

Adequacy of poisoning antidote stocks in the pharmacies of public health service hospitals in the Spanish autonomous community of the Balearic Islands

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Objective: To analyze whether pharmacies in public health service hospitals in the Spanish autonomous community of the Balearic Islands are stocking sufficient amounts of poison antidotes.

Methods: Descriptive cross-sectional study of public hospital pharmacy stocks of antidotes and other medicines for treating acute poisoning. The head of each hospital pharmacy completed a questionnaire about stocks. The results on which antidotes were in stock, the amounts, and the storage locations were assessed for compliance with recommended quality indicators for emergency care in acute poisonings (CALITOX-2006) and the Antidote Stocking Guidelines (ASG-2009).

Results: The 7 hospitals met the CALITOX-2006 availability criteria for over 85% of items and the ASG-2009 criteria for 68%. Inadequate stocking mainly involved sodium sulfate, apomorphine, oral cyanide antidote kits, and crotaline snake antivenom. An average of 83% of the stocks were adequate; pyridoxine was the substance most often found to be understocked. Activated charcoal and N-acetylcysteine were the items most often overstocked. Glucagon and fomepizole were understocked in the referral hospital. Over 80% of items were stored in appropriate locations in the emergency departments of level 1 hospitals (68% in level 2 hospitals; 94% in the referral hospital).

Conclusions: Public health system hospitals are highly compliant with recommendations on stocking antidotes and other medicines to treat acute poisoning (what to stock, where, and in what amounts); the distribution of stocks safely guarantees they will be available when needed. Among level 2 hospitals, a facility's location (proximity to the best-equipped referral hospital for poisonings) had greater influence on compliance than the hospital's level of complexity. [Emergencias 2014;26:354-358]

Keywords: Medicine supply. Antidotes. Hospital Pharmacy Department.

Introduction

Antidotes are a key component for the treatment of poisoning in any care setting, whether out-of-hospital or in-hospital. While not all the different points of care can stock complete antidote kits, it is always necessary to ensure access to these and other drugs of special interest in critical situations. In the composition of the kit in general

or according to hospital level there are two references: quality of care indicators for the acute care of poisoning 2006 (CALITOX)¹ published by the Spanish Association of Toxicology (AETOX) and the consensus document *Guidelines for Stocking of Antidotes in Hospitals That Provide Emergency Care, 2009*, published by the panel of experts *Antidote Summit Authorship Group* (ASG)².

The availability of such substances may be li-

mitted by demographic, economic and geographic factors, and the latter is an important consideration in our case because of the insular nature of the autonomous community of Les Illes Balears, so that hospital pharmacy services (SFH in Spanish) responsible for acquiring, stocking and dispensing antidotes to the different health areas are particularly sensitive to these limitations. The aim of this study was to analyze the availability of antidote kits in the public SFH network of the autonomous community of the Balearic Islands.

Method

A descriptive study was carried out in hospitals forming part of the public network of the autonomous community of the Balearic Islands. A form was elaborated with a list of specific antidotes and drugs considered useful in the management of acute intoxicated patients, whose availability is recommended by CALITOX ASG-2006¹ and 2009² (Table 1). We excluded antidotes for snakebites by snakes not found in our Mediterranean fauna. The study variables were:

1. Qualitative composition: According to CALITOX 2006, Level I hospitals must have 27 antidotes and other drugs available, 29 in level II and 43 for the toxicological reference hospital. To this list must be added 7 drugs defined by the ASG, besides lipid emulsion (Table 1).

2. Quantitative composition: defined as the minimum amount of each antidote and drug needed to treat a patient of 100 kg over a period of 24 hours, and twice that amount for the referral hospital. The stock was considered adequate if it complied with the defined minimum, inadequate if not, and over-stocked if it exceeded the minimum necessary. Over-stocking did not include drugs with therapeutic indications other than for the management of poisoning, and the following were considered: activated charcoal, physostigmine, ipecac syrup, ethanol, methylene blue, hydroxocobalamin, n-acetylcysteine, naloxone, flumazenil, sodium sulfate, dantrolene, anti-viper serum, digoxin antibody, dimercaprol, calcium EDTA, pralidoxime, silibinin, botulinum serum, thiosulfate, fomepizole, Prussian blue, deferoxamine and oral cyanide kit (sodium nitrite and sodium thiosulfate).

