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PERIODICO DI INFORMAZIONE A CURA DELL'U.O. FARMACIA OSPEDALIERA DELL'AZIENDA OSPEDALIERO - UNIVERSITARIA DI FERRARA

# NEWSLETTER

## Centro Regionale Dotazione Antidoti

Il **Servizio di Farmacia** dell'Azienda Ospedaliero Universitaria di Ferrara è stato individuato come **Centro di Riferimento Regionale (CRR)** per la dotazione **antidoti** da giugno del 2011.

Con la **Newsletter** ci proponiamo di fornire tutte le informazioni e le indicazioni relative alle **ultime evidenze** e **novità** riguardo le **dotazioni antidotiche** e le **intossicazioni** estratte dalle più **recenti evidenze scientifiche**, e di **pubblicare elaborati** dei Referenti Regionali Antidoti.

La collaborazione alla Newsletter è aperta a tutto il personale sanitario interessato al tema.

### 39° Congresso Internazionale dell'European Association of Poisons Centres and Clinical Toxicologists (EAPCCT)

Abstract presentati in occasione del 39° Congresso Internazionale dell'European Association of Poisons Centres and Clinical Toxicologists (EAPCCT), 21-24 Maggio 2019, Napoli

#### Eventi di intossicazione nel Pronto Soccorso di Ferrara nel 2017: Centro Riferimento Regionale Antidoti Emilia-Romagna

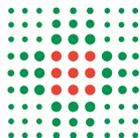
Davide Sighinolfi, Roberto Zoppellari, Riccardo Fontana, Brunella Quarta, Paola Scanavacca, Antonella Tallarico e Angela Ricci Frabattista

**Objective:** Since 2015 there has been activate monitoring of patients accessing the Emergency Department in Ferrara with intoxication diagnosis. Clinicians, closing the medical report, can flag the "Intoxication" option, and information is sent to the hospital pharmacist. The aim is to implement an antidote database accessible via the Internet (Antidotes Internet Portal, AIP) in order to properly manage intoxication-related patients. The aim of the project is to analyze medical reports received via AIP in 2017 in order to understand which intoxications and antidotes have a special relevance for acute medicine.

**Methods:** Medical reports from 2017 involving intoxication were analyzed. Reported intoxications included poisoning involving drugs, chemicals, plants, fungi, animal bites, medical devices, nutritional supplements and pharmaceutical drugs; focus was on the context of the intoxication (accidental, intentional or due to a history of abuse with overdose, according to the E-ICD-9-CM).

Clinical cases were divided by age, gender, toxicant, antidote and context.

**Results:** Overall 71 cases were evaluated with median age 50.7 years; 59.2% were female. In 47.8% the intent was self-harm, 28.2% accidental and 23.9% due to abuse. Responsible toxicants were pharmaceutical drugs, used alone or in combination (64.8%), chemicals (18.3%), ethanol (8.5%), psychotropic drugs (7.0%) and plants (1.4%). Of pharmaceutical drugs, most cases involved benzodiazepines (45.7%), followed by non-opioid analgesics- antipyretics-antirheumatic drugs (15.2%), dabigatran-idarucizumab (8.7%), antidepressants (4.3%), opioids (4.4%), and antidiabetic medications, diuretics, beta-blockers, anti-hypertensive medications (2.2%). In 59.2% of cases an antidote was used (flumazenil 33.3%, activated charcoal 26.2%, idarucizumab 9.5%, N-acetylcysteine 9.5%, naloxone 9.5%, fomepizole 4.8%, and sodium bicarbonate, diazepam and vitamin K 2.4% each). In 21.1% of cases pharmacological treatment without antidotal therapy was required; of these, drugs to treat symptoms were used in 13 cases, including gastroprotectants (8.5%), benzodiazepines for psychomotor activity (4.2%), and aerosolized cortisone after toxic gas inhalation (2.8%). In the remaining 19.7% of cases, the use of an antidote or other drug therapy was not necessary. The second largest group comprised a broad variety of different chemical products: dish-



washing agents, shampoo, but also corrosive drain cleaners and toxic alcohols such as ethylene glycol.

