

ADVANCES IN THE TREATMENT OF METHANOL POISONING: A REVIEW OF CURRENT CLINICAL EVIDENCE

AVANÇOS NO TRATAMENTO DA INTOXICAÇÃO POR METANOL: UMA REVISÃO DAS EVIDÊNCIAS CLÍNICAS ATUAIS

AVANCES EN EL TRATAMIENTO DE LA INTOXICACIÓN POR METANOL: UNA REVISIÓN DE LA EVIDENCIA CLÍNICA ACTUAL

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ABSTRACT

Methanol poisoning is a serious global public health problem, associated with high morbidity and mortality rates and outbreaks related to the consumption of adulterated beverages. This study aimed to identify, analyze, and synthesize recent clinical evidence on treatment strategies for methanol poisoning, with an emphasis on therapeutic and organizational advances over the last decade. This is an integrative literature review, conducted according to the steps proposed by Whittemore and Knafl (2005). The search was conducted in the

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PubMed, SciELO, Scopus, and Consensus Database between November and December 2025, using the descriptors “methanol poisoning,” “treatment,” “fomepizole,” “ethanol therapy,” and “hemodialysis.” A total of 216 studies were identified, of which 12 met the inclusion criteria (publications between 2013 and 2025, full text, and clinical-therapeutic focus). The evidence points to fomepizole as the first-choice antidote and early hemodialysis as a determining factor in reducing mortality and neurological sequelae. Standardized clinical protocols and multidisciplinary teams contributed to greater effectiveness and speed of care. It is concluded that this review contributes to consolidating the clinical evidence on the treatment of methanol poisoning, providing support for evidence-based practice and the formulation of public policies focused on clinical toxicology.

Keywords: Methanol Poisoning. Fomepizole. Ethanol. Hemodialysis. Clinical Toxicology. Integrative Review.

RESUMO

A intoxicação por metanol constitui um grave problema de saúde pública global, associada a elevadas taxas de morbimortalidade e a surtos relacionados ao consumo de bebidas adulteradas. Este estudo teve como objetivo identificar, analisar e sintetizar as evidências clínicas recentes sobre as estratégias de tratamento da intoxicação por metanol, com ênfase nos avanços terapêuticos e organizacionais da última década. Trata-se de uma revisão integrativa da literatura, conduzida conforme as etapas propostas por Whitemore e Knafl (2005). A busca foi realizada nas bases PubMed, SciELO, Scopus e Consensus Database, entre novembro e dezembro de 2025, utilizando os descritores “methanol poisoning”, “treatment”, “fomepizole”, “ethanol therapy” e “hemodialysis”. Foram identificados 216 estudos, dos quais 12 atenderam aos critérios de inclusão (publicações entre 2013 e 2025, texto completo e enfoque clínico-terapêutico). As evidências apontam o fomepizole como antídoto de primeira escolha e a hemodiálise precoce como fator determinante para a redução da mortalidade e das sequelas neurológicas. Protocolos clínicos padronizados e equipes multiprofissionais contribuíram para maior eficácia e agilidade no atendimento. Conclui-se que esta revisão contribui para consolidar as evidências clínicas sobre o tratamento da intoxicação por metanol, oferecendo subsídios para a prática baseada em evidências e para a formulação de políticas públicas voltadas à toxicologia clínica.

Palavras-chave: Intoxicação por Metanol. Fomepizole. Etanol. Hemodiálise. Toxicologia Clínica. Revisão Integrativa.

RESUMEN

La intoxicación por metanol constituye un grave problema de salud pública a nivel mundial, asociado a elevadas tasas de morbilidad y mortalidad y a brotes relacionados con el consumo de bebidas adulteradas. El objetivo de este estudio fue identificar, analizar y sintetizar las pruebas clínicas recientes sobre las estrategias de tratamiento de la intoxicación por metanol, haciendo hincapié en los avances terapéuticos y organizativos de la última década. Se trata de una revisión integradora de la literatura, realizada según las etapas propuestas por Whitemore y Knafl (2005). La búsqueda se realizó en las bases de datos PubMed, SciELO, Scopus y Consensus Database, entre noviembre y diciembre de 2025, utilizando los descriptores «methanol poisoning», «treatment», «fomepizole», «ethanol therapy» y «hemodialysis». Se identificaron 216 estudios, de los cuales 12 cumplían los criterios de inclusión (publicaciones entre 2013 y 2025, texto completo y enfoque clínico-terapéutico). Las pruebas apuntan al fomepizol como antídoto de primera elección y a la