3. Location in the emergency department: following the ASG-2009 guidelines, the stock in an urgent healthcare center should include: atropine, calcium chloride, calcium gluconate, oral cyanide

Table 1. Data sheet showing availability of antidotes and other drugs of special interest in the treatment of acute poisoning for each hospital participating in the study, asked about the presence of each, and whether they available in the emergency department and whether they had a minimum stock

Antidotes and other drugs (recommended minimum)	CALITOX 2006	ASG 2009
Atropine (165 mg)	X	X
Biperiden (10 mg)	X	
Activated charcoal (200 g)	X	
Diazepam (100 mg)	X	
Flumazenil (12 mg)	X	X
Naloxone (40 mg)	X	X
Hypertonic glucose (10 g)	X	
Oxygen (not applicable)	X	
Pyridoxine (24 g)	X	X
Ipecac (60 mL)	X	
Ascorbic acid (10 g)	X	
Ethanol (360 g)	X	X
Apomorphine (6 mg)	X	
Methylene blue (600 mg)	X	X
Sodium bicarbonate (84 g)	X	X
Calcium gluconate (30 g)	X	X
Phytonadione (20 mg)	X	
Folinic acid (2 g)	X	
Hydroxocobalamin (10 g)	X	X
Magnesium sulfate (90 g)	X	
Protamine (50 mg)	X	
Physostigmine (4 mg)	X	X
N acetylcysteine (56 g)	X	X
Penicillin G (48 MIU)	X	
Fresh plasma (not applicable)	X	
Polyethylene glycol (240 g)	X	
Sodium sulfate (undefined)	X	
Bromocriptina (30 mg)	X	
Dantrolene (1.4 g)	X	
Cyproheptadine (36 mg; for toxicological reference hospital 72 mg)	X	
Prothrombin factors (undefined)	X	
Phentolamine (576 mg; for toxicological reference hospital 1,150 mg)	X	
Glucagon (250 mg; for toxicological reference hospital 500 mg)	X	X
D-penicillamine (1 g; for hospital Toxicological guidance 2 g)	X	
Serum anti-viper (8 mL; for toxicological reference hospital 16 mL)	X	X
Digoxin antibody (15 vials; for toxicological reference hospital 30 vials)	X	X
Dimercaprol (1.5 g; for toxicological reference hospital 3 g)	X	X
Calcium EDTA (2.25 g; for toxicological reference hospital 4.5 g)	X	X
Hyperbaric oxygen (not applicable)	X	
Pralidoxime (18 g; for toxicological reference hospital 36 g)	X	X
Silibinin (1, 4 g; for toxicological reference hospital 2.8 g)	X	
Serum botulinum (3 vials, to hospital toxicological reference 6 vials)	X	X
Thiosulfate (10 g; for toxicological reference hospital 20 g)	X	
Octreotide (225 mcg)		X
Fomepizole (4.5 g)		X
Prussian Blue (30 g)		X
Deferoxamine (36 g)		X
Calcium chloride (10 g)		X
Potassium iodide (130 mg)		X
Oral cyanide kit (1 kit)		X
Lipoid emulsion (1.100 mL)		X

CALITOX: Quality indicators for emergency care of patients with acute poisoning; ASG: Antidote Stocking Guidelines.

kit (sodium nitrite and sodium thiosulfate), hydroxocobalamin, digoxin antibodies, flumazenil, glucagon, methylene blue, naloxone, physostigmine, pyridoxine and sodium bicarbonate. To these we added 5 other drugs considered essential by the study working group: activated carbon, hypertonic glucose, syrup of ipecac, phytonadione, normobaric oxygen and lipid emulsion^{3,4}. The presence of all was deemed necessary for 100% compliance.

