

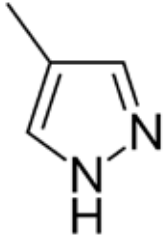
Uso de fomepizol en el tratamiento de la reacción antabus grave

Núria Pi

Servicio de Farmacia

Clínica Girona

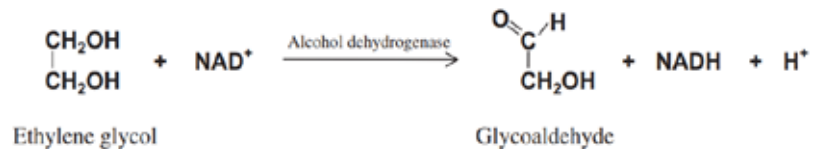
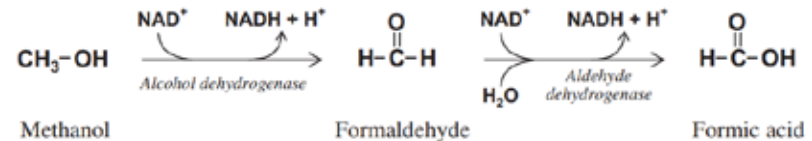
FOMEPIZOL (4-metilpirazol)



ü Inhibidor de la Alcohol deshidrogenasa (ADH)

Indicaciones:

- Intoxicación por metanol
- Intoxicación por etilenglicol



Etanol: Antídoto en intoxicación por metanol y etilenglicol

FOMEPIZOL VS ETANOL

Table 3
Summary comparison of ethanol versus fomepizole for the treatment of methanol and ethylene glycol poisoning

	Ethanol	Fomepizole
Inebriation effect	Yes	No
Sedation effect	Yes	No
Hypoglycemia potential	Yes	No
Acquisition cost of drug	Low	High
Laboratory monitoring required	Yes	No
Duration of action	Short	Long
Potency for ADH inhibition	High	Low
Pharmacokinetics	Unpredictable	Predictable
Ease of administration	More difficult	Less difficult
Gastritis, nausea, vomiting	Yes (if by mouth)	No
Volume overload potential	Yes (if IV)	No
Dialyzable	Yes	Yes
Dose adjustment during dialysis	Yes	Yes
Dose adjustment in alcoholism	Yes	No
Availability	Wide	May be limited
Clinical experience	Long-term	Less, but increasing

Crit Care Clin 2012 Oct;28(4):661-71

EVIDENCIA CIENTIFICA

Curiosamente...

Indicación off-label en la interacción etanol-antabús



American Journal of Emergency Medicine (2012) 34, 262.e3–262.e4

The American Journal of Emergency Medicine

ELSEVIER

Case Report

Fomepizole for severe disulfiram-ethanol reactions^{1,2,3,4}

Abstract

Ingestion of ethanol in the presence of disulfiram may cause a histamine-like reaction due to accumulation of acetaldehyde. These disulfiram-ethanol reactions (DERs) are manifested by hypotension, tachycardia, gastritis, and angioedema. Fomepizole, an inhibitor of alcohol dehydrogenase, may halt progression of this reaction by blocking ethanol metabolism to acetaldehyde. We present 2 cases of disulfiram and alcohol overdose leading to severe reactions unresponsive to fluid resuscitation and treated with a single dose of fomepizole. Case 1: A 20-year-old woman presented after ingestion of vodka and disulfiram. After 11 hours of resuscitation, she had skin flushing, lip swelling, tachycardia, and hypotension. Antihistamines, steroids, and an additional 2 L of normal saline were given without improvement. Fomepizole 15 mg/kg was given with improvement within 1.5 hours, and she was ultimately discharged with no clinical sequelae. Case 2: A 47-year-old woman presented after overdose of vodka and disulfiram. She was tachycardic and hypotensive upon presentation. After administration of 3 L of normal saline, she remained hypotensive and tachycardic. One dose of fomepizole 15 mg/kg was given. Within 1 hour following fomepizole infusion, her blood pressure and heart rate normalized, and she had no further sequelae from her ingestion.

