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Original article

## Availability of antidotes in 70 hospitals in Catalonia<sup>☆</sup>

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### ABSTRACT

**Background and objective:** Antidotes may have a relevant role in acute intoxication management and the time until its administration can influence patient survival.

**Patients and method:** Study conducted by a questionnaire sent in early 2015 to 70 hospitals in Catalonia providing emergency services. Qualitative availability on each antidote was considered adequate when present in at least 80% of hospitals. The quantitative availability was considered adequate when at least 80% of hospitals had the number of units of antidote recommended.

**Results:** Lower complexity hospitals (level A) showed a percentage of adequate qualitative and quantitative availability of 66.7 and 42.9% respectively. In higher complexity hospitals (level B) qualitative and quantitative availability was adequate in 64.5 and 38.7% of the antidotes respectively. Data showed no differences between the different health regions as well as a positive correlation ( $p < 0.05$ ) between the number of emergencies attended and the percentage of adequate qualitative availability.

**Conclusions:** The availability of antidotes in Catalonia hospitals is generally low and shows differences across health regions and depending on level of complexity.

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## Disponibilidad de antidotos en 70 hospitales de Cataluña

### RESUMEN

**Antecedentes y objetivo:** Los antidotos pueden tener un papel relevante en el tratamiento de las intoxicaciones y el tiempo hasta su administración puede condicionar la supervivencia del paciente.

**Pacientes y método:** Estudio realizado mediante cuestionario a principios del año 2015 en 70 hospitales de Cataluña que atienden urgencias. La disponibilidad cualitativa para cada antidoto se consideró adecuada cuando estaba presente en al menos el 80% de los hospitales. La disponibilidad cuantitativa se consideró adecuada cuando se disponía de la cantidad recomendada en al menos el 80% de los hospitales del nivel oportuno.

**Resultados:** Para hospitales de menor complejidad, el porcentaje de antidotos con disponibilidad cualitativa y cuantitativa adecuada fue del 66,7 y 42,9%. En hospitales de mayor complejidad, las disponibilidades cualitativas y cuantitativas fueron adecuadas en un 64,5 y 38,7% de los antidotos. No se observaron diferencias significativas entre las diferentes regiones sanitarias, pero hubo una correlación positiva ( $p < 0,05$ ) entre las urgencias atendidas por los hospitales y el porcentaje de disponibilidad cualitativa adecuada.

#### Palabras clave:

Antidoto

Intoxicación aguda

Botiquín de antidotos

Disponibilidad de antidotos

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**Conclusiones:** La disponibilidad de antídotos en los hospitales de Cataluña es en general baja y muestra diferencias en función de la región sanitaria y de la complejidad asistencial de los hospitales.

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## Introduction

Poisoning is a recurring cause of emergency care. Its treatment requires a multidirectional approach: establish symptomatic measures, try to stop the absorption of the toxin, increase its elimination and avoid or revert the toxic action using antidotes. These drugs can have a very important role in the treatment of poisoning and their efficacy can be time dependent.<sup>1,2</sup>

On the other hand, the availability of antidotes is determined by different factors, such as the frequency of poisoning in a given geographical area, the urgency of antidote administration and its cost.<sup>3,4</sup>

Several publications have offered recommendations on antidotal availability<sup>5,6</sup> and recently, the Antidotes Working Group of the Catalan Society of Clinical Pharmacy (GTA-SCFC), has published an update of the recommendations on qualitative and quantitative availability of antidotes according to the level of healthcare complexity.<sup>7</sup>

The Department of Health of the Generalitat of Catalonia, in collaboration with the GTA-SCFC, conducted a survey among the Catalan hospitals that treat toxicological emergencies to find out whether they had the necessary antidotes, in order to plan, if necessary, future optimisation actions regarding this healthcare resource.

## Patients and method

Descriptive and cross-sectional study carried out by means of a questionnaire sent at the beginning of 2015 to the hospitals of Catalonia that treat emergencies. The document was structured basically in two sections: (a) hospital data, including the number of hospital emergencies in 2015; (b) a table that included 47 drugs with a toxicological or gastrointestinal decontamination indication so as to report the drug's availability (yes/no) and the number of antidotal units available in the Pharmacy and/or Emergency Department. The completed questionnaires were returned by email to the Department of Health of the Generalitat of Catalonia.

