S. However, simplified treatment protocols are readily available elsewhere, for example (https://msf.no/mpi).

Clinicians and Government health authorities must consider available local resources when planning training programs and also criteria prompting an MPO alert.

It is anticipated that ethical issues will be raised with the application of triage tools that seek to prioritize treatments amongst patients. Ethical issues also include misallocation of resources for the treatment of patients for which there is a limited chance of recovery, in particular when there are other

Table 3. Expert consensus statements on the approach to a methanol poisoning outbreak.

Definition of a methanol poisoning outbreak

We recommend (Level 1D)that a methanol poisoning outbreak is defined as a sudden increase in the number of cases of methanol poisoning during a short period of time (days to weeks) above what is normally expected in the population in that specific geographic area. In the absence of such baseline data, we recommend (Level 1D) that three victims in a community or geographical area (e.g., village, town or city) within a limited time (e.g., $<48-72$ h) should be considered an MPO.

Notification of the public and health systems at the onset of an MPO, and active case finding

We suggest (Level 2D) that in the context of an MPO that active case-finding is undertaken.

We suggest (Level 2D) that Government health authorities should be responsible for the active case-finding of poisoned individuals who have not yet presented to hospital.

The use of triaging systems to prioritize patients

It is reasonable (Level 3D) to use a triage system in the context of an MPO in both developed and developing countries.

We recommend (Level 1C) triage using level of consciousness, pH, and pCO_2 when and where these are available (Figure 1)

Administration of antidotes

We recommend (Level 1C)that patients with a high probability of methanol poisoning during an MPO are promptly administered an antidote while further assessment is undertaken.

We recommend (Level 1B)that antidote administration should occur in the pre-hospital setting, where possible.

We recommend (Level 1D) that in the event both fomepizole and ethanol are available, patients with more severe poisoning receive fomepizole and that lesser poisoned patients receive ethanol.

We recommend (Level 1D)that patients who are pregnant or <14 years old are prioritized to receive fomepizole

We recommend (Level 1D)that if sufficient amounts of fomepizole are available then patients at high risk of toxicity, but no current acidosis or end organ damage, receive fomepizole.

We recommend (Level 1D) the published loading dose of fomepizole (15 mg kg^{-1}) for patients with severe poisoning (acidosis, visual disturbance, or coma).

However, in view of the variable availability and expense of fomepizole we recommend (Level 1B) a "use what you have" approach in the selection of ethanol or fomepizole.

We recommend (Level 1D) that patients requiring antidote treatment also receive optimal treatment with bicarbonate, folic/folinic acid, and supportive treatment as necessary.

Administration of extracorporeal elimination treatments

We recommend (Level 1D) the "use what you have" approach to the selection of ECTR modality

We recommend (Level 1D)prioritizing ECTR to those with visual disturbances, particularly when deciding between patients within the same risk category

We recommend (Level 1D) that risk category 3 (Figure 1) is the highest priority for ECTR in the context of an MPO where the need for ECTR exceeds resources.

It is reasonable (Level 3D) that risk category 4 is the next priority due to the severe clinical condition and lower chance of survival without ECTR (see text for more discussion).

We recommend (Level 1D) that risk category 1 is the lowest priority, particularly in those without visual disturbance.

These decisions about ECTRs follow the requirement that all patients have received optimal treatment, notably antidote, bicarbonate, folic/folinic acid, and supportive treatment as necessary.

Transfer of patients to other centers

We recommend (Level 1D)that a preparedness plan is established for the transferring of poisoned patients to other hospitals in each region. Issues to consider include bed capacities, distance of transferring between the hospitals, ability to maintain optimal treatment during transfer, experience, availability of ECTR and antidotes, and expected outcome.

We recommend (Level 1D)that the most stable patients are transferred to other centers when patient numbers exceed local resources or capacity. Specifically, we recommend (Level 1D) that patients in risk categories 1 and 2 (Figure 1) are the highest priority for transfer to another center, when feasible.

poisoned patients who are more likely to benefit from the treatment. These ethical considerations are complicated by substantial limitations in existing data, national and regional variability in cultural beliefs and values, and medico-legal practice. In spite of the difficulties, these are all decisions that clinicians cannot avoid making; a scientific approach to the triaging of these patients may facilitate this process.

Administration of antidotes

Prompt initiation of an antidote has a high priority in methanol poisoning [24], and the work by Zakharov et al. supported the strategy used in Estonia of giving prehospital ethanol to minimize treatment delays. This strategy is particularly feasible during ongoing outbreaks and in case of long transport distances [10,18].

Antidotes might be of limited availability per se, but oral ethanol (e.g., alcoholic beverages) is often available or can be made available in many places. Although data comparing the effectiveness of fomepizole to ethanol are lacking [16,23], fomepizole is generally accepted as superior to ethanol, mainly due to less adverse effects [19,21,25], simplicity of dosing, and more reliable inhibition of alcohol dehydrogenase. This was the basis for recommending fomepizole over ethanol for certain populations.

While acknowledging that fomepizole stocks are likely to be lower than those of ethanol in most areas, we were unable to recommended alternative dosing regimens of fomepizole for the purpose of preserving stocks to allow its use in a higher number of patients.

Administration of extracorporeal elimination treatments

ECTR is a particularly important treatment of methanol poisoning, but in most MPOs it is a limited resource prompting careful decision-making regarding its use. Consensus statements for indications of ECTR in methanol poisoning were recently published [1] which have the potential to reduce unnecessary treatments (e.g., patients with mild poisoning). However, scarce hemodialysis resources require triage to identify patients most likely to benefit from this treatment. Thus, outcome-based data (Figure 1) were utilized for prioritizing ECTR in the context of an MPO (Table 3).

The required duration of ECTR depends on the type of ECTR used, clinical manifestations, and the methanol exposure (based on dose or concentration) [1]. Some researchers have recommended specific calculation of the initial methanol level to estimate the time of dialysis needed [26,27], but most areas do not have ready-access to methanol assays. Thus, most guidelines recommend at least 6–8 h of intermittent hemodialysis (IHD) [24,28] or 18 h for continuous renal replacement therapy (CRRT) [29]. Typically, in the event of mass outbreaks, the lack of both dialysis machines and laboratory equipment makes alternative strategies necessary [1]. Although IHD is more effective than CRRT for methanol clearance and correcting acidemia [29,30], to simplify decision-making in an MPO we recommend the "use what you have" model as documented in the Czech Republic [22].

Transfer of patients to other centers

This is a necessary consideration when the initial center's physical capacity is overwhelmed or are likely to become so, but other hospitals have capacity, including staff, beds, and equipment. Multiple factors must be considered when evaluating the transfer of patient(s) from one healthcare center to another [31].

Although it appears advantageous to spread the more severely poisoned patients across institutions, the sickest patients (those with coma, hemodynamic instability, acidosis, and signs of visual toxicity) should not be transferred unless the distance or time for transfer is very short because of the risk of clinical decline during transfer. Therefore, we recommend that the most stable patients are transferred to other centers.

Otherwise, increasing the capacity of the ICU/HDU in the initial center (including additional personnel), can be a better option. The use of fomepizole simplifies the transfer significantly due to the favorable adverse effect profile and the simplified dosing regimen. Transporting ECTR equipment and especially antidotes to the patients may be more efficient than transporting patients to the treatment facilities.

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Disclosure statement

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