The hospital care level of each participating center was obtained from the Servei Salut Les Illes Balears (Ib-Salut). Ethics committee approval was not sought, since the study involved no therapeutic intervention in patients; it was a logistical exercise to assess the resources available. A pharmacist responsible for each of the SFH in the public network of Les Illes Balears participated in the study and received Table 1 for completion. The survey was conducted in January 2012.

Results

Seven public hospitals of Les Illes Balears participated in the study. Four are Level I (A, B, C and D), 2 Level II (E and F) and one Level III hospital which is the toxicological reference center (G).

1. Qualitative composition: Level I centers complied with 90.7% of the CALITOX recommendations and 67% with those of the ASG. Level II centers complied with 84.5% (CALITOX) and 58% (ASG). And the level III center complied with 95.3% (CALITOX) and 96% (ASG) (Table 2).

2. Quantitative composition: Level I hospitals had adequate stock for 81.4% of antidotes and other drugs. Level II centers had adequate stock for 87.6% of antidotes and other drugs. The referral hospital had adequate stock for 81.2% (Table 2). The main drugs that were understocked were pyridoxine, followed by methylene blue and dantrolene. Understocking was found for N-acetylcysteine at Level II hospitals. Activated carbon was overstocked most frequently.

3. Location of antidotes in the emergency department: The degree of compliance for level I hospitals was 80.2%; 68.4% for Level II and 94.7% for the toxicological reference hospital (Table 3).

Discussion

The ultimate goal of recording the composition of stocks of antidotes and related drugs in a

hospital is to ensure the means for proper care of poisoned patients. The condition of geographic insularity, intrinsic to Les Illes Balears, requires the coexistence of seven public hospitals spread over 4 islands. Such dispersion conflicts with the assignment of hospital resources, which does not always accord with the expected level of complexity.

The differences between CALITOX and ASG recommendations are noteworthy. First, CALITOX proposals on antidote and other drug availability are based on level of care (complexity), which is not the case for ASG which proposes a single list of what should be available in every institution attending emergency patients without distinction. Second, only ASG clearly states what antidotes and other drugs of interest should be stored in the emergency department (ED) itself. We believe their proposals should include other drugs that are only mentioned in the CALITOX recommendations, and their availability in the ED should be immediate: activated charcoal, ipecac, hypertonic glucose, phytomenadione and normobaric oxygen. Third, antidotes appearing on the market after CALITOX recommendations (fomepizole) were not included, nor were active ingredients whose role as an antidote has only been established in recent years (lipid emulsion).

Stock deficiencies (Table 2) suggest the need to revise CALITOX recommendations. Sodium sulfate and apomorphine, drugs not considered by the ASG, without clear therapeutic indications for use, must be re-assessed. No hospital met the ASG recommendation to stock an oral cyanide kit, which is not sold in our country, and only in the reference center is anti-viper serum available, despite the absence of vipers in Les Illes Balears^{5,6}. Excluding the above antidotes, the weighted results show 97.2% compliance with CALITOX for level 1, 91.3% for level 2 and 97.6% for the reference center, while for ASG the respective percentages would be 75%, 66% and 100%. Digoxin antibodies were present in 2 hospitals of different islands, and two islands were without this antidote, whose efficiency is linked to the earliness of administration^{7,8}.

