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The performance of COBRA, a decision rule to predict the need for intensive care interventions in intentional drug overdose

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Background **COBRA was developed as a decision rule to predict which patients visiting the emergency department (ED) following intentional drug overdose will not require intensive care unit (ICU) interventions. COBRA uses parameters from five vital systems (cardiac conduction, oxygenation, blood pressure, respiration, and awareness) that are readily available in the ED. COBRA recommends against ICU admission when all these parameters are normal.**

Objective **The primary aim of this study was to determine the negative predictive value (NPV) of COBRA in predicting ICU interventions. Secondary outcomes were the sensitivity, specificity and positive predictive value (PPV) and the observation time required for a reliable prediction.**

Design **Observational cohort study.**

Settings and participants **Patients with a reported intentional overdose with drugs having potential acute effects on neurological, circulatory or ventilatory function were included, and data necessary to complete the decision rule was collected. The attending physician in the ED made the actual admission decision, on the basis of clinical judgement. COBRA was measured 0, 3 and 6 h after arrival at the ED.**

Outcome measures **Need for ICU interventions (treatment of convulsion; defibrillation; mechanical or noninvasive ventilation; intravenous administration of vasopressive agents, antiarrhythmics, atropine, calcium, magnesium or sedation; continuous hemofiltration or administration of antagonist/antidote and fluid resuscitation).**

Main results **Of 230 new cases (144 unique patients), 59 were immediately referred to the psychiatric services and/or sent home by the attending physician, 27 went to a regular ward, and 144 were admitted to the ICU. Of these 144 cases, 40 required one or more ICU interventions. By the time the first parameters were collected, the NPV of COBRA was 95.6%. After 3 h of observation, NPV was 100%, while sensitivity, specificity and PPV were 100, 61.1 and 35.1%, respectively. None of these values improved by prolonging the observation time to 6 h.**

Conclusion **In patients with a reported intentional overdose with drugs having potential acute effects on neurological, circulatory or ventilatory function, the COBRA decision rule showed good performances in predicting the need for intensive care interventions, with a NPV of 100% after 3 h of observation.** ***European Journal of Emergency Medicine*** **29: 126–133**

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Keywords: clinical decision-making, drug overdose, emergency medical services, intensive care units

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Introduction

Drug overdose is encountered in emergency departments (ED) all over the world [1–6]. The proportion of these patients that is admitted to an ICU varies considerably (3.7–40%) [7–9]. One of the contributing factors for this variability may be the lack of admission guidelines.

According to the current Dutch guideline, patients without symptoms in whom intoxication is suspected should remain under close monitoring for a period of 6 h [10]. In a more recent consensus document, experts proposed ICU admission for the first 6 h for patients with suspected exposure to drugs that can induce organ failure (neurological, cardiovascular and/or respiratory) with few or no symptoms [11]. In many hospitals, 6 h of observation is too long for the ED, almost automatically resulting in an ICU admission.

The present study focused on patients who deliberately took an overdose of prescription drugs. There were three

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reasons for this focus. First, these patients form the largest subset of poisoning patients. In a previous study, 76% of cases of a drug overdose in the ICU records were considered intentional [12]. Second, a large proportion of patients with intentional drug overdose require no interventions (73% in our previous study) [12]. Third, patients with intentional drug overdose have a psychiatric emergency on top of their suspected poisoning, rendering early medical clearance more urgent. The large numbers of asymptomatic patients admitted for observation after suspected poisoning form a burden for acute care systems. Both patients and hospital organisations might benefit from safe discharge criteria applicable before the 6-h mark, particularly for patients with intentional drug overdose.

A study by Hollander *et al.* suggested that patients could be 'safe for discharge' within 2 to 4 h of presentation if the ingested substance was neither a long-acting drug nor had delayed clinical symptoms [13]. They concluded that future studies should develop clinical criteria that can reliably identify the subset of patients who may be eligible for early medical clearance from the ED. The central hypothesis of the present paper is that, in patients with intentional drug overdose, the absence of clinical symptoms may be a reliable predictor of a benign outcome, irrespective of type or dosage used.

