Universitat de Girona
Facultat de Medicina

Is activated charcoal properly indicated in emergency departments from Girona?

A cross-sectional study

END OF TERM PROJECT

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I would like to express my sincere gratitude to all the staff of the emergency departments of Hospital Universitari Doctor Josep Trueta and Parc Hospitalari Martí i Julià for having received me so well. I have learnt a lot from each one of them and from the patients as well.

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1. ABSTRACT

INTRODUCTION: acute oral drug overdose is the toxicological urgency attended most frequently in emergency departments. In the management of these patients, gastrointestinal decontamination plays an important role. Specifically, activated charcoal is the most widely used type of gastrointestinal decontamination. However, according to current recommendations, activated charcoal is used in excess in the management of these patients and this attitude could lead to higher risk of iatrogenic harm. Consequently, Emergency and Pharmacy departments of Hospital Universitari Doctor Josep Trueta (HJT) worked together with the aim to elaborate an intoxication protocol in order to standardize the management of acute intoxications, reduce the high variability of attitudes towards the management of these patients and make easier to take fast decisions in a field where time is crucial.

JUSTIFICATION: the intoxication protocol of the HJT was implemented in 2013 but has never been evaluated. For this reason, this study aims to evaluate if the implementation of this protocol is associated with higher percentage of correct indications of activated charcoal administration.

OBJECTIVE: to evaluate if the implementation of the HJT's intoxication protocol is associated with higher percentage of correct indications of activated charcoal administration in patients with acute oral drug overdose attended in the emergency department of this hospital compared with them attended in the emergency department of Parc Hospitalari Martí i Julià (PHMJ).

METHODOLOGY: this study will be an observational cross-sectional study that will be carried out in the emergency departments of HJT and PHMJ. The sample will be formed by two groups with minimum 180 patients each group with acute oral drug overdose. One group will be formed by patients with acute oral drug overdose attended in the emergency department of HJT (protocol group) and the other group will be formed by patients attended in the emergency department of PHMJ, where there is not an own intoxication protocol (control group). Then, we will compare the percentage of correct indications of activated charcoal administration between the two groups to see if there are differences.

KEY WORDS: activated charcoal, gastrointestinal decontamination, acute intoxication, acute oral drug overdose, poisoning.

2. ABBREVIATIONS

AACT	American Academy of Clinical Toxicology
AC	Activated charcoal
ASA	Acetylsalicylic acid
EAPCCT	European Association of Poison Centres and Clinical Toxicologists
ED	Emergency department
HJT	Hospital Universitari Doctor Josep Trueta
MDAC	Multiple-dose activated charcoal
NAIDs	Nonsteroidal anti-inflammatory drugs
PHMJ	Parc Hospitalari Martí i Julià
SDAC	Single-dose activated charcoal
SSRI	Selective serotonin reuptake inhibitors

3. INTRODUCTION

3.1. TERMINOLOGY

The World Health Organization defines overdose as “the use of any drug in such an amount that acute adverse physical or mental effects are produced” (1).

There are other terms used in literature to describe this situation such as acute intoxication or acute poisoning. In the literature reviewed all these terms has been used as synonyms.

In our study we use the term “acute oral drug overdose” to refer only an acute overdose produced by orally ingested licit drugs regardless of whether it is an accidental poisoning or a self-poisoning. Chronic drug poisonings due to inappropriate treatment or to drug addiction, or adverse reactions to drugs or other agents are not included in this definition.

3.2. EPIDEMIOLOGY

Acute oral drug overdose is, together with alcohol abuse, the toxicological urgency attended most frequently in emergency departments, with psychotropic drugs, particularly benzodiazepines, being the most commonly implicated drugs (2).

Acute intoxication cases represent 0,66% of emergency department (ED) visits. The mean age of these patients is 33 years. Children only represent 4% of cases and teenagers 18,6%. The incidence is higher in male (56%)(3).

Regarding the type of poisoning, according to HISPATOX study (4), the vast majority of acute oral drug overdoses attended in ED are those associated with pharmaceutical drugs (50,2%), followed by alcohol intoxication (29,7%), illicit drug abuse (9,4%) and accidental cases (7,9%). Other studies also indicate pharmaceutical drugs as one of the leading causes of acute intoxications attended in ED (5).

The most frequent drugs involved are benzodiazepines (57%), selective serotonin reuptake inhibitors (SSRI) (6,7%), acetaminophen (4,5%), tricyclic antidepressants (2,8%), neuroleptics (2,2%) and salicylates (1,7%). These drugs are the patient’s own treatment in 59% of cases (3).

On arrival at hospital, less than 20% of patients are symptomatic. Furthermore, a total of 58,84% are discharged within the first 12 hours, 21,41% are discharged after 24 hours of

observation and only 5,3% to 14,1% are hospitalized (2,3% are admitted to intensive care unit)(4,5).

Overall, the mortality from acute oral drug overdose is less than 1%, showing that the vast majority of acute oral drug overdoses are not severe (4,6).

Regarding the treatment of these patients, the indication of any type of gastrointestinal decontamination varies from 29,84% to 63,8%. In these cases, the most widely used type of gastrointestinal decontamination is activated charcoal (AC), ranging from 41,2% to 71,6% (2,4,6–8).

Acute intoxications attended in Girona

According to information provided by Dra Gispert and Dra Guerrero, in one-year period from June 2014 to May 2015, the ED of Hospital Universitari Doctor Josep Trueta (HJT) attended 438 patients with acute intoxication, which represented 0,66% of ED visits. In the same period, the ED of Parc Hospitalari Martí i Julià (PHMJ) attended 295 patients, which represented 0,70% of ED visits.

The overall mortality was 0,46% in HJT and 0% in PHMJ.

Regarding the type of poisoning involved, the most frequent was pharmaceutical drugs, followed by alcohol and illicit drugs (Figure 1).

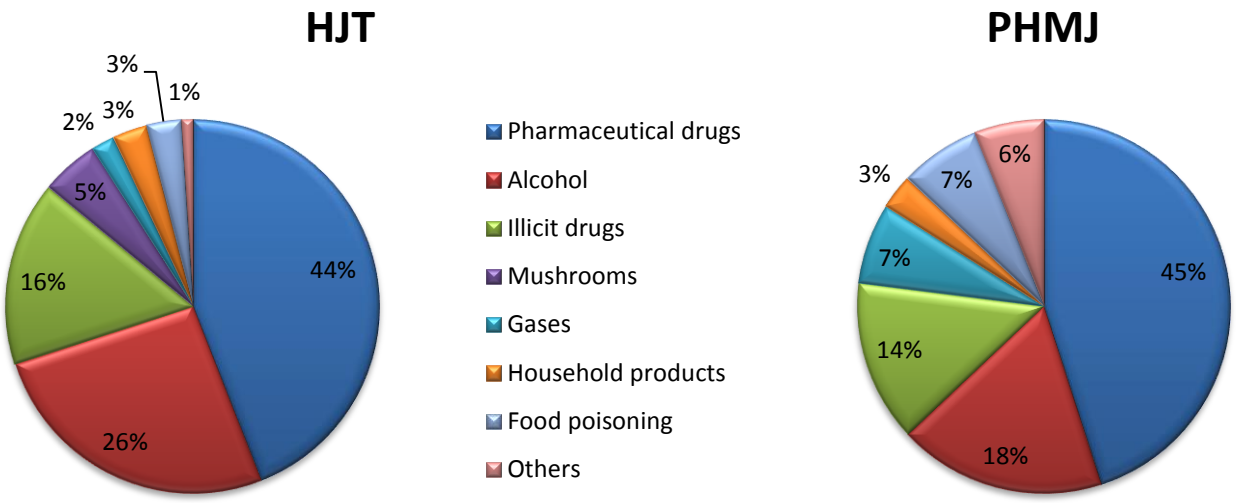


Figure 1: Types of poisonings attended in HJT and PHMJ (Courtesy of Dra Gispert and Dra Guerrero).

3.3. EMERGENCY MANAGEMENT OF ACUTE ORAL DRUG OVERDOSE

In the management of a patient with or potentially with acute oral drug overdose, considerations for both diagnosis and treatment may occur sequentially or simultaneously, depending on the clinical situation and severity of the intoxication (9).

The diagnostic consists of taking an appropriate toxicological history (important information to be gained includes the type of drug involved, the amount ingested and the time since ingestion) and performing a clinical examination with attention to toxidrome recognition (a toxidrome, or toxicologic syndrome, is a constellation of symptoms and signs that lead to a certain class of poisons) (*Annex 1*)(9,10).

Also, depending on the specific situation, certain diagnostic tests may provide useful information regarding the poisoning event and case management. However, the majority of toxicology-related diagnoses and therapeutic decisions are made from the history and clinical examination (10).

In general, the treatment of an acute oral drug overdose involves (9–11):

1) **ABCs of emergency care** -airway, breathing, and circulation- which should be followed ensuring a protected airway, adequate ventilation and hemodynamic stability. It is important to highlight that supportive and symptomatic care should be the cornerstone of acute oral drug overdose treatment.

2) **Gastrointestinal decontamination:** consists on removing the toxin from the body in order to prevent or reduce the absorption of a substance, potentially reducing systemic toxicity. Modalities include syrup of ipecac, gastric lavage, activated charcoal and whole bowel irrigation. These modalities are explained below.

3) **Enhanced elimination:** is the process of removing a toxin from the body after it has been absorbed. Modalities include multiple-dose activated charcoal (MDAC), urinary alkalinisation, and extracorporeal elimination.

4) **Antidote therapy:** there are several specific antidote agents that may be employed with the aim of blocking the effect of the toxic substance on the target organs.

3.4. GASTROINTESTINAL DECONTAMINATION

Removal of the patient from the source of toxicity has been for years the foundation of the treatment of poisoned patients. This includes removing the toxin from the body, a process called decontamination. There are various methods of decontamination. The clinical scenario will determine which method, if any, should be used.

- **Syrup of ipecac:** is an agent that induces emesis through direct irritant action on the stomach and central action at the chemoreceptor trigger zone. The combined position statement of the American Academy of Clinical Toxicology (AACT) and European Association of Poison Centres and Clinical Toxicologists (EAPCCT) concluded that its routine administration in ED should be abandoned due to lack of evidence for improved outcomes and potential risks including delayed administration of oral antidotes and other decontamination products, aspiration, and complications from prolonged emesis and retching. Consequently, the position statement for ipecac syrup, although not condemning its use, says that ipecac should have little or no place in the treatment of oral poisoning (11–13).

- **Gastric lavage:** is the process of irrigating the gastric cavity to remove recently ingested material. Although liquid agents may be lavaged with a smaller diameter nasogastric tube, extraction of pill fragments requires use of a large bore tube. However, placement of an orogastric tube is a distressing procedure to perform in an awake patient and may be complicated by retching and aspiration. Other serious complications such as hypoxia, laryngospasm, dysrhythmia and perforation have also been reported. This procedure is contraindicated in cases of acid, alkali or hydrocarbon ingestion. Gastric lavage is not recommended for routine use in the poisoned patient but, it may be considered in combination with AC for symptomatic patients who present within 1 hour, who have ingested agents that slow gastrointestinal motility, sustained-release medication or massive/life-threatening amounts of a substance (11,12).