**Conclusion:** The monitoring of Emergency Department accesses and data collection in the AIP database helped maintain appropriate clinical practice and ensure proper management of intoxicated patients. Data collection is important at a clinical epidemiologic level and even more in the logistic management of antidote activities (rare antidotes, expiry dates, budget impact) and in order to build a stronger connection between clinicians, pharmacists, and chemical analytical toxicological laboratories, improving the efficiency of the regional health system.

## Pazienti intossicati ricoverati in Rianimazione:: esperienza di trattamenti in una serie di 184 pazienti

Roberto Zoppellari, Anna L Pinamonti, Filippo Tartari, Alessandra Mallozzi Menegatti, Luca Bagnoli, Chiara De Fazio, Alessandra Quaranta, Angela Ricci Frabattista, Anna Talarico e Rosa M Gaudio.

**Objective:** The correct management of some poisoned patients may require admission to the Intensive Care Unit (ICU). We studied the ICU usage in poisoned patients and the related treatments: mechanical ventilation and cardiovascular support, antidotal administration, gastrointestinal decontamination, and extracorporeal removal.

**Methods:** A 17-year (1 July 2001 to 30 June 2018) prospective study including all patients admitted to our adult ICU with a main diagnosis of acute poisoning. We defined three criteria for ICU admission: the presence of vital function impairment (group 1), the perception that significant organ dysfunction could appear in asymptomatic patients on the basis of toxicokinetics or toxicodynamic (group 2), and a clinical judgment for intensive observation in mildly symptomatic patients (group 3).

**Results:** In total 184 poisoned patients (2.7% of admitted patients) were included. All toxic agents were confirmed by toxicological laboratory analysis. The number of patients was 142 for group 1, 17 for group 2 and 25 for the third. For group 1 the main causes of vital function impairment was: respiratory failure requiring ventilatory support (114), severe cardiovascular toxicity (11), neurological dysfunction with a Glasgow Coma Score <11 (14), and metabolic disturbance (3). For this group antidotal administration, gastrointestinal decontamination and extracorporeal removal (dialysis) was used in 66, 99 and 6 patients, respectively. For group 2 mechanical ventilation and/or cardiovascular support was used in 7 patients, antidotal administration in 9 patients, gastrointestinal decontamination in 10 and extracorporeal removal in 4 (2 treated with hemoperfusion and 2 with dialysis). Group 3 required treatment with mechanical ventilation and car-

diovascular support in 5 patients, antidotal administration in 4 and gastrointestinal decontamination in 15; no enhanced elimination was applied in this group.

**Conclusion:** A rational approach to ICU use and treatment is described. For patients who were asymptomatic (group 2) or minimally symptomatic at admission (group 3) mechanical ventilation and/or cardiovascular support was used in some cases due to an unpredictable clinical course.

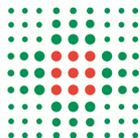
## Intossicazione da Metformina richiedente dialisi: un caso clinico di rimozione extracorporea ed eliminazione renale

Roberto Zoppellari, Milo Vason, Alda Storari, Anna Talarico, Stefano Petri e Margherita Neri

**Objective:** Extrarenal removal in metformin intoxication has been suggested [1]. Metformin can cause severe complications such as severe lactic acidosis, especially in the setting of acute renal failure. We report a case of metformin intoxication treated with dialysis where the metformin concentrations in serum, urine and ultrafiltrate were measured.