Previously, a clinical decision rule was developed to predict which patients visiting the ED with intentional drug overdose will not require ICU interventions [12]. The rule was based on retrospective data of patients admitted to the ICU with an intentional drug overdose with potential acute effects on neurological, circulatory or ventilatory function. It used parameters from six vital systems (cardiac conduction, oxygenation, blood pressure, respiration and awareness and airway) that were readily available in the ED. This rule recommended against ICU admission when all these parameters were normal. For this study, the prediction rule was adjusted; reducing the number of parameters to five, and this new decision rule was given the acronym COBRA (Table 1).

The primary aim of the present study was to determine the negative predictive value (NPV) of COBRA in predicting ICU interventions. Secondary outcomes were the sensitivity, specificity and positive predictive value (PPV) of COBRA, and the observation time will be required for a reliable prediction.

Methods

Study design

A single-centre cohort study was carried out at the 23-room ED and 12-bed ICU of Deventer Hospital, the Netherlands. Though patients were included prospectively, the decision rule was applied afterwards, resulting in a retrospective study design.

Patient and public involvement statement

This study was conducted in accordance with the World Medical Association Declaration of Helsinki. The Medical Ethics Committee of Isala Clinics, Netherlands, concluded that the rules laid down in the Medical Research Involving Human Subjects Act did not apply to this research proposal. Patients were not involved in the design and conduct of this research.

Study population

All ED patients with a reported intentional overdose with drugs having potential acute effects on neurological, circulatory or ventilatory function were included. The list of eligible drug families included benzodiazepines, barbiturates, antidepressants, antipsychotics, opioids, antihypertensives, neurostimulants, antiepileptics, antihistamines, aminoquinolines, antiarrythmics and lithium. The population was similar to the population in which the decision rule was designed [12]. When multiple ED presentations occurred, individual patients could be included more than once.

Patient history was provided by the patient, accompanying persons, and/or paramedics. A drug overdose was considered 'intentional' if the reported ingestion was a deliberate action, with the intention of self-harm or suicide or a desperate act to achieve mental rest, accepting the risk of self-harm. This was for the ED physician to decide.

Not included in the study were exposures to pesticides, insecticides, corrosive agents or other chemicals not being medication; cases of unintentional drug overdose and overdose with recreational drugs only, such as ethanol (because these rarely present asymptomatically); and cases of intentional drug overdose exclusively with drugs not having potentially acute effects on neurologic, cardiovascular or ventilatory function, for example, paracetamol as a single exposure (because the severity of these exposures cannot be evaluated by measuring vital signs).

The study excluded patients aged 15 years and younger (transferred to a paediatric ICU) and patients who were transferred from other hospitals. Coingestion of paracetamol or ethanol with eligible medication was not a reason for exclusion.

Study procedures

Patients were treated in accordance with the Dutch guidelines for the initial treatment of intoxicated patients [10], including paracetamol levels in serum. All parameters required to complete the decision rule, including Glasgow Coma Scale (GCS) and respiratory rate, were routine tests, recorded in the medical records by ED nursing or medical staff. Agitation was scored if it was mentioned in the records. ECG was recorded on admission and automated conduction times were verified manually

Table 1. COBRA: Decision rule for patients with intentional overdose of drugs having potential acute effects on neurological, circulatory or ventilatory function

	Patient may require intervention if one or more of these criteria are positive		
Cardiac conduction	QRS-interval prolonged[a]	or	QTc-interval prolonged[b]
Oxygenation	SpO_2 <90 %	or	Arterial PO_2 <8.0 kPa
Blood pressure	SBP <90 mmHg	or	SBP >200 mmHg
Respiratory rate	RF <8/min	or	RF >30/min
Awareness	GCS <14	or	Agitation

GCS, Glasgow coma scale; PO_2, arterial partial pressure of oxygen; SBP, systolic blood pressure; SpO_2, peripheral capillary oxygen saturation; RF, respiratory frequency.
[a]Prolonged QRS-interval is defined as >0.12 s.
[b]Prolonged QTc is defined as ≥450 ms in men and ≥460 ms in women.