- **Whole bowel irrigation:** is the administration of a laxative agent such as polyethylene glycol to fully flush the bowel of stool and unabsorbed substances. Although data is limited, whole bowel irrigation could be considered for substantial ingestions of substances that are not bound by AC. Contraindications for its use include

compromised airway, hemodynamic instability, seizures and the lack of bowel sounds or a suspected or documented bowel obstruction (10–12).

- **Activated charcoal:** is an agent possessing a large surface area that when administered orally, adsorbs ingested substances within the gastrointestinal track thereby preventing systemic absorption. Although it adsorbs most toxics; some agents such as lithium, heavy metals and alkalis do not bind to charcoal. The most common adverse effects are gastrointestinal and include vomiting and constipation, but the most concerning adverse effect is aspiration, although this is rare. Overall, administration of activated charcoal remains a useful decontamination technique for patients presenting with early, potentially severe poisoning of adsorbable toxics. Nowadays, AC is the preferred method of gastrointestinal decontamination and the most widely used (10–12).

In conclusion, decontamination of the poisoned patient must only be performed after careful consideration of the potential risks and benefits of the decontamination procedure. Although decontamination with ipecac, activated charcoal, gastric lavage and whole bowel irrigation were once common practice, current recommendations of the AACT and the EAPCCT reflect a trend towards more judicious use (6,12,13). These two institutions do not recommend the routine use of gastrointestinal decontamination, but advice that it may be considered in selected cases. Although controversial, emergency physicians must always determine whether the benefits outweigh the associated risks.

3.5. ACTIVATED CHARCOAL

3.5.1. BACKGROUND

For centuries, perhaps millennia, human beings have used purgatives to remove a poison from the body (14).

Since antiquity, physicians have believed in the healing properties of charcoal. Hippocrates (400 BC) used charcoal to treat epilepsy, vertigo, and anthrax. However, scientific study of charcoal began in 1758 when its adsorptive powers were recognized (15).

The first reported use of charcoal as an antidote occurred in 1811, when the French chemist Michel Bertrand ingested charcoal with 5 grams of arsenic trioxide. Afterwards in 1852, another French chemist named Pierre-Fleurus Touéry showed no ill effects after consuming a

large dose of strychnine with charcoal before sceptical colleagues of the French Academy of Medicine (16).

Nevertheless, charcoal was infrequently used in the management of acute poisoning until 1963, when a review article in the Journal of Pediatrics concluded that “this agent, presently somewhat neglected, has a wide spectrum of activity and when properly used is probably the most valuable single agent we possess”. After that, in the 1970s and 1980s, activated charcoal was a common element of gastrointestinal decontamination after acute poisoning (16).

Nowadays, activated charcoal (AC), sometimes mistakenly characterized as a “universal antidote,” is the most frequently employed method of gastrointestinal decontamination in the developed world. Typically administered as a single dose (SDAC), its tremendous surface area permits the binding of many drugs and toxins in the gastrointestinal lumen, reducing their systemic absorption. Like other decontamination procedures the utility of SDAC attenuates with time, and while generally safe it is not free of risk (16).

It bears mention that decontamination with SDAC is conceptually different from the use of multiple-dose activated charcoal (MDAC), a less commonly deployed intervention involving the administration of multiple (typically 2 to 6) smaller doses of AC with the goal of enhancing total body clearance of a limited number of compounds such as dapsone, carbamazepine, and phenobarbital. Thus, the goal of MDAC is enhanced toxin elimination rather than reduced absorption per se (16).

The mechanism by which this modality accomplishes enhancement of elimination is either by interrupting the enterohepatic/enterogastric circulation of drugs or through the binding of any drug that diffuses from the circulation into the gut lumen (called *gut dialysis*). However, it has limited application because the toxin must have a low volume of distribution, low protein binding, prolonged elimination half-life, and low p*K*a, which maximizes transport across mucosal membranes into the gastrointestinal tract. Based on experimental and clinical studies, it should be considered only in patients with a life-threatening ingestion of carbamazepine, dapsone, phenobarbital, quinine or theophylline (17).

3.5.2. HOW IS ACTIVATED CHARCOAL MADE?

Activated charcoal is produced by the controlled pyrolytic decomposition of carbon-based compounds, such as sawdust, peat or coconut shells, followed by "activation" using oxidizing gases (steam, carbon dioxide, sulfuric acid…) at temperatures of 500-900ºC. The activating agent removes substances previously adsorbed on charcoal and erodes the internal surfaces of the product breaking down granules of carbon into smaller ones having larger surface area and thereby increasing its adsorptive surface area, resulting in an exceptionally porous final product (15,16,18).

Typical surface areas for activated charcoals average of 800-1,200 m2/g. Thus, a 50gr dose of activated charcoal has an adsorptive surface area equivalent to about seven football fields (15,16,18).

This results in a powerful, inert, nontoxic, and nonspecific adsorbent that binds intraluminal drugs and interferes with their absorption through weak intermolecular (Van der Waals) forces. It is particularly effective in binding non-ionized, organic and high molecular-weight compounds (16,17).

3.5.3. EFFECTIVENESS OF AC

In vitro and animal studies:

Dozens of *in vitro* simulations and animal studies convincingly show that AC binds a wide range of drugs to varying degrees (*Annex 2*) (6,10,15–17,19).

However, these studies also show that some compounds do not bind to AC and so it is not indicated for their decontamination, such as, heavy metals, iron, lithium, potassium, acids and alkalis. (*Annex 3*) (6,10,15–17,19).

Studies in human volunteers:

The most recent AACT and EAPCCT joint position paper on SDAC observed that 46 drugs have been the subject of 122 evaluations of the effect of SDAC in healthy volunteers. Most of these are small crossover studies examining the extent to which SDAC influences the area-under-the-curve (AUC) of drug concentration versus time (6).

These studies employed varying doses of SDAC (0.5 to 100 g) at intervals of up to 6 hours following ingestion of different drugs. The mean reduction in systemic drug absorption was 74,1% at 5 minutes, 51,7% at 30 minutes, 38,1% at 60 minutes, 34,5% at 120 minutes and 21,1% at 180 min (Figure 2) (6).

TABLE 2

Summary of the reduction of drug absorption by single-dose activated charcoal (0.5–100 g) in human volunteer studies (n=122 comparisons involving 46 drugs) at varying time intervals (0–360 minutes) after drug dosing

	Time (min) of administration of charcoal after drug dosing												
% Reduction in drug absorption	0–5 (n=84)	30 (n=7)	0–30 (n=92)	60 (n=16)	0–60 (n=108)	120 (n=8)	0–120 (n=117)	180 (n=3)	0–180 (n=120)	240 (n=3)	0–240 (n=123)	360 (n=1)	0–360 (n=124)
Mean	74.10	51.70	72.17	38.14	67.13	34.54	64.75	21.13	63.66	29.33	61.44	14.00	60.95
SD	27.59	14.73	27.40	20.25	29.09	26.76	30.00	16.17	30.50	20.50	30.75	0.00	30.94
Median	86.85	49.40	83.00	30.20	74.60	25.00	65.20	13.60	64.65	23.00	63.50	14.00	62.90
Max	100.00	75.00	100.00	77.90	100.00	49.60	100.00	43.60	100.00	80.00	100.00	14.00	100.00
Min	12.30	31.10	12.30	5.70	5.70	7.70	5.70	6.20	5.70	8.00	5.70	14.00	5.70

Figure 2: Summary of the reduction of drug absorption by SDAC in human volunteer studies (6).

Therefore, these volunteer studies demonstrate that the effect of activated charcoal diminished as the time of administration after drug ingestion increased and show that AC is more effective preventing systemic absorption of drugs when given within 1-2h of ingestion and perhaps longer after ingestion of sustained-release preparations (6,18).

However, in addition to recruiting medically well subjects, an important limitation of volunteer studies is that they involve sub-toxic drug exposures (6,15,16).

Studies in poisoned patients:

One of the problems with the clinical studies is that the majority of the patients do not have severe overdoses. Also, in most studies, the power to detect differences between treatment groups in seriously intoxicated patients is poor (15).

Merigian et al. performed a prospective, controlled trial (n=1479) compared administration of AC to supportive care alone on an even/odd day basis. Administration of AC provided no benefit over supportive care and was associated with a higher incidence of vomiting (23% vs. 13% in the supportive care group), longer ED stay, and higher incidence of complications. However, the vast majority of cases (1266 patients) were not admitted to the hospital, reflecting the low risk of serious outcome in most overdoses presenting to the ED. In addition, lopsided numbers in the charcoal (399 patients) and no charcoal (1080 patients) group raises

questions about the randomization method (even/odd day allocation) and data on the temporal separation between the ingestion and the time of charcoal administration were not included in the paper (6,15,18).

Cooper et al. randomized 327 patients with acute drug overdose to receive either 50 g of SDAC or no decontamination within 12 hours of ingestion. They found no difference between SDAC and supportive care only with respect to length of stay, intensive care unit admission and mortality. However, the ability of this study to detect a benefit of SDAC may have been limited by the enrolment of patients destined to do well without AC (they excluded patients with ingestions judged to be too serious to enter a randomized trial) (20).

Nevertheless, other studies suggest that SDAC can be associated not only with reduction in drug absorption, but also with improvements in clinical outcomes. For example, Friberg and colleagues evaluated 53 patients with citalopram overdose. The authors estimated that SDAC reduced citalopram bioavailability by 22% and increased total body clearance by 72%. Comparable studies estimate that early administration of SDAC following overdose reduces the absorption of quetiapine by 35%, sertraline by 27%, escitalopram by 31% and venlafaxine by 29%. Furthermore, another study shows that SDAC, when given within 2 hours of promethazine overdose, reduced the risk of delirium by more than half. Finally, an Australian study performed in 1999 showed that the administration of AC spared some patients the need for hospitalization despite the limitations of the study (14).

These studies yield insights into the utility of SDAC in real-world practice. Despite their observational nature, they provide relevant evidence supporting the use of SDAC shortly after acute overdose (16).

In conclusion, according to current recommendations there is enough evidence from in vitro data and volunteer studies to justify the use of AC in selected circumstances (6,16,18).

3.5.4. ADVERSE EVENTS

While generally safe, activated charcoal is not free of risk. Vomiting and constipation are the most common complications of AC administration. Rates of vomiting in adults range from 5% to 56% (2,9,18,21).

However, pulmonary aspiration is the most widely cited concern associated with AC and the most serious potential complication after AC administration, but the risk of this complication is

low. Nevertheless, aspiration following AC administration is well documented in isolated case reports, some of them dramatic causing even the patient's death (16,21).

More commonly, pulmonary aspiration occurs when the drowsy or convulsing patient regurgitated gastric contents, including activated charcoal, into the unprotected airway. This can result in acute airway obstruction, bronchospasm, hypoxemia, and pneumonitis. Prolonged intubation, death, and permanent lung injury may follow (17,18). In addition, aspiration occurred most often when AC is used in conjunction with gastric emptying techniques (22).

It bears mention that endotracheal intubation decreases, but does not eliminate, the risk of aspiration(17,18).