**Case report:** An 80-year-old woman was admitted to the intensive care unit anuric, with abdominal pain, vomiting and diarrhoea. She had a history of hypertension and diabetes treated with metformin (3 g/day). Arterial blood gas (ABG) analysis showed severe metabolic acidosis (pH 7.07, bicarbonate 6.4 mmol/L). Lactate was 5.5mmol/L. Glycaemia and abdominal ultrasound were normal. Blood urea and serum creatinine were 194 (reference 17-43 mg/dL) and 9.04 (reference 0.5-1.2 mg/dL), respectively. Serum metformin was 18.5 µg/mL (upper limit <4 µg/mL). Dialysis was started. Metformin concentration in serum, ultrafiltrate and urine was measured by ultra-performance liquid chromatography-mass spectrometry. The amount of metformin removed by dialysis was 1460 mg, whereas metformin elimination by urine during the same time was 895 mg. Serum metformin at the end of dialysis was 12.4 µg/mL and ABG improved (pH 7.32, bicarbonate 1-5.5mmol/L, lactate 0.9mmol/L). During the following 12 hours metformin elimination via urine was 1731 mg. At the end of this time the metformin serum concentration was 8.8 µg/mL. On day 3 the patient became polyuric, ABG normalized and the metformin serum concentration was 3.7 µg/mL.

**Conclusion:** A concurrent disease may induce acute renal failure leading to metformin accumulation. Clinical benefit of extrarenal support is to restore an acceptable acid-base status and to remove the drug. In our case the benefit of dialysis was due to direct elimination of the drug itself



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(small removal) and particularly the correction of the metformin-induced severe lactic acidosis [2]. Metformin elimination by diuresis improved with the recovery of renal function and resulted in a lowering of the serum concentration.

## References

- [1] Seidowsky A, Nseir S, Houdret N, et al. Metformin-associated lactic acidosis: a prognostic and therapeutic study. *Crit Care Med.* 2009;37:2191–196.
- [2] Zoppellari R, Felisatti G, Dallochio G, et al. Metformin removal by extracorporeal elimination techniques in cases of overdose: a literature review. *Clin Toxicol (Phila).* 2014;52:404–405.

## TOSSICOLOGIA DI BASE PER EMERGENZA-URGENZA

**Corso per idoneità all'esercizio dell'attività di emergenza sanitaria territoriale AUSL Bologna tenutosi in data 08/04/2019**

### Relatori:

- dott.ssa Alessandra Bologna - dott. Davide Sighinolfi -  
-dott. Giacomo Tagliani - dott.ssa Antonella Tallarico.

### Obiettivi del corso:

La giornata prevedeva una breve introduzione basilare sui meccanismi soprattutto di farmacodinamica, al fine di comprendere gli effetti dei tossici, che sono stati poi approfonditi caso per caso, in particolare quelli ritenuti di più frequente incontro durante la pratica clinica dell'emergenza. Viene inoltre posta l'attenzione sulle intossicazioni da inalanti durante gli incendi; la sezione finale verte invece sulla gestione del paziente intossicato, in particolar modo ci si concentra sugli algoritmi decisionali stilati per rendere il più lineare e condivisibile possibile il trattamento della tipologia di pazienti di cui sopra.

Ogni sezione viene accompagnata da casi clinici esplicativi e interattivi.

### Contenuti del corso:

- **Introduzione all'emergenza tossicologica** (Realtà ed Epidemiologia)
- **Principi di farmacocinetica e farmacodinamica** (ADME: assorbimento, distribuzione, metabolismo, eliminazione, terapia antidotale)
- **Principali quadri di intossicazione:** caratteristiche, trattamento, casi clinici interattivi:

1. Alcool etilico e metilico
2. Benzodiazepine
3. Oppioidi

4. FANS e salicilati
5. Paracetamolo
6. Eroina
7. Cocaina
8. Amfetamine e metamfetamine
9. THC
10. Cenno alle Nuove Sostanze Psicoattive (NPS)

- **Intossicazione da Agenti Fisici:** Fumi (CO, HCN). Casi Clinici interattivi
- **Approccio al paziente intossicato:** anamnesi, esame obiettivo, diagnostica ematochimica e strumentale
- **Gestione del paziente intossicato in Emergenza Urgenza:**

1. Algoritmo ABCDE
2. Algoritmo DEAD (decontaminazione - eliminazione - antidoti - disposizioni successive)
3. Casi Clinici Interattivi

- **Centro di Riferimento Regionale Antidoti Emilia – Romagna** (Rete e Portale Antidoti dell'AOU Di Ferrara)
- **Centro Anti-Veleni**