(QT-duration by the tangent method). Pulse oximetry and blood pressure monitoring were standard.

The intensivist decided about ICU admission, which was considered indicated if a patient was already receiving ICU interventions (Table 2), or if such an intervention was anticipated, on the basis of pharmacological considerations. Patients considered stable for discharge were sent home, or to a mental healthcare facility, at the discretion of the ED physician. When patients were not admitted to a hospital ward, it was assumed that their clinical signs did not worsen after discharge from the ED.

Though recent studies have advocated a more conservative strategy [14], patients in the present study were intubated for only two reasons: respiratory insufficiency or reduced consciousness (GCS below 8). These abnormalities were already covered in other parameters of the decision rule. Therefore, airway intubation was removed from the decision rule as published before [12], leading to identical predictions. The adjusted decision rule was named COBRA (Table 1). To avoid biasing the actual admission decision, COBRA was applied post hoc, on the first set of data after arrival, and at 3 and 6 h after arrival. At each time point, the worst value for each parameter recorded up to that time was used. If patients were admitted to the ICU, data collection was continued, as required by both standard treatment and study protocols. Blood gas analyses and repeat ECGs were done at the discretion of the attending physician; for the completion of COBRA, missing parameters were considered normal.

Study endpoints

The decision rule predicted ICU interventions, not ICU admission. Table 2 lists which interventions were included, illustrating that this definition was taken broadly. It contains all interventions for which continuous monitoring is required, including the administration of a fluid bolus (to know when it should be given) and intravenous sedation (to monitor respiration and consciousness). Continuous administration of flumazenil or naloxone was considered an ICU intervention (because it requires GCS monitoring), but administration of acetylcysteine was not. For the purpose of this study, the term 'ICU' encompasses all wards with facilities to continuously monitor vital functions, including intensive care, coronary care, medium care, intermediate care and stepdown units.

The outcome of COBRA was compared with the ICU interventions that took place (Table 2). The objective of this research project was to find a safe method for recognising patients who will not require ICU interventions; therefore, the NPV of COBRA was the primary endpoint. In this study protocol, a 95% NPV was considered safe. The secondary endpoints were the sensitivity, specificity and PPV of COBRA, and the minimal observation time required for a reliable prediction.

Statistical analysis

The study was powered to determine the NPV of the COBRA decision rule. Regarding these values as proportions (p), sample size (n) was calculated as $n = \frac{p(1-p)}{(\frac{p}{2} \times \left(z1 - \frac{\propto}{2} \right))^2}$. With a power of 80% and α of 0.05, this resulted in a minimum sample of 146 cases.

Statistical Package for Social Sciences (SPSS) version 24 was used. NPV, sensitivity, specificity, and PPV were determined with a 95% confidence interval (CI) by

Table 2 Definition of ICU interventions

Intervention	Number of times used (%)
Treatment of convulsion	0 (0)
Intubation and mechanical ventilation	6 (10.5)
Intravenous administration of vasopressive agents	1 (1.8)
Intravenous administration antiarrhythmics	1 (1.8)
Continuous venovenous hemofiltration	0 (0)
Noninvasive ventilation	1 (1.8)
Fluid resuscitation[a]	15 (26.3)
Intravenous administration of atropine, calcium or magnesium	11 (19.3)
Continuous administration of antagonist/antidote[b]	12 (21.1)
Defibrillation	0 (0)
Intravenous sedation	10 (17.5)
Total interventions	57 (24.8)

ICU interventions, defined as in [12], used in 40 cases from a population of 230 cases presenting to the emergency department with reported intentional overdose with drugs having potentially acute effects on neurologic, circulatory or ventilatory function.
[a]Fluid bolus >1000 ml, or fluid >500 ml explicitly given for hypotension, or continuous infusion >5 L/24 h.
[b]Specific antidote, for example, naloxone and flumazenil.

comparing the outcomes of the decision rule with the ICU interventions that actually took place.

Differences between the ICU intervention and the non-intervention groups were tested using Pearson's chi-squared test for categorical variables (sex, intubation and agitation), and Fisher's exact test when expected frequencies were less than 5. Mann–Whitney *U* test was used for continuous variables. Results were considered significant when $\alpha < 0.05$.