Other pulmonary complications that have also been reported include chronic lung disease, obstructive laryngitis with glottic edema, granulomatous lung mass, charcoal empyema and bronchiolitis obliterans. In general, rates of pulmonary complications in medical literature range from 1,7% to 9,1% (16,17,21).

Gastrointestinal complications, apart from vomiting and constipation, represent another potential risk of AC administration. Published reports describe bowel obstruction, bezoars, gastrointestinal tract perforation with charcoal peritoneum and stercoliths after AC administration. Patients with pre-existing motility disorders, those receiving opioids or antimuscarinic drugs, and those treated with MDAC seem to be at greater risk (16).

In 2010 it was published a Spanish study about adverse reactions to the administration of AC. In this study, 575 cases of acute intoxication were reviewed and adverse reactions occurred in 41 cases (7.1%) and included nausea or vomiting (36 patients), bronchoaspiration (6 patients) and pneumonia (2 patients). Spontaneous vomiting before AC, pre-hospital AC administration, MDAC and the need for specific clinical measures to treat intoxicated patients (e.g., intubation) were all associated with a significantly increased risk for an adverse event (21).

The authors concluded that adverse reactions to charcoal are infrequent and rarely severe, but are associated with a greater emergency department stay and a trend to greater hospital admission. They also asserted that even though these adverse reactions are infrequent, their presence is one more reason to highlight the importance of administering AC only when it is indicated (21).

3.5.5. ACTIVATED CHARCOAL INDICATIONS

The AACT/EAPCCT 1997 guidelines recommend that AC should not be routinely administered to poisoned patients and suggest its effectiveness decreases with time after ingestion. If AC is to be administered, the greatest benefit is seen within 1 h after ingestion of the poison (23). These 1997 recommendations were reaffirmed in 2005 with the observation that "no new evidence" was found to suggest that a revision in the guidelines was needed (6).

In the literature reviewed there is an agreement that the decision to perform gastrointestinal decontamination has to be based upon the specific poison(s) ingested, the amount ingested, the time from ingestion to attendance and the clinical status.

According to that, a recent Up to Date review says that gastrointestinal decontamination would be recommended in patients who (22):

- Present for care soon after ingestion (usually within one to two hours).
- Have ingested a poison and amount suspected to cause toxicity
- Have a protected airway (ie, patient is alert with intact airway reflexes or is intubated)

Based on AACT/EAPCCT guidelines, current evidence, literature review and their own experience, M. Amigó and S. Nogué elaborated an algorithm with criteria on the use of gastrointestinal decontamination in acute oral drug overdoses based upon the specific drug(s) ingested, dose ingested, time since ingestion and patient's clinical status (*Annex 4*) (24,25).

About these criteria, it bears mention that some drugs, such as, anticholinergics, neuroleptics and cyclic antidepressants, are considered to have particular pharmacokinetic characteristics that delays systemic absorption and, therefore, the administration of AC is considered correct up to 6 hours post ingestion (24,25).

In 2006, the *Asociación Española de Toxicología* published a document, called CALITOX, with 24 indicators to evaluate the quality of the assistance of patients with acute intoxications attended in emergency departments. The indicator number 6 evaluates the correct indication of gastrointestinal decontamination. According to this indicator, indication of gastrointestinal decontamination, which includes the use of AC, is considered correct if it meets the M. Amigó and S. Nogué criteria (26).

Apart from SDAC, when considering MDAC, AACT/EAPCCT guidelines and the M. Amigó and S. Nogué criteria suggest that MDAC should only be considered in patients with protected or intact airways and only if a patient has ingested a life-threatening amount of carbamazepine, dapsone, phenobarbital, quinine, theophylline or sustained-release tablets (25,27).

3.5.6. ACTIVATED CHARCOAL CONTRAINDICATIONS

Contraindications to the administration of AC include (6,12,22,27):

- Depressed state of consciousness without airway protection (due to risk of aspiration). The decision to intubate a poisoned patient is often complicated, but it should be made independently of the decision to give AC. In particular, tracheal intubation should not be performed for the sole purpose of giving AC.

- Patients who present to ED when poison absorption is considered complete.

- Nontoxic amount ingested.

- Drugs not bound by AC (e.g., metals including iron and lithium, alkali, acids, alcohols).

- Need for endoscopy (e.g., significant caustic ingestion) because its presence in the gastrointestinal tract severely limits early endoscopic evaluation of caustic injuries.

- Presence of intestinal obstruction (absolute contraindication) or concern for decreased peristalsis (relative contraindication).

3.5.7. CONTROVERSY ON THE USE OF ACTIVATED CHARCOAL

Activated charcoal remains one of the last vestiges of a universal antidote. Currently, AC, as we have shown here, is widely used as a universal antidote in the treatment of acute oral drug overdoses, despite proven efficacy, because it is assumed that there may be some benefit, based on human volunteer studies, and the risk of complication is low. Conviction of efficacy is such that nasogastric tubes are placed for the sole purpose of administering AC. However, this current trend of widespread usage could possibly result in the increase of iatrogenic harm (15,28).

As stated above, no controlled clinical studies have demonstrated that the "routine" use of gastrointestinal decontamination reduces morbidity and mortality in poisoned patients. Nevertheless, evidence from human volunteer trials and clinical studies suggest that decontamination may reduce the absorption of toxins in the gastrointestinal tract and may be helpful in select circumstances. The problem is to decide whether, when and how to remove or neutralize ingested poisons (29).

A study published in 2007 found that the majority of patients who presented to a health care provider received charcoal regardless of the time of toxic ingestion. They concluded that few patients presenting to a health care provider after an acute toxic ingestion are treated in accordance with the current recommendations for activated charcoal (28).

It is worth noting that many authors have referenced the position statements as advocating the administration of SDAC. In fact the position statement does not advocate the use of SDAC. The last paragraph of the Position Statement Abstract on SDAC reads: "SDAC *should not be administered routinely in the management of poisoned patients*. […] The administration of activated charcoal *may be considered* if a patient has ingested a potentially toxic amount of a poison (which is known to be adsorbed to charcoal) up to 1 hour previously; there are insufficient data to support or exclude its use after 1 hour of ingestion. *There is no evidence that the administration of AC improves clinical outcome*."(6,15)

Furthermore, the vast majority of adults with acute oral drug overdose have an uncomplicated course and recover fully with supportive care. As a result of attempts to administer AC, deaths, threatening pulmonary complications, clinically significant long-term pulmonary diseases, charcoal peritoneum, and corneal abrasions have been reported in the literature (14,15,20,22).

Consequently, current recommendations suggest that AC should be used far more selectively. Specifically, according to these recommendations, AC should be restricted to those situations where there is a substantial risk from the poisoning and a significant amount of the poison is likely to still be present in the gut; or what is the same, AC should not be administrated if the agent and amount ingested are clearly nontoxic, if the agent is considered fully absorbed due to delayed presentation, or if the toxin is not adsorbed by AC (6,15,20,22).

In these cases, when gastrointestinal decontamination is indicated, AC, though not strikingly effective, provides the best rationale on which to base treatment of acute oral drug overdoses (29).

In conclusion, the challenge for clinicians managing poisoned patients is to identify those who are most at risk of developing serious complications and who might potentially benefit from AC administration (29).

In order to standardize the management of these patients and make easier to take fast decisions in a field where time is crucial, some protocols have been elaborated, such as, the HJT's intoxication protocol (30).

Nevertheless, some authors emphasize the importance of assessing each case individually instead of using a protocol. They state that based on personal experience and knowledge and unique circumstances of the ingestion, the clinician could make the best judgment of the value or risk of AC administration (18).

3.6. HOSPITAL DOCTOR JOSEP TRUETA'S INTOXICATION PROTOCOL

Emergency and Pharmacy departments of HJT worked together with the aim to elaborate an intoxication protocol in order to standardize the management of patients with acute intoxication and making easier to take fast decisions by the physicians.

The intoxication protocol was finally implemented in 2013 and is based on AACT/EAPCCT guidelines, M. Amigó and S. Nogué criteria and current evidence (30).

This protocol establishes the actions to take by the emergency physician in the management of a patient with acute intoxication regarding the type of poisoning, the amount ingested, the time since ingestion and the clinical status.

With the aim to making easier to take fast decisions, the authors summarized the indications of the gastrointestinal decontamination in an algorithm, which could be an useful tool for the emergency physicians of HJT (Figure 3) (30).

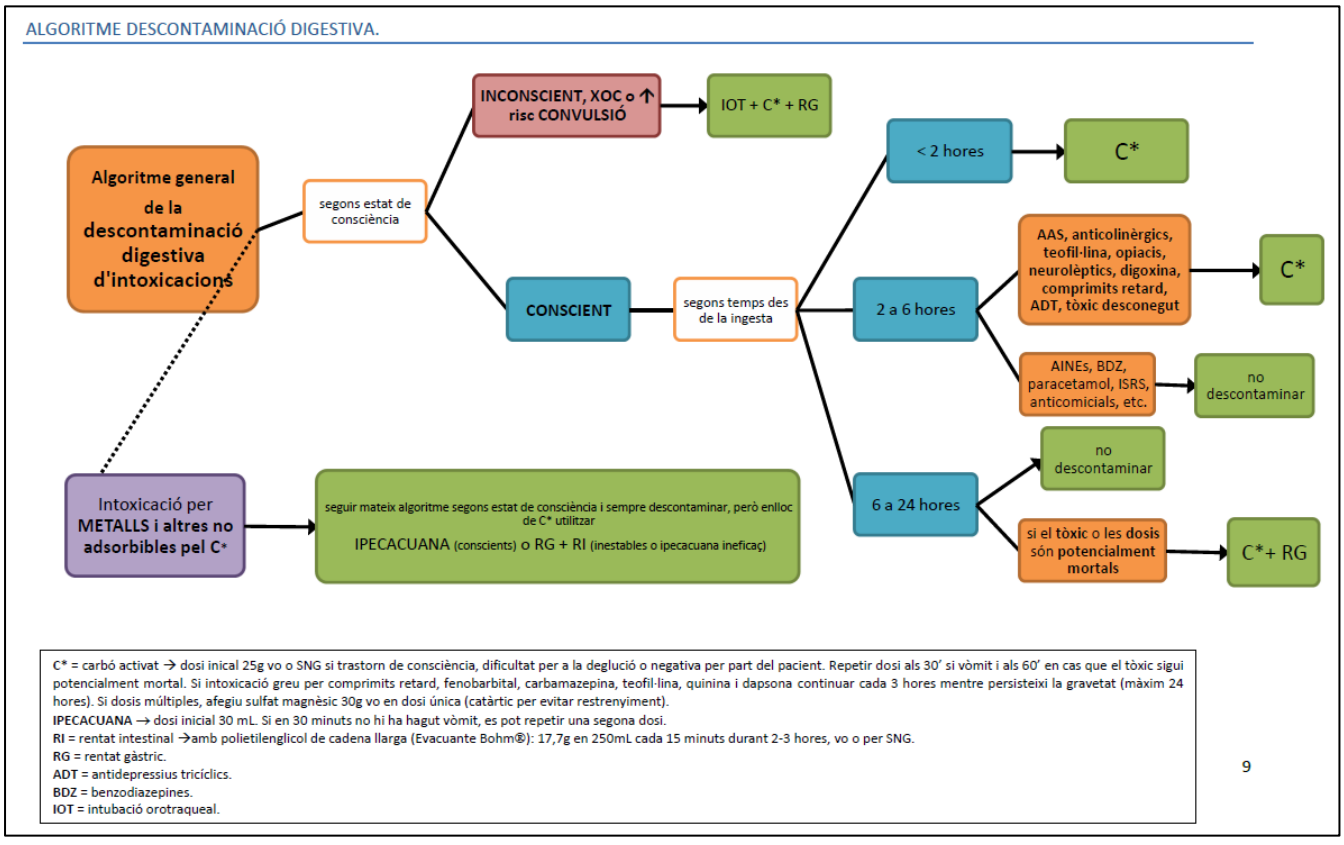


Figure 3: Gastrointestinal decontamination algorithm from HJT's intoxication protocol (30).