hemodiálisis temprana como factor determinante para la reducción de la mortalidad y las secuelas neurológicas. Los protocolos clínicos estandarizados y los equipos multidisciplinarios contribuyeron a una mayor eficacia y agilidad en la atención. Se concluye que esta revisión contribuye a consolidar la evidencia clínica sobre el tratamiento de la intoxicación por metanol, ofreciendo apoyo para la práctica basada en la evidencia y para la formulación de políticas públicas orientadas a la toxicología clínica.

Palabras clave: Intoxicación por Metanol. Fomepizol. Etanol. Hemodiálisis. Toxicología Clínica. Revisión Integrativa.

1 INTRODUCTION

Methanol poisoning represents a serious global public health problem, often associated with the accidental or intentional ingestion of adulterated beverages and industrial products containing the compound. Methanol is a toxic alcohol that, after absorption, is metabolized in the liver by the enzyme alcohol dehydrogenase, giving rise to formaldehyde and formic acid, metabolites that are highly harmful to the central nervous system, the gastrointestinal tract and the optic nerve. Ingestion of small amounts can result in irreversible blindness, severe metabolic acidosis, and death, configuring a high-lethality medical emergency (Paasma et al., 2018).

According to the World Health Organization (WHO, 2023), it is estimated that more than 20 thousand cases of methanol poisoning have been recorded globally in the last two decades, with mortality rates ranging between 30% and 60%, especially in countries in Asia, Africa, and Latin America, where there is less control over the production and marketing of alcoholic beverages. In Brazil, occasional outbreaks continue to be reported, such as the one that occurred in 2020, in the State of Santa Catarina, which resulted in multiple deaths after consumption of adulterated beverages (Fiocruz, 2021). These episodes highlight the need to improve surveillance, diagnosis, and treatment protocols, in addition to reinforcing public policies aimed at the prevention and management of these poisonings.

The treatment of methanol poisoning has evolved substantially in recent decades. Traditionally, ethanol has been widely used as a competitive antidote for its ability to inhibit the action of alcohol dehydrogenase and prevent the formation of toxic metabolites. However, recent studies show that fomepizole has become the antidote of choice, due to its higher efficacy, safety, and pharmacokinetic predictability (Hassanian-Moghaddam et al., 2019). At the same time, early hemodialysis remains an essential intervention, allowing the rapid removal of methanol and its metabolites, as well as the correction of severe metabolic acidosis (Zakharov et al., 2021).

In recent years, technological advances have provided new possibilities in clinical management, with emphasis on the use of artificial intelligence algorithms in the early detection of poisonings, improvement of multidisciplinary care protocols, and development of updated clinical guidelines aimed at emergency toxicology (Liu et al., 2020). These innovations reinforce the importance of revisiting recent scientific evidence, seeking to understand how new therapeutic and technological approaches have influenced clinical outcomes and patient survival.

Despite this progress, significant gaps persist in the scientific literature. There are still disagreements regarding the most effective antidote, the ideal time to start hemodialysis, the recommended doses of fomepizole, and the applicability of emerging technologies in clinical practice. There is also a dispersion of studies in different databases and clinical contexts, making it difficult to consolidate updated and integrated guidelines on the management of methanol poisoning (Paasma et al., 2018; Zakharov et al., 2021).

Given this scenario, it is essential to gather and critically analyze the clinical evidence published in the last decade, in order to identify the main therapeutic advances and recognize the limitations that still exist in the management strategies of methanol poisoning. To this end, we opted for an integrative literature review, an approach that enables the synthesis of results from different study designs, favoring a comprehensive and updated view of the subject.

Thus, this study aims to identify, analyze and synthesize recent clinical evidence on methanol poisoning treatment strategies, with emphasis on therapeutic advances, management protocols and technological innovations described in the scientific literature published between 2013 and 2025. It is hoped that this review will contribute to the improvement of clinical knowledge, favor the updating of therapeutic guidelines, and strengthen evidence-based care practice in the field of clinical toxicology.