Results

Between January 2018 and November 2019, 452 cases of reported drug overdose came to the ED. Of these, 222 cases (49.1%) did not meet the inclusion criteria (Fig. 1). The remaining 230 cases (50.9%, 144 unique patients) were included.

Patient characteristics

Table 3 lists the patient characteristics of those cases who received an ICU intervention (intervention group, 40 cases) and those who did not (nonintervention group, 190 cases).

Compared to the nonintervention group, patients in the intervention group spent significantly less time in the ED. The number of missing data was limited: in the nonintervention group, respiratory frequency was not recorded in two cases and QRS-/QTc-duration upon arrival was missing in two other cases. Arterial PO_2 was measured 18 times in the intervention group and 20 times in the nonintervention group.

Table 4 shows the prevalence of the reported agents. As this information came from the patients, paramedics or bystanders, these data may be less reliable. In 46 cases (20.0%) a single agent was reported. The median number of reported co-ingested agents was three. Benzodiazepines were the most frequently reported drugs (31.5%), followed by antipsychotics (13.8%), analgesics (13.6%) and antidepressants (9.1%). Of all ingested agents, 86 (12.4%) were a modified-release formulation. No significant differences were found in the nature and prevalence of substances ingested between the group requiring ICU intervention and the group who did not.

Study endpoints

Of 230 cases with reported intentional drug overdose, 59 were immediately referred to the psychiatric services and/or sent home by the attending physician, and 27 went to a regular hospital ward. On the basis of clinical judgement (and not COBRA), 144 cases (62.6%) were admitted to the ICU of which 40 (27.8%) required one or more ICU interventions (Table 2). The most common intervention was fluid resuscitation, representing 26.3% of the total number of interventions (in 9 cases as a single intervention), followed by intravenous administration of magnesium, and continuous administration of an antidote (19.3 and 21.3%, respectively). The antagonists/antidotes used were flumazenil for benzodiazepines and sodium bicarbonate for TCA overdose with cardiac toxicity. Intubation was needed in six cases (10.5%) and intravenous sedation in 10 cases (17.5%).

Table 3 shows which COBRA parameters were positive using the first set of parameters collected after arrival at the ED. Most cases in the ICU intervention group had a positive score on more than one parameter. At baseline, 136 cases had a negative score on COBRA, of which 130 did not require an ICU intervention, resulting in an NPV of 95.6% (95% CI 91.6–98.4%), while 34 of 40 interventions were identified by the test (sensitivity 85%, 95% CI 70.1–94.2%). Of the 190 cases not requiring an intervention, 130 had a negative score on COBRA (specificity 68.4%, 95% CI, 61.3–74.9%), while 34 of 94 cases with a positive test result received an ICU intervention (PPV 36.2%, 95% CI, 26.5–46.7%; see Fig. 2).