4. JUSTIFICATION

The World Health Organization defines quality care as that which ensures that all patients receive the most complete diagnostic and therapeutic care to achieve the best possible result and maximum satisfaction with the least possible risk of iatrogenic harm (26).

According to that, the previous aggressive approach to gastrointestinal decontamination in patients with acute oral drug overdose is increasingly being replaced by less emphasis on it and more emphasis on supportive care, based on current evidence (11).

However, although trends are changing, it seems clear that AC continue to be used in excess according to current recommendations, even though it has not been shown to improve the outcome of patients with acute oral drug overdose. Consequently, this attitude could lead to higher risk of iatrogenic harm.

In order to reduce this overuse of AC and make clear indications on the use of any type of gastrointestinal decontamination for the treatment of acute oral drug overdoses and make easier to take fast decisions in a field where time is crucial, the Emergency and Pharmacy departments of HJT developed an intoxication protocol.

Nevertheless, it has never been evaluated if the implementation of this protocol is associated with higher percentage of correct indications of gastrointestinal decontamination and, specially, of activated charcoal, which is the most widely used type of gastrointestinal decontamination.

For that reason, this study aims to evaluate if the implementation of HJT's intoxication protocol is associated with higher percentage of correct indications of AC administration in patients with acute oral drug overdose.

In order to do that, we will compare the management of patients with acute oral drug overdose attended in the ED of HJT, with them attended in the ED of PHMJ where there is not an own intoxication protocol and the decision whether use or not AC is based only on the emergency physician judgment.

5. HYPOTHESIS

The implementation of the Hospital Universitari Doctor Josep Trueta's intoxication protocol is associated with higher percentage of correct indications of activated charcoal administration in patients with acute oral drug overdose attended in the emergency department of this hospital compared with them attended in the emergency department of Parc Hospitalari Martí i Julià.

6. OBJECTIVE

This study aims to analyse if the implementation of the Hospital Universitari Doctor Josep Trueta's intoxication protocol is associated with higher percentage of correct indications of activated charcoal administration in patients with acute oral drug overdose attended in the emergency department of this hospital compared with them attended in the emergency department of Parc Hospitalari Martí i Julià.

7. MATERIALS AND METHODS

7.1. STUDY DESIGN

This study is designed as an observational cross-sectional study.

7.2. STUDY POPULATION

The study population will be all patients admitted to the emergency departments of HJT and PHMJ due to an acute oral drug overdose, with the following inclusion and exclusion criteria:

7.2.1. Inclusion criteria

1) **Patients with acute oral drug overdose**

- Diagnosis of acute oral drug overdose was established on the basis of clinical history (excessive ingestion of any therapeutic drug, alone or in combination with other drug or alcohol) and/or clinical symptoms.
- Furthermore, the diagnosis could rely on the toxicological analysis when it was done (*Annex 5*).

2) **Patients of 15 years old or more**

7.2.2. Exclusion criteria

1) Patients referred from another medical centre.
2) Patients assisted by doctors working in both emergency departments (HJT and PHMJ), because they could manage patients attended in PHMJ according to the HJT's intoxication protocol that they already know.
3) Chronic poisonings.
4) Alcohol intoxication alone.
5) Adverse reactions and drug secondary effects.
6) Food, mushrooms and plants intoxication.
7) Gas intoxication.
8) Poisonous animals bite.
9) Intravenous or inhaled route of administration.
10) Drugs of abuse (illicit drugs) intoxication.

7.3. SAMPLE

7.3.1. Sample selection

A non-probabilistic consecutive sampling method will be performed with patients of 15 years old or more admitted to the emergency departments of HJT and PHMJ due to an acute oral drug overdose.

Therefore, sampling recruitment will carry out in the emergency department of two health centers: Hospital Universitari Doctor Josep Trueta and Parc Hospitalari Marti i Julià from Girona.

The study sample will be formed by two groups:

- The first group (protocol group) will be formed by patients meeting the inclusion and exclusion criteria admitted to HJT's ED.

- The second group (control group) will be formed by patients meeting the inclusion and exclusion criteria admitted to PHMJ's ED.

Sample recruitment will take place during 18 months.

7.3.2. Sample size

To calculate the sample size the online free application GRANMO was used (31).

Accepting an alpha risk of 0.05 and a beta risk of 0.2 in a two-sided test, 180 subjects are necessary in the first group and 180 in the second group (360 subjects in total) to recognize as statistically significant a proportion difference, expected to be of 0.7 in group 1 (proportion of cases in which activated charcoal is correctly indicated in HJT) and 0.55 in group 2 (proportion of cases in which activated charcoal is correctly indicated in PHMJ). It has been anticipated a drop-out rate of 10%, corresponding to incomplete data collection sheets.

As stated before, in one-year period 2014-2015, the ED of HJT attended 438 patients and the ED of PHMJ attended 295 patients with the diagnosis of acute intoxication. Then, the number of patients is estimated to be enough to carry out the study.

7.4. VARIABLES AND METHODS OF MEASUREMENT

All variables will be collected prospectively during 18 months using a data collection sheet, designed by physicians of HJT's ED to collect data regarding patients with acute intoxication (*Annex 6*).

7.4.1 Main variables

- **Correct indication of activated charcoal administration:** it is a nominal dichotomous qualitative variable (Yes/No).

  - On the basis of the drug(s) ingested, the amount ingested, the time from ingestion to attendance and the presence of symptoms and according to AACT/EAPCCT guidelines (6,27) and M. Amigó and S. Nogué algorithm (25), will be considered that the indication of AC was correct if it meets the following criteria:

  1) The drug is adsorbed by AC or it is unknown which drug(s) has ingested (*Annex 2*).
  2) The amount ingested is considered toxic or is unknown (*Annex 7*).

  If these 2 criteria are met, then the indication of AC will be considered correct in the following circumstances:

  1) The patient is unconscious (GCS ≤ 8), shocked or the risk of convulsion is high. The risk of convulsion is considered high if the patient has ingested isoniazid, antimalarials or theophylline, or in case of history of previous seizures.
  2) The patient is conscious and the time since ingestion is less than 2 hours or is unknown.
  3) The patient is conscious and the time since ingestion ranges from 2 to 6 hours. In this case, the indication of AC will be considered correct if the patient has ingested some of the next drugs: cyclic antidepressants, neuroleptics, opioids, salicylates, anticholinergics, digoxin, sustained-release tablets or the drug ingested is unknown.
  4) The patient is conscious and the time since ingestion is less than 24 hours and the amount ingested is considered life threatening.

- If the patient is unconscious (GCS ≤ 8) or loss of pharyngeal reflex or there are swallowing problems, the airway has to be protected with endotracheal intubation and AC has to be administrated by nasogastric tube.

- In case of caustic ingestion or intestinal obstruction, the administration of AC is contraindicated.

- In case of severe intoxication with carbamazepine, dapsone, phenobarbital, quinine, theophylline or sustained-release tablets, MDAC could be indicated.

- If the patient has ingested more than one drug, the decision has to be based on the most potential life-threating drug.

- **Emergency department in which patient was admitted**: it is a nominal dichotomous qualitative variable (HJT/PHMJ). It will be assessed by HJT if the patient was attended in HJT's ED or PHMJ if the patient was attended in PHMJ's ED.

7.4.2. Covariates

Covariates that will be measured are:

- **Gender**, which is a nominal qualitative variable. It will be assessed by male / female / unknown.

- **Age**, which is a discrete quantitative variable. It will be collected from the ID card of the patient. It will be assessed by years.

- **Type of drug involved**, which is a nominal qualitative variable. According to the most common drugs involved in acute oral overdoses, it will be assessed by benzodiazepines, SSRI, acetaminophen, cyclic antidepressants, acetylsalicylic acid (ASA), nonsteroidal anti-inflammatory drugs (NAIDs), neuroleptics, lithium or others (3,20,21,32).

- **Time from ingestion to ED attendance**, which is a continuous quantitative variable. It will be measured from the time of ingestion to the time of ED attendance and it will be calculated by "time of ED attendance" minus "time of ingestion" from the data collection sheet. It will be assessed by hours.

VARIABLE	TYPE OF DATA	CATEGORIES OR VALUES	MEASURE INSTRUMENT
Correct indication of AC	Nominal dichotomous qualitative	Yes/No	Defined criteria
Emergency department admission	Nominal dichotomous qualitative	HJT/PHMJ	Data collection sheet
Gender	Nominal qualitative	- Male - Female - Unknown	ID card or other documentation of the patient
Age	Discrete quantitative	Number of years	ID card or other documentation of the patient
Type of drug involved	Nominal qualitative	- Benzodiazepines - SSRI - Acetaminophen - Cyclic antidepressants - ASA - NAIDs - Neuroleptics - Lithium - Others	Clinical history, clinical examination (toxindromes), and/or toxicological analysis
Time from ingestion to ED attendance	Continuous quantitative	Hours	Calculate the “Time of ED attendance” minus “Time of ingestion” from data collection sheet

Figure 4: variables of the study

7.5. DATA COLLECTION

All data will be collected prospectively during 18 months using a data collection sheet elaborated by physicians of HJT's ED with the aim to collect data about patients with acute intoxications (*Annex 6*).

Emergency physicians from the ED of HJT and PHMJ, previously informed about the study and asked for their collaboration, will have to fill this data collection sheet when they attend a patient with acute oral drug overdose who meets the study population criteria. In order to do that correctly, we will teach them how to fill it.

Patients will be informed about the study and will have to sign an informed consent before being included in the study. If the patient is unconscious, informed consent will be required to first-degree relatives.

Then, after an 18 months period, these data collection sheets will be collected and introduced in a database created for this study in order to analyse the information obtained.

8. STATISTICAL ANALYSIS

8.1. UNIVARIANT ANALYSIS

A descriptive analysis of the variables will be performed.

For qualitative variables (correct indication of AC, ED admission, gender and type of drug involved), results will be expressed as frequencies and percentages for each category.

For quantitative variables (age and time from ingestion to ED attendance), results will be expressed as mean and standard deviation (in case of variables with normal distribution) and as median and quartiles (in case of variables without normal distribution).

8.2. BIVARIATE ANALYSIS

For the analysis between the main variable correct indication of activated charcoal and the main variable emergency department in which patient was admitted, which are nominal qualitative variables, it will be applied a Chi-square test (χ^2).