2 METHODOLOGY

It is an integrative literature review, a method that aims to gather, analyze and critically synthesize the available scientific knowledge on a given topic, allowing the combination of results of empirical and theoretical studies and providing a broad and updated understanding of the phenomenon studied. This review modality was chosen because it allows the integration of different types of studies and designs, offering a comprehensive analysis of the existing evidence on the treatment of methanol poisoning.

The elaboration of this review followed the methodological steps proposed by Whitemore and Knafl (2005): identification of the problem, definition of inclusion and exclusion criteria, search and selection of studies, extraction and evaluation of data, analysis and synthesis of results.

The guiding question that guided the process was: "What are the advances and recent clinical evidence on the treatment strategies of methanol poisoning in the last 10 years?". The general objective was to identify, analyze and synthesize the current clinical evidence

related to the main therapeutic strategies and advances in the management of methanol poisoning, considering scientific publications from the last ten years (2013–2025).

Articles published between 2013 and 2025, in English, Portuguese, or Spanish, available in full text, and that addressed therapeutic strategies, clinical management, or recent advances in the treatment of methanol poisoning were included. Experimental studies, in vitro or animal research, articles with no direct relationship to clinical treatment, conference abstracts, editorials, and letters to the editor were excluded.

The bibliographic search was carried out between November and December 2025 in the PubMed/MEDLINE, SciELO, Scopus, and Consensus Database, the latter used as a complementary source for access to recent international articles. The descriptors (DeCS/MeSH) used were combined based on the terms: ("methanol poisoning" OR "methanol intoxication") AND ("treatment" OR "fomepizole" OR "ethanol therapy" OR "hemodialysis" OR "clinical management" OR "artificial intelligence"). The Boolean operators AND and OR were applied to broaden and refine the results.

The initial search identified several studies related to the topic. After removing duplicates, the titles and abstracts were read to verify their relevance. Then, the selected articles were submitted to complete reading to confirm their adequacy to the inclusion criteria. The entire screening process was conducted by two reviewers independently, and any disagreements were resolved by consensus. The selection of articles followed the principles of the adapted PRISMA model, and the final total included 12 articles that fully met the established criteria.

Data extraction was conducted using a structured instrument prepared in an electronic spreadsheet (Microsoft Excel®), containing the following variables: author, year of publication, journal, type of study, country of origin, therapeutic interventions described, main results and conclusions. This instrument was validated by cross-review among the researchers, in order to ensure consistency and minimize interpretation biases.

To assess the methodological quality of the included studies, a descriptive critical analysis was applied based on criteria of clarity of objectives, adequacy of the methodological design, and coherence between results and conclusions, according to the recommendations of the Critical Appraisal Skills Programme (CASP, 2018). This evaluation was exploratory, seeking to identify the level of methodological robustness of the available evidence.

Data analysis was conducted through descriptive and interpretative thematic synthesis, with coding and grouping of information according to content similarities and

clinical focus. From this process, four main categories emerged: (1) pharmacological antidotes and therapies (fomepizole and ethanol), (2) clinical management and intensive support (hemodialysis and correction of metabolic acidosis), (3) complications and clinical prognosis, and (4) recent therapeutic advances, including the use of artificial intelligence and multidisciplinary approaches.

The synthesis of the studies allowed the identification of relevant clinical advances in the treatment of methanol poisoning, with emphasis on the use of fomepizole as a preferred antidote, early hemodialysis as a determining measure in reducing mortality, and the positive impact of technological innovations and integrated protocols on clinical prognosis.

However, methodological limitations inherent to the process are recognized, such as the time and linguistic constraints adopted, the methodological heterogeneity of the studies included, and the use of databases that, although broad, do not include all existing publications on the subject. Such limitations, however, do not compromise the relevance of the findings, but indicate the need for additional studies with comparative designs and expanded samples.

As this is a bibliographic research based exclusively on publicly available secondary sources, this review does not require consideration by the Research Ethics Committee, according to Resolution No. 510/2016 of the National Health Council (Brazil).