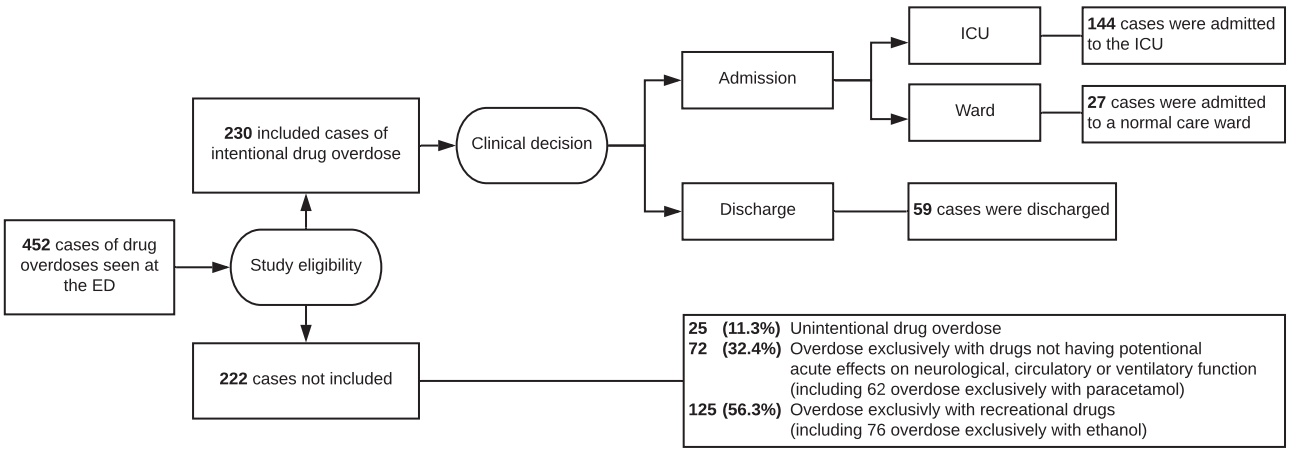
Table 3 also shows which COBRA parameters were positive using the most abnormal parameters after 3 h of observation. Three hours after arrival at the ED, 116 cases had a negative score on COBRA, none of which required an ICU intervention, resulting in an NPV of 100% (one-sided 97.5% CI, 96.9–100%), while 40 of 40 interventions were identified by the test, resulting in a sensitivity of 100% (one-sided 97.5% CI, 91.2–100%). Of the 190 cases not requiring an intervention, 116 had a negative score on COBRA (specificity 61.1%, 95% CI, 53.7–68.0%), while 40 of 114 cases with a positive test result received an ICU intervention (PPV 35.1%, 95% CI, 26.4–44.6%). These values did not change by prolonging the observation period to 6 h (Fig. 2).

Discussion

This study investigated the NPV of COBRA, a newly developed decision rule to predict which patients visiting the ED with a reported intentional overdose with drugs having potential acute effects on neurological, circulatory or ventilatory function will not require ICU interventions. After only 3 h of observation, the NPV was 100%. This means that the decision rule did not miss one case that needed a specific ICU intervention, later on, indicating that this decision rule can reliably predict, at an early stage, which patients will not benefit from admission to an ICU or a similar monitoring facility.

The NPV was chosen as the primary endpoint because it represented the probability that a person will not require an intervention, given a negative test result. In theory, the NPV depends on the incidence of ICU interventions in the population of ED patients with a reported intentional overdose with drugs having potential acute effects on neurological, circulatory or ventilatory function. It is, therefore, not an intrinsic characteristic of the decision rule. In this cohort, 40/230 cases (17.4%) required one or more ICU interventions.

Fig. 1



Flow diagram of participants. ED, emergency department.

Table 3 Characteristics and positive COBRA parameters of intervention and nonintervention groups

	Baseline characteristics		
	ICU intervention Median [IQR]	Nonintervention Median [IQR]	*P* value
Cases ED (*n*)	40	190	
Sex, men (*n* (%))	8 (20.0)	36 (19.1)	0.828
Age (years)	39 [29–57]	34[23–51]	0.163
Estimated time between reported exposure and ED arrival (h)	5:17 [3:00–:10:50][a]	5:22 [2:03–12:16][b]	0.859
Time between ED arrival and admission/discharge (h)	1:18 [0:54–1:58]	2:21 [1:33–3:41]	0.000[c]
Positive parameter COBRA2 at baseline (*n* (%))			
QRS-duration >120 ms	2 (5)	3 (1.6)	0.209
Prolonged corrected Qtc-duration[d]	21 (52.5)	37 (19.5)	0[c]
Saturation (%) <90	1 (2.5)	3 (1.6)	0.537
Arterial PO_2 (kPa) <8.0	2 (5.0)	3 (1.6)	0.209
Systolic blood pressure <90 mmHg	3 (7.5)	2 (1.6)	0.0381[c]
Systolic blood pressure >200 mmHg	0	0	–
Respiratory frequency <8/min	0	0	–
Respiratory frequency >30/min	0	0	–
Glasgow coma scale <14	25 (62.5)	34 (17.9)	<0.00001[c]
Agitation	1 (2.5)	0	0.174
Positive parameter COBRA2 after 3 h (*n* (%))			
QRS-duration > 120 ms	2 (5)	3 (1.6)	0.209
Prolonged corrected Qtc-duration[d]	21 (52.5)	37 (19.5)	0[c]
Saturation (%) <90	3 (7.5)	9 (4.7)	0.443
Arterial PO_2 (kPa) <8.0	2 (5.0)	4 (2.1)	0.280
Systolic blood pressure <90 mmHg	14 (35.0)	11 (5.8)	<0.00001[c]
Systolic blood pressure >200 mmHg	0	0	–
Respiratory frequency < 8/min	0	1 (0.5)	1
Respiratory frequency >30/min	2 (5.0)	4 (2.1)	0.280
Glasgow coma scale <14	29 (72.5)	46 (24.2)	<0.00001[c]
Agitation	1 (2.5)	0	0.174