To compare qualitative and quantitative variables, the t test or Mann-Whitney and ANOVA or Kruskal-Wallis tests will be used to compare 2 groups or ≥ 3 groups, respectively.

8.3. MULTIVARIATE ANALYSYS

The analysis of the proportion of cases in which activated charcoal was correctly indicated depending on the emergency department in which patient was admitted will be performed by Logistic Regression Model.

The analysis will be adjusted for covariates statistically significant ($p<0,05$) in order to adjust for potential confounders.

9. ETHICAL CONSIDERATIONS

This study will be conducted according to the ethical principles for medical research established by the World Medical Association (WMA) in the *Declaration of Helsinki of Ethical Principles for Medical Research Involving Human Subjects* (1964). Last revision was in 2013 (33).

As this research is an observational study involving an authorized drug, it will be conducted under the normative framework of these laws:

- *Ley 29/2006, de 26 de julio, de garantías y uso racional de los medicamentos y productos sanitarios.*
- *Real Decreto Legislativo 1/2015, de 24 de julio, por el que se aprueba el texto refundido de la Ley de garantías y uso racional de medicamentos y productos sanitarios. Título III, artículo 58.2.*
- *Orden SAS/3470/2009, de 16 de diciembre, por la que se publican las directrices sobre estudios posautorización de tipo observacional para medicamentos de uso humano.*

This study protocol will be presented to the Clinical Research Ethics Committee (CEIC, "Comitè Ètic d'Investigació Clínica") of HJT and PHMJ before the study begins in order to be evaluated and get its approval. Furthermore, it will be presented to the *Agencia Española de Medicamentos y Productos Sanitarios (AEMPS)* for its classification according to "*Orden SAS/3470/2009".*

Personal and clinical information of participants will be anonymous, codified when collected and only used for the purpose of the research according to *"Ley Orgánica 15/1999, de 13 de Diciembre, de Protección de Datos de Carácter Personal."*

All participants will be personally informed by emergency physicians and an information document about the study will be given to them (*Annex 8.1*). Participants will have to sign voluntarily the informed consent (*Annex 8.2*) before being included in the study. If the patient is unconscious, informed consent will be required to first-degree relatives.

10. STUDY LIMITATIONS

This study is designed as an observational cross-sectional study. Therefore, it can demonstrate association between our main variables but cannot prove causality. To attribute causality we would need a prospective study.

To collect data we will use a data collection sheet that personnel from the ED of HJT and PHMJ will have to fill when they attend a patient with acute oral drug overdose who meets the study population criteria. This may cause an information bias if the data collection sheet is incorrectly filled or due to the Hawthorne effect because doctors will think that they are being evaluated so they may change their decisions. However, we think that using a form is a good way to standardize information and to reduce missing information. So, we will teach them how to fill the data collection sheet and we will train them to do it.

Furthermore, it is difficult to precisely define a toxic dose for each drug. To solve it, we use different sources of information specialized in toxicology and the drug information sheet of the main drugs involved in acute oral drug overdoses in order to define its toxic doses.

Finally, due to our study design it is difficult to control the possible confounding variables. In order to avoid this problem we will analyse the confounding variables in a multivariate analysis to reduce the confusion.

11. WORK PLAN

The research team will carry out the tasks of coordination, interpretation and dissemination of the results. The sequence of activities is detailed below:

- **<u>Stage 0:</u> study design → November 2015 – January 2016.**

  - Bibliographic research and protocol elaboration.

  - Investigator 1.

- **<u>Stage 1:</u> ethical evaluation of the protocol → February 2016.**

  - Clinical Research Ethics Committee of HJT and PHMJ.

  - Presentation to AEMPS for its classification.

- **<u>Stage 2:</u> meeting with emergency physicians to inform about the study → March 2016.**

  - First meeting for task organization and teach how to fill the data collection sheet.

  - Meeting with physicians of the emergency departments of HJT and PHMJ

  - Investigators 1, 2 and 3.

- **<u>Stage 3:</u> patient recruitment and filling data collection sheets →April 2016 – September 2017.**

  - Physicians of the emergency departments of HJT and PHMJ.

- **<u>Stage 4:</u> data treatment and generation of the database → October 2017.**

  - Collection of the data collection sheets of both groups (HJT and PHMJ) and generation of the database with the information obtained.

  - Investigators 1, 2 and 3.

- **<u>Stage 5:</u> statistical analysis → November 2017 – January 2018.**

  - A qualified statistician will process the data.

  - Qualified statistician.

- **<u>Stage 6:</u> interpretation of the results → February – March 2018.**

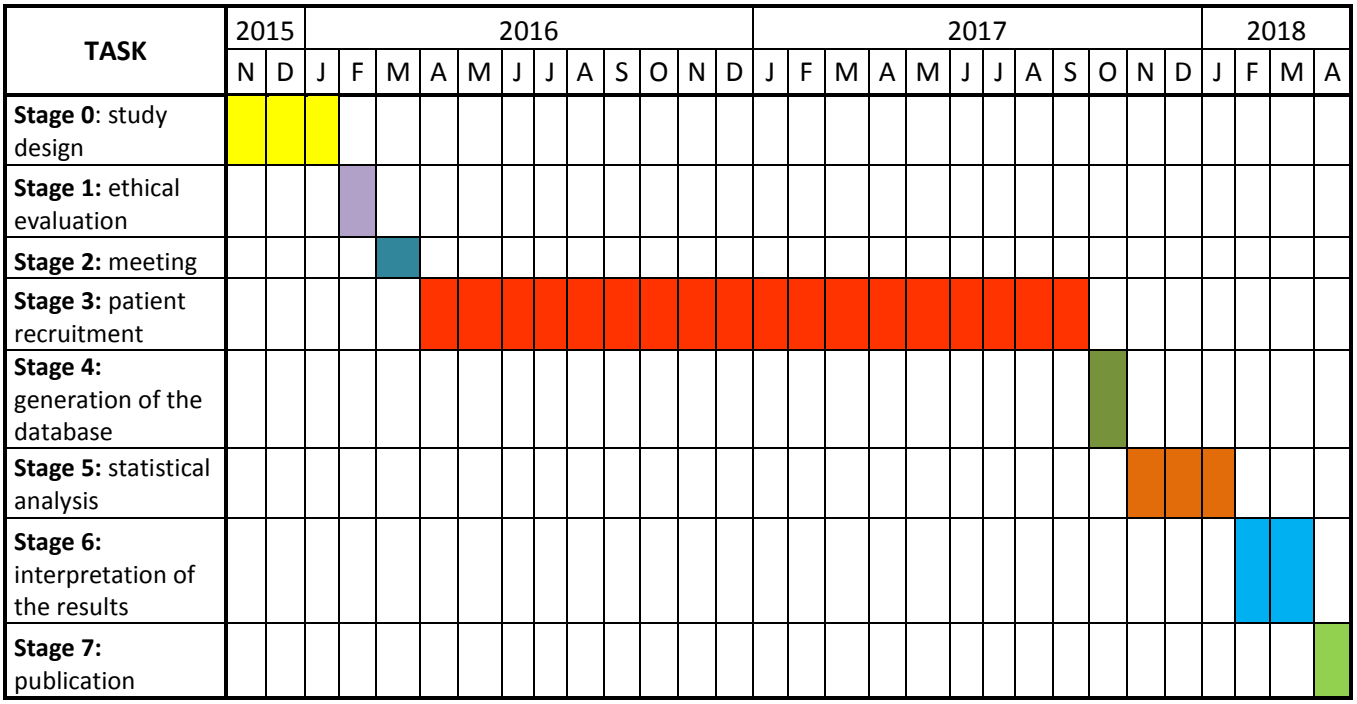
  - The research team will keep in contact and meet to analyse and interpret the results.

  - Investigators 1, 2 and 3.

- **<u>Stage 7:</u> publication of the results → April 2018.**

  - The results will be presented in national conferences. We will also attempt to publish the study in an emergency journal.

  - Investigators 1, 2 and 3



12. BUDGET

EXPENSES	COSTS (€)
Personnel expenses	0 €
Goods and services costs - Qualified statistician: • 30€/h x 4h/day x 2 day/week x 12 weeks	2880 €
National conferences attendance	950 €
Publication expenses	1000 €
TOTAL:	4830 €

Investigators 1, 2 and 3 will not receive any financial compensation for their contribution to the study.

13. CLINICAL AND HEALTHCARE IMPACT

According to current recommendations, AC is used in excess in the management of patients with acute oral drug overdose and this attitude could lead to higher risk of iatrogenic harm.

Furthermore, few physicians have read the current guidelines on the appropriate us of gastrointestinal decontamination, which leads to a high variability of attitudes towards the treatment of these patients (34).

Therefore, if the results of our study show that the implementation of the HJT's intoxication protocol is associated with higher percentage of well indicated use of activated charcoal then, we can highly recommend with facts the implementation of an intoxication protocol in all the emergency departments which do not have one.

In contrast, if our study fails to demonstrate that the implementation of this protocol is associated with higher percentage of correct indication of AC, it will be the first step to make a review of the protocol and to investigate why this protocol has not worked well.

14. BIBLIOGRAPHY

1. Lexicon of alcohol and drug terms. Geneva: World Health Organization (WHO); 1994.

2. Amigó M, Nogué S, Sanjurjo E, Faro J, Ferró I, Miró Ò. Eficacia y seguridad de la descontaminación digestiva en la intoxicación medicamentosa aguda. Med Clin (Barc) [Internet]. 2004 [cited 2015 Nov 18];122(13):487–92. Available from: http://www.sciencedirect.com/science/article/pii/S0025775304742839

3. Burillo-Putze G, Munné P, Dueñas A, Pinillos MA, Naveiro JM, Cobo J, et al. National multicentre study of acute intoxication in emergency departments of Spain. Eur J Emerg Med. 2003;10(2):101–4.

4. Burillo-Putze G, Munné P, Dueñas A, Trujillo MDM, Jiménez A, Adrián MJ, et al. Intoxicaciones agudas : perfil epidemiológico y clínico , y análisis de las técnicas de descontaminación digestiva utilizadas en los servicios de urgencias españoles en el año 2006 – Estudio HISPATOX –. Emergencias. 2008;20:15–26.

5. García MC, Arias Á, Rodríguez C, Morcillo A, Aguirre-Jaime A. Time series analysis of poisonings treated in a hospital emergency department. Emergencias. 2011;23(3):193–9.

6. American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists. Position Paper: Single-Dose Activated Charcoal. Clin Toxicol. 2005;43(2):61–87.

7. Karim A, Ivatts S, Dargan P, Jones A. How feasible is it to conform to the European guidelines on administration of activated charcoal within one hour of an overdose? Emerg Med J [Internet]. 2001 [cited 2015 Nov 25];18(5):390–2. Available from: http://emj.bmj.com/content/18/5/390.long

8. Vernet D, García R, Plana S, Amigó M, Fernández F, Nogué S. Descontaminación digestiva en la intoxicación medicamentosa aguda: implementación de un triaje avanzado con carbón activado. Emergencias. 2014;26(6):431–6.