The availability assessment was based on the availability recommendations of the GTA-SCFC,<sup>7</sup> with the level of complexity of the hospital being the factor that determines the need to have a specific antidote and in what quantity. Therefore, the hospitals were classified into two levels: A, which included the regional hospitals, and B, which encompassed the high-tech general hospitals and general reference hospitals. For a given antidote, it was considered that qualitative and/or quantitative availability was adequate when it was present in at least 80% of hospitals. It was also considered that 21 antidotes should be present in all level A hospitals and 32 antidotes in level B hospitals.

To establish the optimal quantitative availability, the patient/day treatment (PDT) variable was used,<sup>2</sup> equivalent to the maximum amount of antidote that would be necessary to treat an adult of 70 kg during a period of 24 h. The quantitative availability was considered adequate when the amount of antidote was equal or superior to one PDT in level A hospitals and 3 PDT in level B hospitals. In the case of antidotes of very difficult availability, such as anti-digoxin antibodies, the quantitative availability for level B hospitals was reduced to one or 2 PDT.

The cost involved in maintaining an adequate stock of antidotes was calculated by multiplying the units recommended at each level by the purchase price of the antidote in April 2016. The antidotes that, together, accounted for more than 90% of the total cost of the stock were defined as high cost antidotes.

Fisher's exact test was used to establish the differences between the qualitative and quantitative availability of each antidote. The qualitative and quantitative antidote availability results were also analysed by grouping the different hospitals by healthcare areas, in order to see if there were availability differences due to the geographical location of the hospital, applying the Kruskal–Wallis test. To study the correlation between the number of emergencies treated and the percentage of qualitative and quantitative availability of each hospital, the Pearson correlation coefficient was used. A *p* value <0.05 was considered significant.

## Results

72 questionnaires were sent to 42 hospitals in Barcelona, 11 in Tarragona, 7 in Lleida and 12 in Girona, which corresponded to 59 level A hospitals and 13 level B. The participation of the centres surveyed was 97.2%, since 70 responses were obtained (57 level A and 13 level B).

The percentage of antidotes with adequate qualitative availability was 66.7% for level A hospitals and 64.5% for level B hospitals. Regarding quantitative availability, it was adequate in 42.9% of antidotes for level A hospitals and of 38.7% for those of level B.

Table 1 shows the availability results of the different antidotes in level A and B hospitals. Fomepizol, included in the availability recommendations, could not be evaluated due to a global shortage of the active ingredient at the time of the study. In the comparison between the two levels of hospital complexity (A and B), significant differences were found at the level of qualitative availability for folic acid, intravenous lipid emulsion and physostigmine ( $p < 0.05$ ). Regarding quantitative availability, significant differences were obtained for folic acid ( $p < 0.02$ ).

The availability results according to healthcare areas are shown in Table 2. No significant differences were found between the different healthcare areas, but the global data show a lower adequate qualitative availability in the Healthcare Area of Barcelona with respect to the rest of the areas.

Antidotal availability was analysed according to the number of annual emergencies treated in the 53 hospitals that provided this information (Table 3). The correlation coefficient between the number of emergencies treated and the percentage of qualitative availability was 0.288 ( $p < 0.05$ ), showing a positive correlation between these two variables. On the other hand, the correlation coefficient between the number of emergencies treated and the percentage of quantitative availability did not achieve statistical significance (0.108 [ $p > 0.05$ ]).

The cost of maintaining an adequate stock of antidotes was €5804.64 for a level A hospital. Four antidotes had the highest cost (dantrolene, physostigmine, glucagon and hydroxocobalamin), the sum of their stock maintenance representing 94.7% of the total amount. In level B hospitals, the cost was €36,056 (excluding fomepizole due to shortage in Spain at the time of the study) with 8 being the high-cost antidotes (antidigoxin, dantrolene, physostigmine, glucagon, hydroxocobalamin, silibinin, botulism antitoxin and anti-venom serum) representing 92.9% of the total amount.

## Discussion

The availability of antidotes in healthcare centres is a challenge for all healthcare systems. Deficiencies are repeatedly confirmed even though the lack of availability of antidotes can alter the treatment of the poisoned patient.<sup>8</sup> In our study, the recommended

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