ED, emergency department; IQR, interquartile range.
Number of missing values:
[a] 6;
[b] 13.
[c]Statistically significant at $\alpha = 0.05$
[d]Prolonged QTc is defined as ≥450 ms in men and ≥460 ms in women.

There is no reason to believe that this percentage in other hospitals will differ from ours to a degree that will significantly influence the NPV of COBRA. It is likely that COBRA will perform equally well in other institutions, provided it is applied to a group of patients with similar characteristics.

After 3 h of observation, the sensitivity of COBRA was also 100%. PPV was substantially lower (35.1%), indicating that COBRA is not a good test to predict who will need ICU interventions later on. However, it is a tool designed to identify with a high degree of safety which patients can be medically cleared if they do not need supportive

Table 4 Suspected (co-)ingested agents

Ingested substances (*n* (%))	ICU intervention 138 (100)	Nonintervention 553 (100)
Benzodiazepines	36 (26.1)	181 (32.7)
Barbiturates	0 (0)	0 (0)
Antidepressants		
SSRIs	7 (5.1)	36 (6.5)
TCAs	2 (1.4)	15 (2.7)
Other antidepressants	0 (0)	3 (0.5)
Antipsychotics	26 (18.8)	69 (12.5)
Analgesics		
Paracetamol	6 (4.3)	25 (4,5)
NSAIDs	8 (5.8)	22 (4.0)
Opioids	7 (5.1)	26 (4.7)
Antihypertensives	1 (0.7)	3 (0.5)
Neurostimulants	4 (2.9)	7 (1.3)
Antiepileptics	7 (5.1)	37 (6.7)
Antihistamines	7 (5.1)	26 (4.7)
Aminoquinolines	0 (0)	0 (0)
Antiarrhythmics	1 (0.7)	8 (1.4)
Lithium	0 (0)	2 (0.4)
Ethanol	14 (10.1)	46 (8.3)
Other	12 (8.6)	47 (8.5)
Slow-release preparations	19 (13.8)	67 (12.1)

Suspected (co-)ingested agents in numbers. There was no significant difference in any of the drug groups between cases requiring an ICU intervention and those that did not. SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants; NSAIDs, nonsteroidal anti-inflammatory drugs; slow release preparations: venlafaxine, valproic acid, quetiapine, bupropion, alprazolam, doxazosin, carbamazepine, lithium, dipyridamole, methylphenidate, barnidipine, propranolol.

treatment for coingested drugs. For future practice, we anticipate that ED clinicians approach patients with intentional drug overdose, according to standard protocols [10,11]. After 3 h of observation, when ECG and lab results are available, COBRA can be applied. The results of this study show that it is safe to medically clear patients with a negative score on the decision rule, and proceed to psychiatric assessment.