9. Thompson T, Theobald J, Lu J, Erickson T. The general approach to the poisoned patient. Dis Mon [Internet]. 2014 Nov [cited 2015 Nov 9];60(11):509–24. Available from: http://www.sciencedirect.com/science/article/pii/S0011502914001436

10. Van Hoving DJ, Veale DJH, Müller GF. Clinical Review: Emergency management of acute poisoning. African J Emerg Med [Internet]. 2011 [cited 2015 Nov 10];1(2):69–78. Available from: http://www.afjem.org/article/S2211-419X(11)00042-5/fulltext

11. Albertson T, Owen K, Sutter M, Chan A. Gastrointestinal decontamination in the acutely poisoned patient. Int J Emerg Med [Internet]. 2011 [cited 2015 Nov 13];4(1):65. Available from: http://www.intjem.com/content/4/1/65

12. Boyle J, Bechtel L, Holstege C. Management of the critically poisoned patient. Scand J Trauma Resusc Emerg Med [Internet]. 2009 [cited 2015 Nov 16];17(1):29. Available from: http://www.sjtrem.com/content/17/1/29

13. American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists. Position Statement: Ipecac Syrup. Clin Toxicol [Internet]. 1997 [cited 2015 Nov 18];35(7):699–709. Available from: http://informahealthcare.com/doi/abs/10.3109/15563659709162567

14. Randall G. The role of activated charcoal and gastric emptying in gastrointestinal decontamination: A state-of-the-art review. Ann Emerg Med [Internet]. 2002 Mar [cited 2015 Nov 9];39(3):273–86. Available from: http://www.sciencedirect.com/science/article/pii/S0196064402070658

15. Seger D. Single-dose activated charcoal-backup and reassess. J Toxicol Clin Toxicol [Internet]. 2004 [cited 2015 Nov 6];42(1):101–10. Available from: http://www.tandfonline.com/doi/full/10.1081/CLT-120028754

16. Juurlink D. Activated charcoal for acute overdose: a reappraisal. Br J Clin Pharmacol [Internet]. 2015 [cited 2015 Nov 6];1–6. Available from: http://onlinelibrary.wiley.com/doi/10.1111/bcp.12793/full

17. Mokhlesi B, Leiken J, Murray P, Corbridge T. Adult toxicology in critical care: Part I: General approach to the intoxicated patient. Chest [Internet]. 2003 [cited 2015 Nov 3];123(2):577–92. Available from: http://journal.publications.chestnet.org/article.aspx?articleid=1081295

18. Olson K. Activated Charcoal for Acute Poisoning: One Toxicologist's Journey. J Med Toxicol [Internet]. 2010 [cited 2015 Nov 5];6(2):190–8. Available from: http://link.springer.com/article/10.1007/s13181-010-0046-1/fulltext.html

19. Lloret J, Nogué S, Amigó M. Descontaminación digestiva de tóxicos. Técnicas e indicaciones. In: Morán I, Baldirà J, Marruecos L, Nogué S, editors. Toxicología Clínica. Barcelona: Grupo difusión; 2011. p. 79–91.

20. Cooper GM, Le Couteur DG, Richardson D, Buckley NA. A randomized clinical trial of activated charcoal for the routine management of oral drug overdose. Q J Med [Internet]. 2005 Sep 1 [cited 2015 Nov 6];98(9):655–60. Available from: http://qjmed.oxfordjournals.org/content/98/9/655.long

21. Amigó M, Nogué S, Miró Ò. Carbón activado en 575 casos de intoxicaciones agudas. Seguridad y factores asociados a las reacciones adversas. Med Clin (Barc) [Internet]. 2010 [cited 2015 Dec 5];135(6):243–9. Available from: http://www.sciencedirect.com/science/article/pii/S0025775310004537

22. Hendrickson R, Kusin S. Gastrointestinal decontamination of the poisoned patient. Up to Date [Internet]. 2015 [cited 2015 Dec 3];1. Available from: http://www.uptodate.com/contents/gastrointestinal-decontamination-of-the-poisoned-patient

23. American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists. Position Statement: Single-Dose Activated Charcoal. J Toxicol Clin Toxicol [Internet]. 1997 [cited 2015 Nov 16];35(7):721–41. Available from: http://www.tandfonline.com/doi/full/10.3109/15563659709162569

24. Amigó M, Faro J, Estruch D, Cascán M, Gallego S, Gómez E, et al. Descontaminación digestiva en pacientes con intoxicación medicamentosa aguda. Validación de un algoritmo para la toma de decisiones sobre la indicación y el método prioritario. Emergencias. 2003;15:18–26.

25. Amigó M, Nogué S. Descontaminación digestiva en la intoxicación medicamentosa aguda. JANO. 2005;77–80.

26. Nogué S, Puiguriguer J, Amigó M. Indicadores de calidad para la asistencia urgente de pacientes con intoxicaciones agudas (Calitox-2006). Barcelona: Asociación Española de Toxicología, Sección de Toxicología Clínica.; 2006.

27. American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists. Position Statement and Practice Guidelines on the Use of Multi-Dose Activated Charcoal in the Treatment of Acute Poisoning. J Toxicol Clin Toxicol. 1999;37(6):731–51.

28. Lo Vecchio F, Shriki J, Innes K, Bermudez J. The feasibility of administration of activated charcoal with respect to current practice guidelines in emergency department patients. J Med Toxicol [Internet]. 2007 Sep [cited 2015 Nov 6];3(3):100–2. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3550070/pdf/13181_2009_Article_BF03160918.pdf

29. Henry J, Hoffman J. Continuing controversy on gut decontamination. Clin Toxicol [Internet]. 1998 [cited 2015 Nov 20];36(7):753–5. Available from: http://informahealthcare.com/doi/pdf/10.3109/15563659809162631

30. Aguilar R, Gispert À, Limón G, Ramió C, Tarrés M. Protocol d'intoxicacions. Servei d'Urgències i Farmàcia hospitalària. Girona: Hospital Universitari Doctor Josep Trueta; 2013.

31. Calculadora de grandària mostral GRANMO [Internet]. Barcelona: Institut Municipal d'Investigació Mèdica; 2012 [cited 2015 Dec 4]. Available from: http://www.imim.cat/ofertadeserveis/software-public/granmo/

32. Echarte J, Aguirre A, Clemente C, Iglesias M, León N, Labordeta V, et al. Calidad de los registros en las intoxicaciones voluntarias por fármacos en un Servicio de Urgencias. Rev Toxicol. 2011;28(2):166–9.

33. WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects [Internet]. World Medical Association. 2013 [cited 2015 Dec 28]. Available from: http://www.wma.net/en/30publications/10policies/b3/

34. Wood D, Greene S, Jones A, Dargan P. Gut decontamination of acutely poisoned patients: what do doctors really know about it? Emerg Med J. 2007;24(11):774–5.

15. ANNEXES

ANNEX 1: TOXINDROMES

SÍNDROME	PARÀMETRES VITALS	MANIFESTACIONS CLÍNIQUES	PUPIL·LES	Agents responsables	Antídot
Colinèrgica	Bradicàrdia Taquipnea Hipotèrmia	Diaforesi Diarrea Sialorrea Broncospasme Broncorrea	Miosi	Organofosforats Carbamats Pilocarpina *Amanita muscaria*	Atropina Oximes
Anticolinèrgica	Hipertensió Taquicàrdia Taquipnea Hipertèrmia	Confusió Retenció urinària Pell seca Disminució del peristaltisme Deliri Rubor facial	Midriasi	ADT Antihistamínics Antiparkinsonians Antipsicòtics Atropina Amantadina Alcaloides Belladona Bromur d'ipratropi Escopolamina	Fisostigmina
Narcòtica o opiàcia	Hipotensió Xoc Bradicàrdia Bradipnea Apnea Hipotèrmia	Coma profund	Miosi	Opiacis Propoxifè Dextrometorfan	Naloxona
Hipnòtica-sedant	Hipotensió Bradicàrdia	Coma superficial	Miosi	Barbitúrics Benzodiazepines Etanol Antiepilèptics	Flumacenil (si BDZ)
Al·lucinògena	Hipertensió Taquicàrdia Taquipnea	Augment peristaltisme Diaforesi Desorientació Al·lucinacions (visuals) Atacs de pànic	Midriasi	LSD Mescalina Psilocina/psilocibina Alcaloides anticolinèrgics Amfetamines Cannabinoids Cocaïna	
Serotoninèrgica	Hipertensió Taquicàrdia Hipertèrmia	Diaforesi Augment del peristaltisme Hiperreflèxia Clonus Tremolor Agitació	Midriasi	ISRS IMAO ADT Triptòfan Valproat Liti Antiemètics LSD Cocaïna	Ciproheptadina Clorpromazina
Simpaticomimètica	Hipertensió Taquicàrdia (o bradicàrdia reflexa i agonista α pur) Taquipnea Hipertèrmia	Diaforesi Piloerecció Disminució del peristaltisme Hiperreflèxia Agitació psicomotorora	Midriasi	Cocaïna Amfetamines Agonistes α o β adrenèrgics (efedrina, teofil·lina...) IMAO	

Figure from: Aguilar R, Gispert À, Limón G, Ramió C, Tarrés M. Protocol d'intoxicacions. Servei d'Urgències i Farmàcia hospitalària. Girona: Hospital Universitari Doctor Josep Trueta; 2013.

ANNEX 2: SUBSTANCES ADSORBED BY ACTIVATED CHARCOAL

TABLA I

SUSTANCIAS ADSORBIBLES POR EL CARBÓN ACTIVADO

Acetona	Doxepina	Nicotina
Ácido mefenámico	Estricnina	Nortriptilina
Aconitina	Fenciclidina	Opiáceos y derivados
Aflatoxina	Fenilbutazona	Organoclorados
Amanitinas	Fenilpropanolamina	Organofosforados
Anfetaminas	Fenitoína	Paracetamol
Amiodarona	Fenobarbital	Paraquat
Amitriptilina	Flecainida	Pentobarbital
Amlodipino	Fluoxetina	Piroxicam
Anilinas	Furosemida	Porfirinas
Aspirina	Glipizida	Propanteline
Astemizol	Glutetimida	Propoxifeno
Atropina	Hexaclorofeno	Queroseno
Barbital	Hidralazina	Quinidina
Benceno	Ibuprofeno	Salicilamida
Benzodiazepinas	Imipramina	Salicilato sódico
Bilirrubina	Ipecacuana	Secobarbital
Bupropión (*)	Isoniazida	Sulfametoxazol
Carbamazepina	Isopropanol	Sulfonilureas
Cianuro (†)	L-tiroxina	Teofilina
Ciclosporina	Malation	Tetraciclinas
Dapsona	Meprobamato	Tolbutamida
Dietilcarbamazina	Metilsalicilato	Toxina botulínica
Difenhidramina	Metotrexate	Valproato sódico
Digitoxina	Mitomicina	Vancomicina (*)
Digoxina y alcaloides derivados	Moclobemida	Verapamilo (*)
Diltiazem (*)	N-acetilcisteína	Yohimbina
	Nadolol	

(*) Efecto de adsorción controvertido.

(†) Es poco adsorbible por el carbón activado: 1 gramo de carbón activado puede adsorber unos 35 mg de cianuro. Pero dado que dosis tan bajas como 200 mg de cianuro pueden ser letales, se puede indicar junto a otras medidas complementarias: aspirado y lavado gástrico, antídotos, medidas de apoyo, etc.