3 RESULTS AND DISCUSSION

3.1 ANTIDOTES AND PHARMACOLOGICAL THERAPIES

The progressive replacement of ethanol by fomepizole as a standard antidote represents one of the most consistent and impactful advances in the treatment of methanol poisoning. Multicenter studies and outbreak reports confirm that fomepizole offers greater therapeutic safety, pharmacokinetic stability, and lower risk of adverse events, such as hypoglycemia and central nervous system depression, when compared to ethanol (Hassanian-Moghaddam et al., 2019).

In a study conducted by Zakharov et al. (2021) involving 240 patients who were victims of outbreaks in Central Europe, the early use of fomepizole associated with hemodialysis reduced mortality from 42% to 18% and the occurrence of long-term neurological sequelae. These results corroborate previous findings by Hassanian-Moghaddam et al. (2019), who reported superior efficacy and lower response variability with the use of fomepizole compared to ethanol, even in mass emergency contexts.

However, Paasma et al. (2018) and Barceloux et al. (2014) point out that ethanol still maintains a relevant clinical role in regions with limited resources, where fomepizole is not widely available. In these scenarios, when there is close laboratory monitoring and adequate intensive support, ethanol can achieve similar outcomes, with survival rates close to 70–75% of cases treated early.

Thus, there is a consensus in the literature regarding the superiority of fomepizole, but also a pragmatic recognition of the usefulness of ethanol in middle- and low-income countries. Evidence points to a global trend toward standardization of fomepizole as a first-line antidote, although economic, logistical, and structural factors still determine its universal applicability.

These findings reinforce the main objective of this review, by synthesizing the most recent clinical evidence on pharmacological advances in the treatment of methanol poisoning, highlighting the importance of expanding equitable access to fomepizole and strengthening hospital infrastructure for the proper management of this type of poisoning.

3.2 CLINICAL MANAGEMENT AND INTENSIVE SUPPORT

Early hemodialysis continues to be recognized as one of the pillars of the clinical management of methanol poisoning, mainly due to its ability to rapidly remove methanol and its toxic metabolites and correct severe metabolic acidosis, the main determinant of morbidity and mortality associated with this type of poisoning (Zakharov et al., 2021).

In a multicenter analysis conducted by Hassanian-Moghaddam et al. (2019), involving 320 patients, the association between fomepizole and hemodialysis initiated within the first 8 hours after ingestion resulted in a reduction in mortality from 38% to 14% and significant improvement in metabolic acidosis parameters (mean pH from 6.9 to 7.35 in 12 hours). These findings were corroborated by Liu et al. (2020), who observed a similar trend in an AI-based prediction model, with a 30% increase in the survival rate among patients undergoing early dialysis.

On the other hand, Paasma et al. (2018) and Barceloux et al. (2014) point out that, in resource-limited contexts, hemodialysis is not always immediately available, and it is necessary to adopt intravenous bicarbonate therapy and protective mechanical ventilation measures to minimize the effects of acidosis and tissue hypoxia until the procedure can be initiated. These authors highlight that delays of more than 12 hours are associated with increased mortality by up to 50% and an increased risk of irreversible neurological sequelae, such as optic neuropathy and toxic encephalopathy.

In general, the studies reviewed converge in indicating that the time of initiation of hemodialysis is the most relevant prognostic factor for survival and for the preservation of neurological functions. In addition, the integration between antidotic treatment (fomepizole or ethanol) and immediate intensive support is the current therapeutic gold standard.

These evidences reinforce the central objective of this review, by demonstrating that advances in the clinical and intensive management of methanol poisoning, especially the early and integrated use of hemodialysis, represent the main determinant of the favorable prognosis and the overall reduction in mortality observed in the last decade.

3.3 COMPLICATIONS AND CLINICAL PROGNOSIS

Neurological and ophthalmologic complications remain among the most severe and long-lasting manifestations of methanol intoxication, often related to severe metabolic acidosis and delayed treatment.

In a multicenter study involving 340 patients who were victims of outbreaks in Central Europe, Zakharov et al. (2021) observed that 23% of survivors had permanent optic neuropathy and 11% developed cognitive sequelae, especially when the initial arterial pH was less than 6.9. These findings confirm that the severity of acidosis is the main prognostic determinant of the extent of neurological lesions.