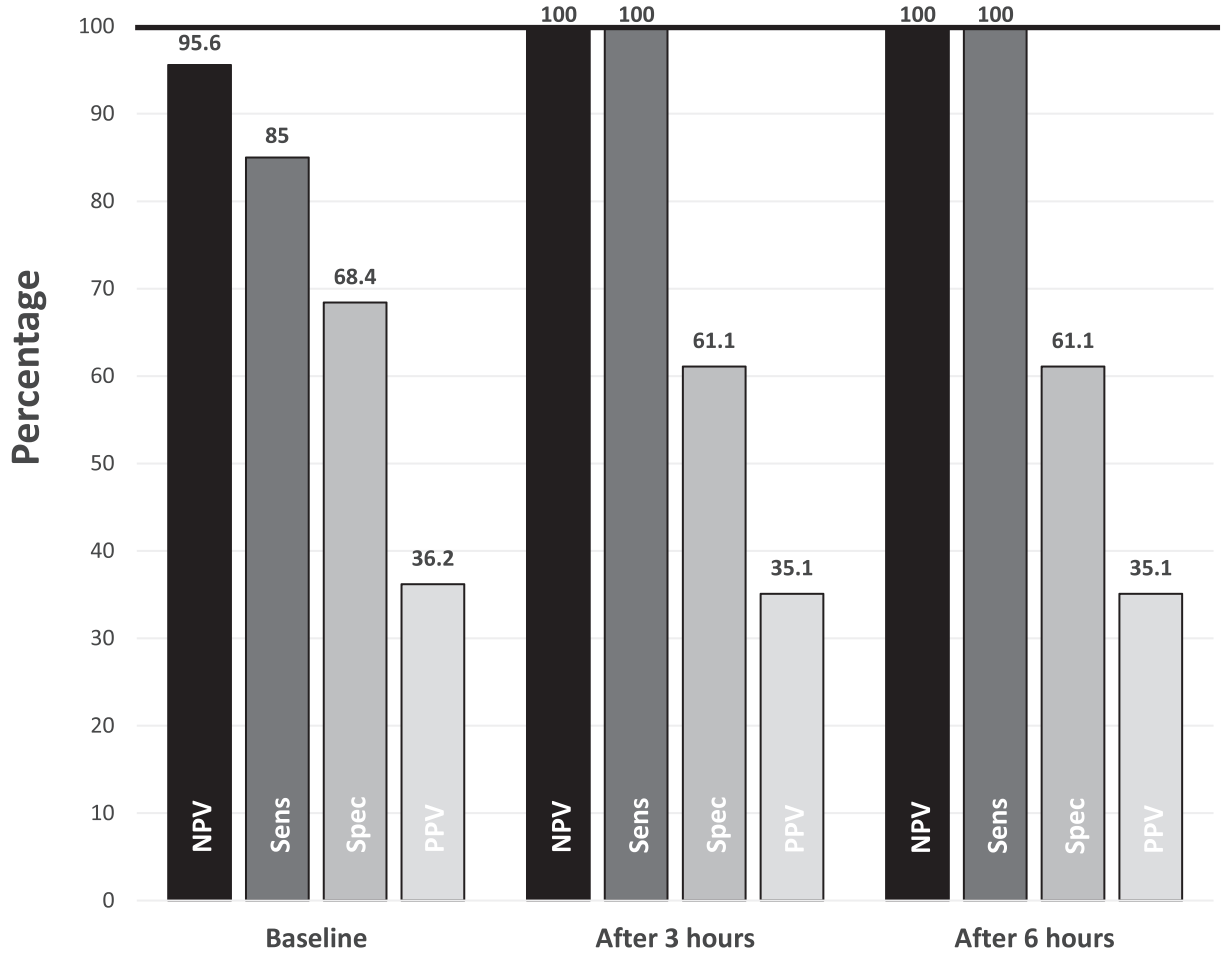
Not all patients seen in the ED with a history of intentional drug overdose were admitted to the ICU. In this study, the attending medical team used their clinical judgment to send 86 patients home, or refer them to a mental healthcare facility. Because the decision rule was designed to have a high sensitivity (one would not want to send patients home whose condition was at risk for deteriorating), the specificity of the decision rule was rather low, 61.1%. Nevertheless, this was higher than the specificity of 29.7% reported in the previous retrospective study, in which COBRA was developed COBRA[12]. This increase in specificity may be attributed to selection bias: cases that were selected in the previous study had already been admitted to the ICU. One could surmise that the retrospective study would not include the subset of patients who did not require any intervention and would have bypassed the ICU altogether, leading to a lower specificity of the test. In contrast, the present study was carried out on all cases presenting to the ED, including more cases with a negative result on the decision rule, resulting in higher specificity.