Figure from: Lloret J, Nogué S, Amigó M. Descontaminación digestiva de tóxicos. Técnicas e indicaciones. In: Morán I, Baldirà J, Marruecos L, Nogué S, editors. Toxicología Clínica. Barcelona: Grupo difusión; 2011. p. 79–91.

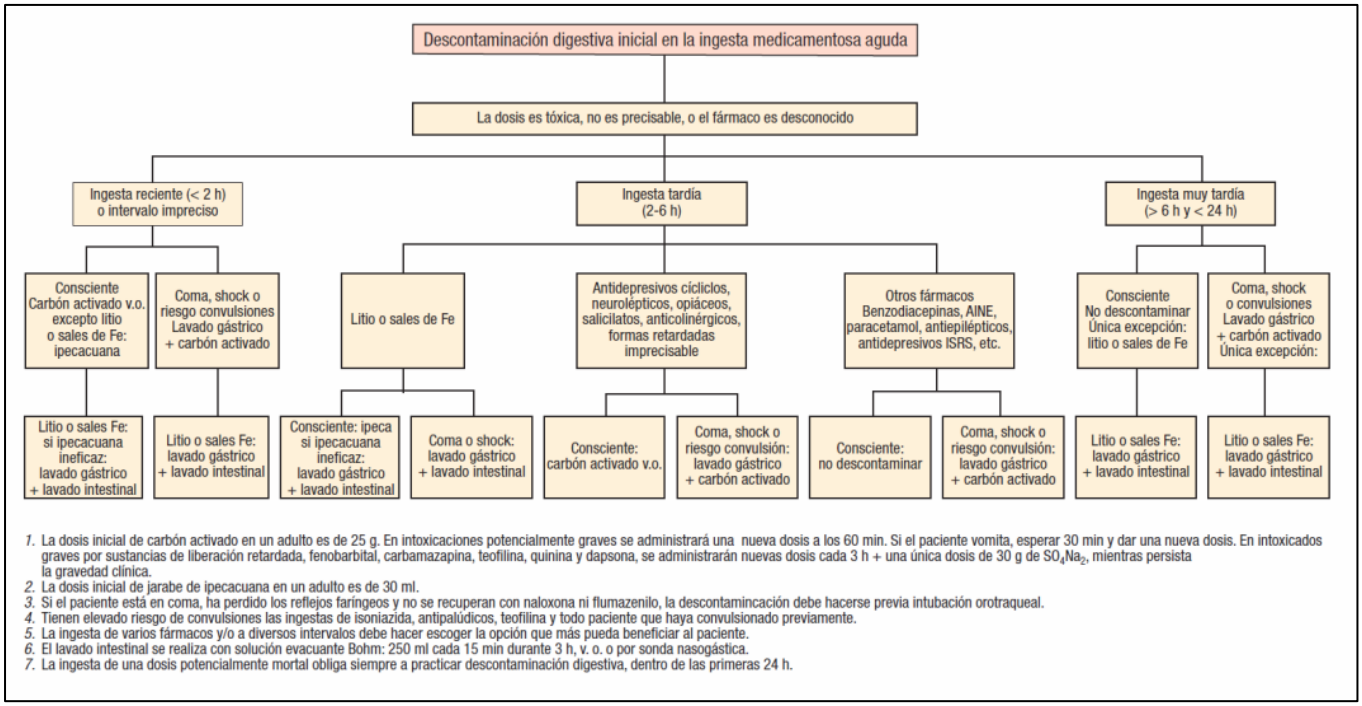
ANNEX 3: SUBSTANCES NOT ADSORBED BY ACTIVATED CHARCOAL

TABLA II
SUSTANCIAS QUE NO SON ADSORBIBLES POR EL CARBÓN ACTIVADO

Ácidos	Cesio	Metales pesados (Ni, Co, Zn,
Álcalis	Etanol, metanol y otros	Pb, Hg)
Arsénico	alcoholes	Petróleo y algunos derivados
Bromo	Etilenglicol y otros glicoles	(gasolina)
Cáusticos	Hierro	Potasio
	Litio	Yodo

Figure from: Lloret J, Nogué S, Amigó M. Descontaminación digestiva de tóxicos. Técnicas e indicaciones. In: Morán I, Baldirà J, Marruecos L, Nogué S, editors. Toxicología Clínica. Barcelona: Grupo difusión; 2011. p. 79–91.

ANNEX 4: M. AMIGÓ AND S. NOGUÉ ALGORITHM FOR GASTROINTESTINAL DECONTAMINATION



1. La dosis inicial de carbón activado en un adulto es de 25 g. En intoxicaciones potencialmente graves se administrará una nueva dosis a los 60 min. Si el paciente vomita, esperar 30 min y dar una nueva dosis. En intoxicados graves por sustancias de liberación retardada, fenobarbital, carbamazapina, teofilina, quinina y dapsona, se administrarán nuevas dosis cada 3 h + una única dosis de 30 g de SO_4Na_2, mientras persista la gravedad clínica.
2. La dosis inicial de jarabe de ipecacuana en un adulto es de 30 ml.
3. Si el paciente está en coma, ha perdido los reflejos faríngeos y no se recuperan con naloxona ni flumazenilo, la descontamincación debe hacerse previa intubación orotraqueal.
4. Tienen elevado riesgo de convulsiones las ingestas de isoniazida, antipalúdicos, teofilina y todo paciente que haya convulsionado previamente.
5. La ingesta de varios fármacos y/o a diversos intervalos debe hacer escoger la opción que más pueda beneficiar al paciente.
6. El lavado intestinal se realiza con solución evacuante Bohm: 250 ml cada 15 min durante 3 h, v. o. o por sonda nasogástica.
7. La ingesta de una dosis potencialmente mortal obliga siempre a practicar descontaminación digestiva, dentro de las primeras 24 h.

Figure from: Amigó M, Nogué S. Descontaminación digestiva en la intoxicación medicamentosa aguda. JANO. 2005;77–80.

ANNEX 5: TOXICOLOGICAL ANALYSIS

Valors de referència fàrmacs i tòxics. Laboratori Hospital Trueta.

NOM	UNITAT	VALORS DE REFERÈNCIA			MOSTRA	DEMORA
Acetaminofen (paracetamol)	mg/L	Terapèutic: 10-25 Tòxic: 4h post-ingesta >300 12h post-ingesta >50			sèrum	2 hores (URG)
Àcid acetil salicílic	mg/L	Terapèutic: analgèsic 20-100 antiinflamatòri 100-250 Tòxic >300			sèrum	2 hores (URG)
Barbiturats	mg/dL	vida mitja curta>3mg/dL Vida mitja llarga>9mg/dL			sèrum	2 hores (URG)
Benzodiacepines	ng/mL	Benzodiacepina	Nivell terapèutic	Nivell tòxic	sèrum	2 hores (URG)
		Alprazolam	2-22			
		Clordiazepòxid	500-1600	>3000		
		Clorazepam	7-30	>70		
		Diacepam	30-1500	>3000		
		Fluorazepam	30-1100	>500		
		Lorazepam	20-240	>300		
		Oxazepam	100-1500	>3000		
		Triazolam	0'1-8			
Carbamazepina	mg/L	Terapèutic: 4-11 Tòxic:>12			sèrum	2 hores (URG)
Ciclosporina	ng/mL	Terapèutic: 360-1200 ng/mL Control transplantament:100-875ng/mL			sang total (heparina-Li)	2 hores (URG)
Cooximetria-carboxihemoglobina	%	0-0'8			sang total (heparina-Li)	1 hora (URG)
Cooximetria-metahemoblobina	%	0'2-0'6			sang total (heparina-Li)	1 hora (URG)
Cooximetria-oxihemoglobina	%	94-99			sang total (heparina-Li)	1 hora (URG)
Digoxina	mcg/L	Terapèutic: 0'8-2 Tòxic>2			sèrum	2 hores (URG)
Fenitoïna	mg/L	Terapèutic: 10-40 Tòxic>40			sèrum	2 hores (URG)
Fenobarbital	mg/L	Terapèutic: 10-40 Tòxic>40			sèrum	2 hores (URG)
Liti	mEq/L	Terapèutic: 0.5-1.5 mEq/L			sèrum	2 hores (URG)
Teofilina	mcg/mL	Terapèutic: 8-20 Tòxic>20			sèrum	2 hores (URG)
Valproat	mg/L	Terapèutic: 50-100			sèrum	2 hores (URG)
Amfetamina	qualitatiu	abscència			orina	2 hores (URG)
Barbiturats	qualitatiu	abscència			orina	2 hores (URG)
Benzodiacepines	qualitatiu	abscència			orina	2 hores (URG)
Cannabinoids	qualitatiu	abscència			orina	2 hores (URG)
Cocaïna	qualitatiu	abscència			orina	2 hores (URG)
Fenciclidina	qualitatiu	abscència			orina	2 hores (URG)
Metadona	qualitatiu	abscència			orina	2 hores (URG)
Metamfetamina	qualitatiu	abscència			orina	2 hores (URG)
MDMA	qualitatiu	abscència			orina	2 hores (URG)
Morfina	qualitatiu	abscència			orina	2 hores (URG)

Figure from: Aguilar R, Gispert À, Limón G, Ramió C, Tarrés M. Protocol d'intoxicacions. Servei d'Urgències i Farmàcia hospitalària. Girona: Hospital Universitari Doctor Josep Trueta; 2013.

ANNEX 6: DATA COLLECTION SHEET (to fill by emergency physicians)

Hospital Universitari de Girona Doctor Josep Trueta — IAS Institut d'Assistència Sanitària

Hospital Universitari Josep Trueta ☐

Parc Hospitalari Martí i Julià ☐

CODITOX: intoxicacions via oral.

HORA ARRIBADA URGÈNCIES __:__
PREAVÍS SEM: SI ☐ NO ☐ HORA:__:__
ACTIVACIÓ CODI SEM: SI ☐ NO ☐

CONSTANTS ARRIBADA URGÈNCIES:
GLS: __ (O: __/ V: __/ M:__)
TA: __/__ FC:__ FR:__ SatO2: __%

Valoració a triatge

Edat (anys): _____

Sexe: Home ☐ Dona ☐ Història de crisis comicials prèvies? si ☐ no ☐

Hora ingesta: __:__

Tipus ingesta: voluntària ☐ accidental ☐ altres ☐ _____

Tipus de tòxic: benzodiazepines ☐ antidepressiu cíclics ☐ ISRS ☐ AAS ☐ AINEs ☐ paracetamol ☐ neurolèptic ☐ b-bloquejant ☐ digoxina ☐ opiacis ☐ liti ☐ Carbamazepina ☐ Altres ☐ Desconegut ☐

Actuació pre-hospitalària:

CONSTANTS PRE-HOSPITALÀRIES:
GLS: __ (O: __/ V: __/ M:__)
TA: __/__ FC:__ FR:__ SatO2: __%

.Via aèria: permeable ☐ Guedel ☐ IOT ☐ Fastrach ☐ crico. ☐
.Ventilació mecànica: si ☐ no ☐
.Vies: si ☐ no ☐: perifèriques ☐ número __ calibre __ // centrals ☐ // intraòssia ☐
.Carbó actiu: si ☐ hora: __:__ no ☐
.Antídot: flumazenil ☐ naloxona ☐ altres ☐: quin_____
.Sonda nasogàstrica: si ☐ no ☐
.Seroteràpia: si ☐ _____ ml no ☐

Valoració hospitalària

Nom del tòxic o tòxics: _____

Dosi ingerida via oral: _____ Dosi tòxica: si ☐ no ☐ desconeguda ☐

Símptomes: _____

Actuació hospitalària:

.Via aèria: permeable ☐ Guedel ☐ IOT ☐ Fastrach ☐ crico. ☐
.Ventilació mecànica: si ☐ no ☐
.Vies: si ☐ no ☐: perifèriques ☐ número __ calibre __ // centrals ☐ // intraòssia ☐
.Seroteràpia: si ☐ no ☐ _____ ml
.Carbó actiu: si ☐ hora: __:__ no ☐ Dosis repetides: si ☐ no ☐
.Antídot: flumazenil ☐ naloxona ☐ altres ☐: quin_____
.Sonda naso-gàstrica: si ☐ no ☐
.Rentat gàstric: si ☐ no ☐

Proves compl.

