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BRIEF REPORT

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Incidence, risk factors, and outcome of aspiration pneumonitis in ICU overdose patients

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Abstract *Objective:* To assess the incidence and outcome of clinically significant aspiration pneumonitis in intensive care unit (ICU) overdose patients and to identify its predisposing factors. *Design:* Retrospective cohort study. *Setting:* Medical ICU of an academic tertiary care hospital. *Patients:* A total of 273 consecutive overdose admissions. *Measurements and results:* Clinically significant aspiration pneumonitis was defined as the occurrence of respiratory dysfunction in a patient with a localised infiltrate on chest X-ray within 72 h of admission. In our cohort we identified 47 patients (17%) with aspiration pneumonitis. Importantly, aspiration pneumonitis was associated with a higher incidence of cardiac arrest (6.4 vs 0.9%; $p = 0.037$) and an increased duration of both ICU stay and overall hospital stay [respectively: median 1 (interquartile range 1–3) vs 1 (1–2), $p = 0.025$; and median 2 (1–7) vs 1 (1–3), $p < 0.001$]. In multivariate logistic regression analysis, Glasgow Coma Scale (GCS) score [odds ratio (OR) for each point of GCS 0.8; 95% confidence interval (CI) 0.7–0.9; $p = 0.001$], ingestion of opiates (OR 4.5; 95% CI 1.7–11.6; $p = 0.002$), and white blood cell count (WBC) (OR for each increase in WBC of 10^9/l 1.05; 95% CI 1.0–1.19; $p = 0.049$) were identified as independent risk factors. *Conclusions:* Clinically relevant aspiration pneumonitis is a frequent complication in overdose patients admitted to the ICU. Moreover, aspiration pneumonitis is associated with a higher incidence of cardiac arrest and increased ICU and total in-hospital stay.

Keywords Aspiration · Pneumonitis · Overdose · Intensive care

Introduction

Drug overdose is an important and increasingly frequent cause of admission to the ICU, and accounts for significant morbidity and mortality [1, 2, 3]. In 2001, approximately 15.9 million Americans had used an illicit drug at least once in the month prior to being interviewed [2]. Moreover, hospital use due to overdose has increased. Mortality rate was 3.9% in a recent report of patients with acute poisoning admitted to the emergency department [3].

Aspiration pneumonitis (AP) is a common complication of drug overdose [2, 4, 5]. AP results from the aspiration of gastric contents, which causes acute chemical inflammation and shows a broad spectrum of clinical outcomes, ranging from asymptomatic and self-limiting episodes to the development of severe pneumonitis with rapid progression to acute respiratory distress syndrome [6, 7]. Bacterial colonisation leading to aspiration pneumonia and sepsis are uncommon sequelae, although in severe cases they may occur.

There are only few studies of aspiration in overdose patients, and most focus on the risk of aspiration with gastric emptying [5]. In addition, overlap between the clinical entities of AP and aspiration pneumonia complicates epidemiological and clinical studies of AP. Therefore,

little is known about the incidence and risk factors of AP [6]. This study sought to determine the frequency and outcome of clinically significant AP in an ICU population of overdose patients, and to identify its predisposing factors.

Materials and methods

Setting and study population

We performed a retrospective observational study in consecutive overdose patients admitted to the medical ICU of the University Hospital Basel, Switzerland, within a 3-year period. AP was recorded as the primary endpoint. Management in general included repetitive administrations of activated charcoal [8]. Gastric emptying was not performed in any of the patients. Prospective data collection was approved by the local ethics committee and was in accordance with the principles of the Declaration of Helsinki.

Endpoints

Clinically significant AP was defined as the occurrence of respiratory dysfunction in a patient with a localised pulmonary infiltrate on chest X-ray [5]. Chest X-ray was routinely performed in this cohort. All patients with an obvious or at least suspected local infiltrate were identified as potential cases and therefore reviewed for significant respiratory dysfunction. Respiratory dysfunction was defined as at least one of the following: invasive or non-invasive mechanical ventilation for hypoxaemia or hypercapnia, supplemental oxygen > 4 l/min; respiratory rate > 20/min, arterial oxygen saturation $< 92\%$, $PaO_2 < 10$ kPa within the first 72 h after admission.

We identified ingested drugs using ambulance charts, history, urine screening and blood analysis. Patients were contacted 6 months after discharge by telephone.

Statistical analysis

Results are expressed as means $\pm$ SD for continuous normally distributed variables. For non-parametric data, medians with interquartile ranges are used. To describe baseline characteristics, comparisons were made using the *t*-test, Mann–Whitney *U*-test, Fisher's exact test and chi-square test as appropriate. Univariate and multivariate analyses were conducted using logistic regression. The following variables were entered in multivariate analysis: Glasgow Coma Scale (GCS) score on admission, opiate ingestion, APACHE II, heart rate on admittance, serum sodium, serum potassium, white blood cell count (WBC). Risk-adjusted mortality rates (observed/expected) were compared for patients with and without AP, using the diagnostic category weight of drug overdose for the expected rates [9, 10]. Tests were two-sided, and a p value of less than 0.05 was considered to indicate statistical significance. Statistical analyses were performed using SPSS/PC (version 12.0, SPSS Inc.).