Despite this relatively low specificity, application of the decision rule would have resulted in not admitting 116 patients to the ICU, instead of 86 using clinical judgement alone. Thus, with proper use of this tool, we could have spared 30 (13.0%) additional patients an ICU admission, and instead directed them to psychiatric care.

The study results also showed that the optimal test results were achieved within 3 h of observation. Prolonging the observation period to 6 h did not improve the sensitivity, specificity, PPV or NPV of the decision rule. The median time that this study population spent in the ED was 2:09 h. It takes approximately 30 min to gather the parameters of the decision rule, that is, oxygen saturation, respiratory frequency, blood pressure, coma score, ECG and blood gas analysis if necessary. The time may increase to 1 h if routine blood analysis is done. In the Deventer Hospital, determination of serum paracetamol levels at 4 h after the presumed ingestion, and storage of serum for later drug analysis, are also part of the protocol. In addition, a psychiatrist assessed all patients with a reported intentional drug overdose before discharge. This explains why patients who were not admitted to the hospital were often not discharged before the 3-h mark. However, reducing the recommended observation period from 6–3 h may be relevant for many EDs seeking to limit the organisational burden associated with intentional drug overdose patients. In line with the findings of this study, Hollander *et al.* suggested that drug overdose patients could be identified as safe for discharge within 2–4 h, provided no slow-release preparations were involved [13]. On the basis of the results, shortening the recommended observation time should be considered in future guidelines.

Baseline population characteristics in this study were comparable with previously published studies on intentional drug overdose patients [8,12]. As in previous studies, more women than men met the inclusion criteria

Fig. 2



Diagnostic performance of COBRA in predicting ICU interventions in 230 cases with a reported intentional overdose with drugs having potential acute effects on neurological, circulatory or ventilatory function, at baseline, and after 3 and 6 h of observation. The primary test characteristics negative predictive value (NPV) and secondary test characteristics sensitivity (sens), specificity (spec) and positive predictive value (PPV) after 3 and 6 h of observation were identical.

[15]. The parameter that most often lead to a positive COBRA score was impaired consciousness (Table 3), which is in keeping with earlier reports suggesting that coma score was an important predictor for ICU admission in this patient group [16,17], followed by ECG abnormalities, which also corresponds to previous findings [18]. Furthermore, the results of this follow-up study were in line with the results of our previous, retrospective study [12].

Previous studies have shown that alcohol, benzodiazepines, analgesics, antidepressants and antipsychotics were the most common agents in cases of intentional drug overdoses [1,12,19–20]. This study had comparable findings, with benzodiazepines as the most frequently used agent (31.5%), and slow-release preparations in 12.4% (Table 4). However, it is important to note that the list of ingested drugs was on the basis of information from the patient, the accompanying person or the available history, and not toxicological analysis, and can be unreliable.

The COBRA decision rule was specifically designed to predict ICU interventions, and not ICU admissions. Other studies, focusing on predicting ICU admissions, are subject to the fallacy of self-fulfilling prophecy. Using ICU interventions as the endpoint means that the chances of subjective decision-making are lessened. This study was carried out in a real-life situation. Despite that, there was no interference with daily practice, which limited the amount of missing data.

Limitations

This study has some limitations. The outcomes of ingesting corrosive substances, or potentially harmful drugs that may cause organ failure later on, such as paracetamol or

metformin, cannot be predicted with this tool. The predictive values of the decision rule are therefore restricted to the reported ingestion of drugs with potential acute effects on neurological, circulatory or ventilatory function. Yet, even with these restrictions, the decision rule was applicable to more than half of all patients admitted to the ED with some sort of intoxication.

Additionally, the present study was done with a small study population in a single centre. Therefore, a larger multicentre trial, designed along STARD guidelines [21], would be required to confirm these results with good external validity.

Conclusion

In patients with a reported intentional overdose with drugs having potential acute effects on neurological, circulatory or ventilatory function, the COBRA decision rule showed good performances in predicting the need for intensive care interventions, with a NPV of 100%. The results also suggested that this decision could be reached after 3 h of observation in the ED.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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