Analítica: si ☐ no ☐ / Gasometria arterial: si ☐ no ☐
Proves creuades: si ☐ no ☐
Tòxics en orina: si ☐ no ☐
Rx tòrax: si ☐ no ☐ / Rx abdomen: si ☐ no ☐ / Altres ☐: _____

Destinació

Observació urgències ☐
UCI ☐
Quiròfan ☐
Reanimació ☐
Planta ☐
Alta ☐
Èxitus ☐

Hora sortida urgències: __:__

CONSTANTS SORTIDA URGÈNCIES:
GLS: __ (O: __/ V: __/ M:__)
TA: __/__ FC:__ FR:__ SatO2: __%

Observacions:

Nº col·legiat metge responsable: _____

ANNEX 7: TOXIC DOSES OF MAIN DRUGS INVOLVED IN ACUTE ORAL DRUG OVERDOSES

Tipus de fàrmac	Principi actiu	Dosi màxima adult	Dosi tòxica oral adult	Indicació carbó actiu
Benzodiazepines	Midazolam	10 mg/dia	La dosi tòxica és molt variable i depèn de cada tipus de BDZ. Es considera **dosi tòxica més de 10 vegades la dosi terapèutica.**	≤ 2 hores post-ingesta, excepte els comprimits retard en que es pot administrar si ≤ 6 hores post-ingesta.
	zolpidem	10 mg/dia		
	alprazolam	6 mg/dia		
	clorazepat dipotassic	30 mg/dia		
	lormetacepam	3 mg/dia		
	clonacepam	20 mg/dia		
	lorazepam	20 mg/dia		
	loprazolam	2 mg/dia		
	bromazepan	36 mg/dia		
	diazepam	40 mg / dia		
	flunitrazepam	2 mg /dia		
Antidepressius Tricíclics	amitriptilina	300 mg/dia	< 500 mg molt baixa tox. 500 a 1000 mg mitjana tox. 1000 a 2500 mg alta tox. >2500 mg dosi potencialment mortal.	≤ 6 hores post-ingesta.
	clomipramina	250 mg/dia		
Antidepressius Heterocíclics	Trazodona	600 mg/dia		
	Bupropi	300 mg/dia	≥ 9 gr, ≥ 23 gr dosi potencialment mortal	
ISRS	Citalopram	40 mg/dia	≥ 600 mg	≤ 2 hores post-ingesta.
	Escitalopram	20 mg/dia	≥ 600 mg	
	Fluoxetina	60 mg/dia	≥ 600 mg	
	Paroxetina	60 mg/dia	≥ 400 mg	
	Sertralina	200 mg/dia	≥ 1000 mg	
	Venlafaxina	375 mg/dia	≥ 1000 mg	
Paracetamol	Paracetamol	4 gr/dia	≥ 125 mg/Kg o 100 mg/kg si factors de risc (alcoholisme, caquèxia, malnutrició, hepatopatia, inducció enzimàtica citocrom p450) Dosi potencialment mortal si ≥ 20 gr	≤ 2 hores post-ingesta.

Salicilats	Àcid acetil salicílic	4 gr/dia	≥ 150 mg/Kg o concentració plasmàtica ≥ 30 mg/dL. Dosi potencialment mortal si ≥ 500 mg/Kg	≤ 6 hores post-ingesta.
AINEs	Ibuprofè	2400 mg/dia	≥ 400 mg/kg	≤ 2 hores post-ingesta.
	Dexketoprofè	75 mg/dia		
	Naproxè	1250 mg/dia		
Neurolèptics Típics	Haloperidol	6 mg/dia	dosi potencialment mortal a partir de 15-150 mg/kg segons el compost	≤ 6 hores post-ingesta.
	Clorpromazina	300 mg/dia		
	Clotiapina	360 mg/dia		
Neurolèptics Atípics	Sulpirida	2400 mg/dia		
	Risperidona	10 mg/dia	≥ 270 mg	
	Ziprasidona	80 mg/dia	≥ 4 gr	
	Quetiapina	800 mg/dia	≥ 10 gr	
	Olanzapina	20 mg/dia	≥ 600 mg	
Digital	Digoxina	1,5 mg/dia	≥ 0,05 mg/kg. Dosi potencialment mortal ≥ 10 mg	≤ 6 hores post-ingesta
Morfics d'administració oral	Tramadol	400 mg/dia	No existeix una clara dosi tòxica, depèn de l'individu i la clínica. *es considera ingesta tòxica si apareix miosi, depressió respiratòria i/o disminució nivell de consciència	≤ 6 hores post-ingesta.
	Codeina	240 mg/dia		
	Fentanil	6400 mcg/dia		
	Metadona	120 mg/dia		
	Morfina sulfato	120 mg/dia		
Betabloquejants	Atenolol	100 mg /dia	≥ 3 vegades la dosi terapèutica	≤ 2 hores post-ingesta.
	Bisoprolol	20 mg/dia		
Liti	Liti	1800 mg/dia	concentració plasmàtica > 1,2 mEq/L	No indicat
Carbamazepina	Carbamazepina	1600 mg/dia	Concentració plasmàtica ≥ 12 µg/ mL	≤ 2 hores post-ingesta.
Teofil·lina	Teofil·lina	20mg/kg/dia	Concentració plasmàtica ≥ 20 µg/mL, potencialment mortal si ≥ 100 µg/ml	≤ 2 post ingesta o ≤ 6 hores post-ingesta si comprimits retard.
Barbitúric	Fenobarbital	400 mg/dia	≥ 5 gr o concentració plasmàtica ≥ 40 µg/ml	≤ 2 hores post-ingesta

The drugs included in this table are the vast majority of drugs involved in acute oral drug overdoses. However, if we register some acute oral drug overdose in the data collection sheets caused by other drug not included in this table, we will consult information sources specialized in toxicology and, if it is necessary, we will contact to "Servicio de Información Toxicológica" from the "Instituto Nacional de Toxicología y Ciencias Forenses" in order to determine the toxic dose of the specific drug involved.

Information sources used for determining toxic doses:

- *Fundación Española de Toxicología clínica*: www.fetoc.es/toxicologianet/pages/x/search.htm

- *Agencia Española de Medicamentos y Productos Sanitarios:* www.aemps.gob.es/cima

- *Toxiconet*: www.murciasalud.es/toxiconet

- *Medscape*: http://emedicine.medscape.com

- www.vademecum.es

- Dueñas-Laita A. iTox urgencias intoxicación. Valladolid: Farma SL; 2010.

- Aguilar R, Gispert À, Limón G, Ramió C, Tarrés M. Protocol d'intoxicacions. Servei d'Urgències i Farmàcia hospitalària. Girona: Hospital Universitari Doctor Josep Trueta; 2013.

ANNEX 8: INFORMATION DOCUMENT AND INFORMED CONSENT

8.1. Information document for the study

FULL D'INFORMACIÓ PEL PARTICIPANT

INVESTIGADORS PRINCIPALS: Àngels Gispert, Laia Guerrero, Ignasi Viñas.

CODI DEL PROJECTE: _____

1) **Generalitats del projecte:** el present estudi serà dut a terme pels serveis d'Urgències de l'Hospital Universitari Doctor Josep Trueta i del Parc Hospitalari Martí i Julià, en un període de temps aproximat de dos anys. El projecte de recerca ha estat valorat i aprovat pel Comitè Ètic d'Investigació Clínica dels dos hospitals. Els participants en l'estudi col·laboraran en la recollida de dades aportant informació personal i mèdica.

2) **Objectius i finalitats de l'estudi:** amb aquest estudi es pretén determinar si la implementació d'un protocol d'intoxicacions al servei d'Urgències de l'Hospital Universitari Doctor Josep Trueta s'associa amb un percentatge més alt d'indicacions correctes de carbó activat en el tractament de pacients amb intoxicacions agudes per fàrmacs via oral.

3) **Participació:** la seva participació en l'estudi és totalment voluntària. El participant és lliure d'abandonar l'estudi si així ho desitja en qualsevol moment, sense necessitat de justificacions i sense que aquest fet afecti la seva assistència sanitària. La participació en l'estudi és totalment gratuïta i no s'obtindrà cap compensació econòmica per la participació.

4) **Confidencialitat i protecció de dades**: S'adoptaran les mesures per garantir la confidencialitat de les seves dades en compliment de la *Llei Orgànica* 15/1999 i les dades recollides seran gestionades de forma anònima i només utilitzades amb fins d'investigació.

5) **Tasca del participant en l'estudi:** el participant haurà de cedir informació personal i mèdica sobre l'episodi d'intoxicació aguda que ha patit, per tal que el metge d'urgències que l'ha atès pugui emplenar el full de recollida de dades amb la informació facilitada.

6) **Resultats i beneficis de la investigació:** el participant està en el seu dret de ser informat dels resultats de la investigació. Els beneficis mèdics derivats de l'estudi seran adequadament utilitzats per millorar l'atenció als pacients amb intoxicacions agudes als serveis d'Urgències i serviran de base per futures investigacions en aquest àmbit.

Gràcies per la seva participació.

8.2. Informed consent

CONSENTIMENT INFORMAT

Declaració del participant:

Jo, _____

- He llegit la fulla informativa sobre l'estudi que se m'ha entregat.
- He pogut fer totes les preguntes necessàries respecte l'estudi.
- He rebut suficient informació sobre l'estudi.
- He estat informat de les implicacions i finalitats de l'estudi.
- Entenc que la meva participació és voluntària.
- Entenc que es respectarà la confidencialitat de les meves dades.
- Entenc que puc revocar el meu consentiment de participació a l'estudi, sense haver de donar justificacions i sense afectar la meva assistència sanitària.

➢ Accepto que els investigadors principals de l'estudi puguin contactar amb mi si en un futur es considera oportú?

Sí ☐ No ☐

En cas afirmatiu, telèfon o correu electrònic de contacte: _____

➢ Lliurement, dono la meva conformitat per participar en l'estudi facilitant informació personal i mèdica?

Sí ☐ No ☐

Signatura del participant,

Data: __ / __ / __