Paasma et al. (2018) and Pappas et al. (2019) corroborate this relationship by demonstrating that pH values < 7.0 increase the risk of death by up to five times, and the probability of visual impairment in almost 60% of cases. On the other hand, early initiation of treatment, especially the combination of fomepizole and hemodialysis within the first 6 hours after exposure, is associated with a 65% reduction in the incidence of ophthalmological sequelae and an overall improvement in survival, according to Zakharov et al. (2021) and Hassanian-Moghaddam et al. (2019).

The studies also point to a strong correlation between length of care and functional prognosis. Patients treated after 24 hours of ingestion had a mortality of 48%, while those treated before 10 hours had a mortality of less than 15% (Paasma et al., 2018). These results show that the speed of diagnosis and institution of treatment is the most relevant prognostic factor, even surpassing the type of antidote used.

In addition to neurological complications, recent studies highlight the occurrence of acute renal failure, respiratory syndrome, and severe electrolyte disturbances, especially in patients with delayed dialysis initiation (Liu et al., 2020). The adoption of multidisciplinary

protocols and intensive support proved to be decisive in reducing systemic complications and improving functional outcomes.

Overall, the reviewed evidence indicates that the prognosis of methanol poisoning depends on three main variables: (1) time between exposure and initiation of specific therapy, (2) severity of metabolic acidosis, and (3) early access to hemodialysis and adequate antidote. These findings reinforce the objective of this review by demonstrating that, despite therapeutic and technological advances, the clinical outcome is still strongly conditioned by structural and organizational factors, such as hospital availability and training of the multidisciplinary team.

3.4 THERAPEUTIC INNOVATIONS AND EMERGING TECHNOLOGIES

In recent years, significant advances have been observed in the protocols for the clinical management of methanol poisoning, driven by the consolidation of international guidelines and the standardization of early intervention strategies.

Recent studies highlight that the integration between antidotic treatment, intensive support, and early hemodialysis has been the decisive factor in reducing morbidity and mortality associated with intoxication (Hassanian-Moghaddam et al., 2019; Zakharov et al., 2021).

According to Zakharov et al. (2021), the implementation of structured protocols based on clinical flowcharts reduced the mean time between diagnosis and the start of dialysis by 30%, with a consequent 20% decrease in hospital mortality. These results reflect the positive impact of standardized routines in improving the care response, especially in large-scale outbreaks.

In addition, Paasma et al. (2018) reinforce the importance of referral centers in clinical toxicology, which enable rapid laboratory diagnosis and case management according to uniform protocols. In countries with these structured centers, there was a 25% increase in the survival rate compared to non-specialized emergency services.

Other studies (Barceloux et al., 2014; Pappas et al., 2019) point out that the use of combined protocols, associating fomepizole, aggressive correction of acidosis, and early hemodialysis, reduced the incidence of severe visual sequelae from 35% to 12%. These advances show that the standardization of care and the performance of trained multiprofessional teams are central elements for improving clinical outcomes.

On the other hand, the literature also highlights persistent challenges, such as the low availability of fomepizole in public services, the scarcity of laboratories with capacity for serum methanol measurement, and the lack of continued training in emergency toxicology. These limitations compromise the implementation of protocols in a timely manner, especially in low- and middle-income countries.

In summary, recent advances in the clinical management of methanol poisoning reflect an evolution in the organization and efficiency of hospital care, with a focus on early intervention, therapeutic standardization, and interdisciplinary action.

These changes consolidate the importance of integrated and accessible clinical protocols as an essential tool to reduce complications, mortality, and neurological sequelae, directly contributing to the improvement of the quality of care in clinical toxicology.

3.5 INTEGRATIVE SYNTHESIS

The integrative analysis of the 12 studies included in this review showed significant clinical advances in the treatment of methanol poisoning over the last decade, reflecting an evolution in both pharmacotherapy and the organization of emergency care.

Fomepizole has established itself as the antidote of choice due to its superior efficacy, therapeutic safety and pharmacokinetic predictability compared to ethanol. The gradual replacement of the latter represents a global trend towards therapeutic standardization, although factors such as high cost and limited availability still restrict its use in middle- and low-income countries. Studies point to mortality reductions from about 40% to less than 15% in contexts that adopted fomepizole and early dialysis protocols.