Fomepizole may be a safe and effective treatment of severe DERs. We suggest that 1 dose of fomepizole for severe DERs with hypotension unresponsive to fluid resuscitation or for angioedema unresponsive to antihistamines be administered.

Disulfiram (DSM) has been the preferred pharmacotherapy for the treatment of ethanol dependence since its approval by the Food and Drug Administration in 1951 [1]. Disulfiram is an irreversible inhibitor of aldehyde dehydrogenase (Fig. 1), and when ethanol is consumed in the presence of DSM, acetaldehyde pruritus accumulates. This results in an unpleasant histamine-like reaction termed the DSM-ethanol reaction (DER) [1–3]. Clinical effects range from mild facial flushing and nausea to severe gastritis, angioedema, hypotension, refractory shock, and death [1,4]. Symptoms of DERs typically peak within 1 hour of alcohol consumption and improve over the subsequent few hours [4]. Disulfiram also inhibits dopamine β-hydroxylase, an enzyme involved in norepinephrine synthesis [5,6]. Acetaldehyde accumulation in combination with a relative norepinephrine deficiency may result in more severe DER reactions [4]. Standard treatment for a severe DER reaction includes intravenous fluids, antihistamines, and vasopressors for refractory hypotension [4,7–9]. Fomepizole may halt the accumulation of acetaldehyde and thus halt severe DER reactions. We describe 2 cases of DSM and ethanol overdose resulting in severe DSM reactions successfully treated with a single dose of fomepizole.

A 20-year-old woman presented approximately 1 hour after ingestion of an unknown amount of vodka and intentional overdose of 7500 mg DSM in a suicide attempt. Presenting heart rate (HR) was 125 beats per minute (bpm), blood pressure (BP) was 119/83 mm Hg, and physical examination was significant only for intoxication. Blood alcohol concentration was 448 mg/dL. Drugs of abuse screen, serum electrolytes, and cell counts were normal. The patient developed progressive tachycardia and hypotension over 11 hours of observation and was given a bolus of 2 L of normal saline. At 11 hours, she was noted to have skin flushing, lip swelling, tachycardia (166 bpm), and hypotension (systolic BP, 88 mm Hg). Antihistamines, steroids, and an additional 2 L of normal saline were given without improvement of hypotension or tachycardia. At this time, BP was 94/38 mm Hg and HR was 148 bpm, and one dose of fomepizole (15 mg/kg) was given. Blood pressure improved within 1.5 hours (BP, 118/70 mm Hg), and HR decreased to 86 bpm. No additional doses of fomepizole were administered, and there was no recurrence of tachycardia or hypotension. Ethanol intoxication improved over 16 hours, and she was discharged with no clinical sequelae. Fig. 2 shows ethanol elimination kinetics.

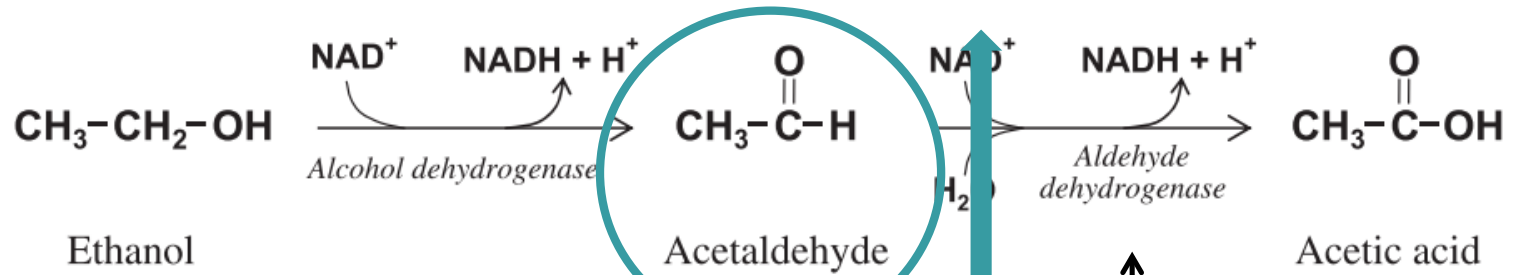
A 47-year-old woman presented 4 hours after an intentional overdose of an unknown amount of vodka and 6250 mg DSM. Heart rate was 136 bpm, and BP was 78/34 mm Hg upon presentation. Her skin was flushed, and she was intubated; otherwise, her physical examination was unremarkable. Blood alcohol concentration was