In the analysis of the specific location in the ED, discounting the oral cyanide kit, the referral hospital and hospital B complied 100% with the recommendations. Hospitals with the most significant deficiencies (D, E, F) are located on the same island as the center of reference, so patients can be transferred there in case of need. Despite not figuring in the recommendations, lipid emulsion was available in all SFH as a component for preparing parenteral nutrition. The preparation of

Table 2. Qualitative and quantitative composition of antidote kits and other drugs of special interest in the treatment of acute poisoning

Hospital	CALITOX (%)	ASG (%)	Not available	Adequate stock	Under-stocked (available but less than the minimum)	Over-stocked with
Level I						
A	23/27 (85.2%)	13/25 (52%)	CALITOX: apomorphine, penicillin G, polyethylene glycol and sodium sulfate. ASG: anti-viper serum, digoxin antibody, dimercaprol, EDTA, pralidoxime, botulinum serum octreotide, fomepizole, Prussian blue, deferoxamine, potassium iodide, cyanide oral kit.	15/23 (65.2%)	Activated carbon, pyridoxine, ascorbic acid, ethanol, methylene blue, folic acid, hydroxocobalamin, N-acetylcysteine.	--
B	25/27 (92.6%)	19/25 (76%)	CALITOX: apomorfina and sodium sulfate. ASG: anti-viper serum, botulinum serum, fomepizole, Prussian blue, potassium iodide and cyanide oral kit.	21/25 (84%)	Pyridoxine, ethanol, methylene blue, N-acetylcysteine.	Activated carbon, flumazenil.
C	24/27 (88.8%)	17/25 (68%)	CALITOX: ipecac syrup, apomorphine and sodium sulfate. ASG: anti-viper serum digoxin antibody, EDTA, botulinum serum, octreotide, fomepizole, Prussian blue, potassium iodide, oral cyanide kit.	22/24 (91.6%)	Pyridoxine, hydroxocobalamin.	Activated carbon, ethanol, physostigmine, N-acetylcysteine.
D	26/27 (96.3%)	18/25 (72%)	CALITOX: sodium sulfate. ASG: anti-viper serum digoxin antibody, botulinum serum fomepizole, Prussian blue, potassium iodide and cyanide oral kit.	22/26 (84.6%)	Pyridoxine, methylene blue, folic acid, hydroxocobalamin.	Activated charcoal, ipecac syrup, ethanol, physostigmine, N-acetylcysteine.
Nivel II						
E	25/29 (86.2%)	13/25 (52%)	CALITOX: ascorbic acid, apomorphine, bromocriptine sodium sulfate. ASG: anti-viper serum digoxin antibody, dimercaprol, EDTA, pralidoxime, botulinum serum octreotide, fomepizole, Prussian blue, deferoxamine, oral potassium iodide and cyanide kit.	23/25 (92%)	N-acetylcysteine and dantrolene.	Activated carbon, ethanol, physostigmine, methylene blue hydroxocobalamin.
F	24/29 (82.8%)	16/25 (64%)	CALITOX: ascorbic acid, apomorphine, physostigmine, bromocriptine and sodium sulfate. ASG: physostigmine, anti-viper serum digoxin, dimercaprol, EDTA, botulinum serum fomepizole Prussian Blue, oral cyanide kit.	20/24 (83.3%)	Hydroxocobalamin, N-acetylcysteine, pyridoxine, dantrolene.	Activated carbon, ethanol.
Level III and toxicological reference						
G	41/43 (95.3%)	24/25 (96%)	CALITOX: sodium sulfate and hyperbaric oxygen (centralized at a nearby private hospital) ASG: oral cyanide kit.	39/48 (81.2%)	Pyridoxine, methylene blue, dantrolene, phentolamine, glucagon, anti-viper serum, botulinum serum, fomepizole and deferoxamine.	Activated charcoal, ipecac syrup, dimercaprol, N-acetylcysteine, pralidoxime, silibinin thiosulfate.

CALITOX: Quality indicators for emergency care of patients with acute poisoning; ASG: Antidote Stocking Guidelines

this work, alongside recently published recommendations to stock lipid emulsion for severe poisoning⁴, has prompted a review of this new indication. The quantitative adequacy of antidote parallels the levels of hospitals: the average distributions were 81.4%, 87.6% and 81.2%, for levels

I, II and III respectively. This provision is clearly insufficient in the referral hospital for fomepizole, which is disturbing and obviously needs rectification. The most frequently detected antidote deficiency was pyridoxine, although exclusively in the ED, as this drug is usually found in all SFH. This