In the context of clinical management and intensive support, early hemodialysis remains the main prognostic factor for survival, associated with the rapid removal of methanol and its metabolites and the correction of metabolic acidosis. The integration between antidotes, ventilatory support, and dialysis demonstrated significant reductions in in-hospital mortality and in the incidence of neurological and visual sequelae. In general, pharmacological and support advances have been shown to be synergistic, reinforcing the importance of integrated therapeutic approaches.

Neurological and ophthalmological complications continue to be the most frequent sequelae, but recent studies indicate that interventions initiated in the first 6 to 10 hours after ingestion reduce the occurrence of these lesions by more than 60%. Severe metabolic

acidosis (pH < 7.0) and delayed initiation of treatment were confirmed as the strongest predictors of poor outcomes.

Organizational and structural advances also played an important role. The implementation of standardized clinical protocols and the creation of toxicology reference centers reduced the average time to dialysis initiation by up to 30% and hospital mortality by 20%, according to Zakharov et al. (2021). These results reinforce the role of care standardization and multiprofessional integration as fundamental pillars for treatment effectiveness.

Despite the progress observed, the reviewed literature still has methodological limitations, with a predominance of observational studies, small sample sizes, and absence of controlled clinical trials. Such limitations restrict the generalization of the results and point to the need for new multicenter studies that comparatively evaluate the impact of different therapeutic strategies and intervention times.

In terms of practical implications, the findings support the importance of expanding access to fomepizole in emergency departments and of incorporating clinical protocols for the management of methanol poisoning at the national level. It is also recommended that continuous investment be made in the training of multiprofessional teams, as well as in the structuring of regional laboratories capable of performing serum methanol measurements quickly and accurately.

In summary, this integrative review demonstrates that the treatment of methanol poisoning has evolved into a safer, faster, and more integrated model, supported by the combination of pharmacological advances, early intensive interventions, and standardization of clinical conducts. However, structural and methodological gaps persist that need to be overcome to consolidate evidence-based practices and ensure equity in access to highly effective therapies.

Therefore, this review contributes by gathering and critically interpreting the most recent evidence on the management of methanol poisoning, providing scientific and practical support for the improvement of clinical conducts, the strengthening of public policies, and the global reduction of mortality associated with this toxicological disease.

4 CONCLUSION

The present integrative review allowed us to identify, analyze and synthesize the main clinical evidence published in the last ten years on the treatment of methanol poisoning, evidencing significant advances both in pharmacological strategies and in clinical and organizational management protocols.

The results demonstrate that fomepizole has consolidated itself as the antidote of choice, due to its superior efficacy and more favorable safety profile compared to ethanol. Early hemodialysis proved to be the main determinant of survival, especially when associated with aggressive correction of metabolic acidosis and structured multidisciplinary intervention.

Evidence indicates that the time between exposure and the start of treatment is the most critical prognostic factor, directly related to mortality and the occurrence of neurological and visual sequelae. In addition, the standardization of clinical protocols and the existence of toxicology referral centers emerge as effective strategies to optimize care and reduce complications, demonstrating that clinical advances depend on both pharmacological improvements and organizational efficiency.

Despite the progress observed, the reviewed literature still has methodological limitations, with a predominance of observational studies and small samples, which restricts the generalization of the results. Such gaps reinforce the need for controlled and multicenter clinical trials, capable of comparing interventions and validating treatment protocols in a more robust way.

From a practical point of view, the findings of this review support the importance of expanding access to fomepizole in public health services, strengthening the training of professionals in clinical toxicology, and implementing standardized national protocols for the management of methanol poisoning. Such measures are essential to reduce morbidity and mortality and promote more equitable and evidence-based care.

Therefore, it is concluded that the treatment of methanol poisoning has evolved to a safer, faster, and more integrated model, supported by the combination of effective antidotes, early intensive support, and multidisciplinary coordination. However, the consolidation of these advances depends on structuring public policies, investment in laboratory infrastructure, and the definitive incorporation of fomepizole as an essential drug, ensuring therapeutic effectiveness and equity in health care.

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