¹ Financial support: None.

^{2,3,4} Presented at North American Congress of Clinical Toxicology Annual Meeting, Denver, CO, October 8, 2010 [Abstract].

0735-6757/\$ – see front matter © 2012 Elsevier Inc. All rights reserved.

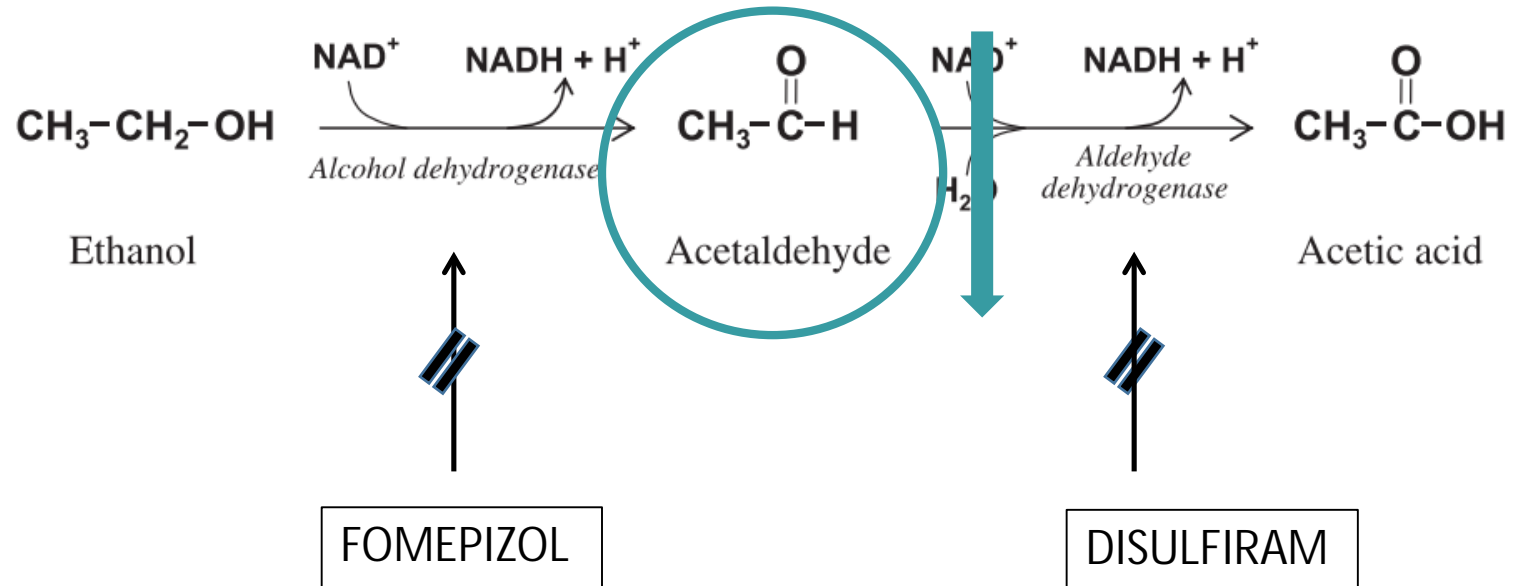
MECANISMO DE ACCIÓN



DISULFIRAM

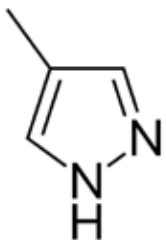


MECANISMO DE ACCIÓN



- Inhibidor de la Alcohol deshidrogenasa
- Afinidad 1000 veces superior a la del etanol

DOSIFICACIÓN



Dosis de carga:

- 15 mg/kg IV en 100 ml SF o SG5% y administrado en 30 min.