Table 3. Compliance with the location of essential antidotes and other drugs of special interest in the treatment of acute poisoning in the emergency department (n = 19)

Hospital	Compliance	Not available
Level I		
A	16/19 (84,2%)	Digoxin antibody, cyanide kit and oral lipid emulsion.
B	17/19 (89,5%)	Oral cyanide kit and lipid emulsion.
C	12/19 (63,2%)	Oral cyanide kit, methylene blue, hydroxocobalamin physostigmine, digoxin antibody, Ipecac syrup and lipid emulsion
D	16/19 (84,2%)	Digoxin antibody, oral cyanide kit and lipid emulsion.
Level II		
E	13 /19 (68,4%)	Oral cyanide kit, hydroxocobalamin, digoxin antibody, physostigmine, methylene blue and lipid emulsion.
F	13/ 19 (68,4%)	Syrup of ipecac, oral cyanide kit, hydroxocobalamin, digoxin antibody, methylene blue and lipid emulsion.
Level III and toxicological reference		
G	18/19 (94,7%)	Oral cyanide kit.

drug has few indications as an antidote⁹, but should be reviewed.

The geographical constraints of different islands could imply a tendency to over-stocking, but this was not found. With the exception of activated charcoal and syrup of ipecac, over-stocking seems to respond more to previous literature references^{10,11} than intrinsic care needs. Particularly striking is the under-stocking of N-acetylcysteine in level II hospitals, but this is mitigated by the fact that both are close to the reference hospital. The additional costs resulting from overstocking in the referral hospital is about 1,000 euros per year, equivalent to 0.4% of total pharmaceutical costs for the ED in the same period.

This study has prompted some centers to revise their stocks which might not have occurred otherwise. We believe it is essential to perform this logistical exercise in geographical regions or areas with limited accessibility or foreseeable problems in communications, in order to coordinate any emergency situation of poisoning.

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Adecuación de los botiquines de antídotos de los servicios de farmacia en hospitales públicos de la comunidad autónoma de Les Illes Balears

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Objetivo: Analizar la adecuación del botiquín de antídotos en los servicios de farmacia de los hospitales de la red pública de la comunidad autónoma de *Les Illes Balears*.

Método: Estudio descriptivo y transversal que revisa la composición del botiquín de antídotos y otros fármacos para el tratamiento de intoxicaciones agudas disponible en los servicios de farmacia de los diversos hospitales públicos de la Comunidad Autónoma, mediante cumplimentación de un formulario específico por un responsable de cada centro. Los resultados obtenidos se compararon con las recomendaciones CALITOX-2006 y las recomendaciones *Antidote Stocking Guidelines* (ASG-2009), se analizó la disponibilidad, cantidad y ubicación.

Resultados: En los 7 hospitales, la disponibilidad supera el 85% según CALITOX y el 68% según ASG. Las carencias principales fueron el sulfato sódico, la apomorfina, la cianida kit oral y el suero anticrotálide. La adecuación cuantitativa media es del 83%, y la piridoxina es el que más veces está infradotado. Hay un exceso de carbón activado y de N-acetilcisteína. Se detectó una infradotación de glucagón y de fomepizol en el hospital de referencia. Los criterios de ubicación en el servicio de urgencias se siguieron en más del 80% (hospital de nivel I), 68% (hospital de nivel II) y 94% (hospital de referencia).

Conclusiones: El grado de cumplimiento de las recomendaciones consultadas en cuanto a composición, accesibilidad y dotación del botiquín de antídotos y otros fármacos para el tratamiento de intoxicaciones agudas en los hospitales públicos de *Les Illes Balears* es alto, con una distribución en cada una de las islas segura para garantizar su disponibilidad. La situación geográfica del hospital y su proximidad al centro de referencia más dotado de antídotos predominan sobre el grado de complejidad del hospital en los de nivel 2. [*Emergencias* 2014;26:354-358]

Palabras clave: Botiquines. Antídotos. Servicio de farmacia hospitalarios.