Dosis de mantenimiento:

- 10 mg/kg/12h x 4 dosis
- 15 mg/kg/12h hasta que los niveles de tóxico hayan disminuido.

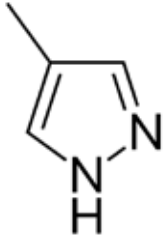
Si HD:

- 15 mg/kg/4h en 30 min
- Al finalizar HD: Última dosis a las 3h, entre 1-3h 50% de la dosis

En pediatría mismas dosis



CARACTERÍSTICAS



Farmacocinética:

- Volumen de distribución: 0,6-1 l/kg
- Baja unión a proteínas plasmáticas
- Metabolismo a través del cit P450 con cinética no-lineal
- Baja eliminación renal
- Semivida: 5 horas aunque en presencia del etanol se prolonga

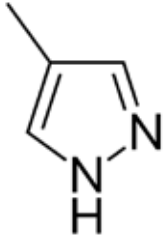
Contraindicaciones:

- Alergia a pirazolonas (metamizol, fenilbutazona..)

Conservación:

- Puede solidificar a T^a <25°C → Calentar el vial con agua caliente o con las manos.

EFECTOS SECUNDARIOS



- Cardiovasculares: Bradicardia, taquicardia e hipotensión.
- Tromboflebitis del acceso vascular, dolor en el lugar de administración
- Dermatológicos: Prurito, rash
- Gastrointestinales: Dolor abdominal, diarrea, vómitos y **náuseas**
- Hematológicos: Anemia, eosinofilia, coagulación intravascular diseminada (CID)
- Hepáticos: Elevación de transaminasas
- Musculares: Rabdomiólisis
- Neurológicos: Vértigo, **cefalea**, convulsiones, agitación, ansiedad, *nistagmus*, vértigo
- Renales: Anuria
- Metabólicos: Hipertrigliceridemia.
- Oculares: Alteraciones visuales



DISPONIBILIDAD



Gestión de Medicamentos en Situaciones Especiales

Código	Principio Activo	Presentación	Proveedor	Precio Facturación(€)	Uso Hospitalario	Estudio Especial	Estado	ATU / Protocolo	Conformidad Expresa	Observaciones	Fecha Última Actualización
000403	FOMEPIZOL	ANTIZOL 1,5 ML(INTRO COD 1389) 1 g/ml gramo(s)/mililitro 4 Polvo y disolvente para solución inyectable	PHARMA INTERNATIONAL, S.A.	0	SI	SI	NO DISPONIBLE	NO	NO	ORPHAN MEDICAL COMUN.A PHARMA NO LO PUEDE ENVIAR A EUR. (9/03	22/04/2010
000173	FOMEPIZOL	FOMEPIZOLE EUSA PHARMA 20 ML (ENVASE DE 5 VIALES) 5 mg/ml miligramo(s)/mililitro 5 Concentrado para solución para perfusión	BCN FARMA DISTRIBUCIÓN Y ALMACENAJE DE MEDICAMENTOS, S.L.	988	SI	NO	DISPONIBLE	NO	NO	PODRA PEDIRSE TAMBIEN UN MINIMO Nº DE UNIDADES PARA TENER UN "STOCK DE URGENCIA" SOLICITÁNDOLO A TRAVES DE LA APLICACION DE MSE CON UN PROTOCOLO DE USO	28/02/2019
014800	FOMEPIZOL	FOMEPIZOLE FOR INJECTION (ENVASE DE 2 VIALES DE 1,5 ML/VIAL) 1 g/ml gramo(s)/mililitro 2 Solución para perfusión	WAAS-ANITA, S.A.	1747.2	SI	NO	DISPONIBLE	NO	NO		15/02/2019
014282	FOMEPIZOL	FOMEPIZOLE INJECTION (ENVASE DE 1 VIAL) 1 g/ml gramo(s)/mililitro 1 Solución para perfusión	WAAS-ANITA, S.A.	873.6	SI	NO	NO DISPONIBLE	NO	NO		12/02/2019

Presentación:

- Fomepizol 100mg/20ml x 5 viales
- Fomepizol 1500mg/1,5ml x 2 viales

MEDICAMENTO EXTRANJERO

- Elevado coste
- Dificultad de adquisición

RED DE ANTÍDOTOS



[Quiénes somos](#)
[La Red](#)
[Centros](#)
[Guía](#)
[Fuentes Información](#)
[Consultas](#)
[Formación](#)
[Noticias](#)
[Agenda](#)



ANTÍDOTOS INCLUIDOS EN LA RED

ANTÍDOTOS	PRESENTACIONES COMERCIALES
ANTICUERPOS ANTIDIGOXINA	Digifab® 40 mg vial
DANTROLENO	Dantrolen® 20 mg vial
DEFEROXAMINA	Desferin® 500 mg vial
DEFIBROTIDE	Defibrotide® 200 mg/2,5 mL vial
DIMERCAPROL (BAL)	Dimercaprol® amp 200 mg/2ml
EDETATO CÁLCICO DISÓDICO (EDTA)	Calcium Edetate sodium® 500 mg/10mL amp EDTA Disodico Calcico (FM) 935 mg/5 mL amp EDTA Disodico Calcico (FM) 935 mg/10 mL amp
ETANOL (ALCOHOL ABSOLUTO)	Alcohol absolut 100% amp 10 ml (FM) Alcohol absolut 100% amp 5 ml (FM) Alcohol absoluto 100% amp 20 ml (FM)
FOMEPIZOL	Fomepizol® vial 100 mg
GLUCARPIDASA	Voraxaze® 1.000 U vial
HIDROXOCOBALAMINA	Cyanokit® 5g vial Hidroxocobalamina 2,5g vial (FM)
IDARUCIZUMAB	Praxbind® 2,5g solución inyectable
PRALIDOXIMA (PAM)	Contrathion® 200 mg/10mL vial
SILIBININA	Legalon® vial 350 mg
SUERO ANTIBOTULÍNICO	BAT (Botulism Antitoxin Heptavalent) (A,B,C,D,E,F,G) 50 ml Solución inyectable
SUERO ANTIOFÍDICO	Snake Venom Antiserum (Bulbio)® 100 ml vial Viperfav® vial 4ml
URIDINA TRIACETATO	Vistonuridine® 10 g sobre

FM= Fórmula magistral

RED DE ANTÍDOTOS

Desde su inicio en 2015...



Antídoto	Del hospital	Al hospital	Viales	Indicación
Fomepizol	H. St Pau	H. Clínic	15	Intoxicación por metanol
Fomepizol	H. Trueta	H. Clínic	20	Intoxicación por metanol
Fomepizol	H. Trueta	H. Clínic	20	Intoxicación por etilenglicol
Fomepizol	H. Trueta	H. St Pau	11	Intoxicación por etilenglicol
Fomepizol	H. St Joan de Déu	H. Clínic	30	No registrada
Fomepizol	H. Trueta	H. Clínic	10	Intoxicación por etilenglicol

CONCLUSIONES



El fomepizol es un fármaco aprobado en la intoxicación por metanol y etilenglicol, que también tienen su uso como antídoto en la **interacción etanol-antabus**.



El fomepizol es un **fármaco seguro** con efectos secundarios descritos de baja gravedad.



Es un fármaco incluido en la **Red de Antídotos** por su elevado coste, su urgencia en la administración y por sus dificultades de adquisición (medicamento extranjero).