Results

Between January 1998 and August 2001, of a total of 3499 ICU patients 273 were admitted for intoxication. Using the predefined criteria, 61 patients (22%) showed a localised infiltrate on chest X-ray. Of these, 47 (17%) additionally had respiratory dysfunction. Thus, a total of 47 patients (17%; 95% CI 13–22%) met the criteria for clinical relevant AP. As shown in Table 1, there were important differences among baseline characteristics in patients with and without AP. Values are given as median (interquartile range), if not otherwise indicated.

The GCS score on admittance of patients with AP was 7 (3–9), compared with 14 (7–15) in patients without AP. Sixty-one per cent of all patients (167 of 273) had a GCS score of 14 or less, 26% (70 of 273) a GCS score of less than 8. APACHE II score was significantly higher in patients with AP than in patients without (Table 1).

Mixed drug intoxication was present in most patients. Ingestion of opiates was identified in 38% of patients with AP and only in 12% of those without. Other substances were ingested in similar frequency by patients with and without AP.

Outcome

A total of 7 patients (2.6%) died during the hospitalisation, with similar risk-adjusted mortality rates in patients with and without AP. The high O/E ratios are caused by the chosen diagnostic category weight of drug overdose, which leads to relatively low expected mortality rates.

The length of stay was significantly longer in patients with AP than in patients without AP, both in the ICU and overall in hospital. Three patients with AP suffered a cardiac arrest (6.4%) while in the ICU, against two patients without AP (0.9%; $p = 0.037$). There were no deaths during the 6-month follow-up period.

Risk factor analyses for aspiration pneumonitis

Several predictors of AP could be identified in univariate logistic regression (Table 2). Of these, GCS score on admittance, opiate ingestion, and WBC remained statistically significant independent predictors of AP in multivariate logistic regression.

Table 1 Baseline characteristics and outcome

	All overdose patients	Aspiration pneumonitis		
		Yes	No	*p* Value
	n = 273 (100)	*n* = 47 (17)	*n* = 226 (83)	
Age, years, median (IQR)	37 (29–47)	39 (34–48)	36 (28–46)	0.066
Sex				0.126
Female, *n* (%)	172 (63)	25 (53)	147 (65)	
Male, *n* (%)	101 (37)	22 (47)	79 (35)	
Before admission				
Cardiac arrest, *n* (%)	3 (1.1)	1 (2.1)	2 (0.9)	0.434
Seizure, *n* (%)	11 (4)	4 (8.5)	7 (3.1)	0.101
Arrhythmia, *n* (%)	7 (2.6)	2 (4.3)	5 (2.2)	0.346
On admission				
GCS, median (IQR)	13 (7–15)	7 (3–9)	14 (9–15)	< 0.001
APACHE II score, median (IQR)	8 (5–14)	15 (10–18)	7 (4–12)	< 0.001
Heart rate, per minute, median (IQR)	90 (76–105)	104 (77–119)	88 (75–100)	0.013
Systolic blood pressure, mmHg, mean ± SD	122 ± 22	117 ± 23	123 ± 22	0.161
Serum sodium, mmol/l, median (IQR)	139 (137–142)	139 (136–142)	139 (137–142)	0.321
Serum potassium, mmol/l, median (IQR)	3.7 (3.5–4.1)	3.9 (3.6–4.3)	3.7 (3.5–4.0)	0.018
White blood cell count, 10^9/l, median (IQR)	8.6 (6.8–11.2)	9.9 (7.1–14.9)	8.4 (6.7–10.7)	0.008
Ingested drugs (incl. co-ingestion)				
Cyclic antidepressants, *n* (%)	76 (28)	18 (38)	58 (26)	0.079
SSRI, *n* (%)	28 (10)	4 (9)	24 (11)	0.796
Neuroleptics, *n* (%)	51 (19)	6 (13)	45 (20)	0.253
Benzodiazepines, *n* (%)	130 (48)	27 (57)	103 (46)	0.138
Alcohol, *n* (%)	60 (22)	8 (17)	52 (23)	0.367
Opiates, *n* (%)	45 (17)	18 (38)	27 (12)	< 0.001
Cocaine, *n* (%)	16 (6)	5 (11)	11 (5)	0.164
Other sedative, *n* (%)	43 (16)	7 (15)	36 (16)	0.859
Paracetamol, *n* (%)	15 (6)	2 (4)	13 (6)	1.000
Others, *n* (%)	96 (35)	11 (23)	85 (38)	0.063
Ventilation				
Non-invasive ventilation, *n* (%)	6 (2.2)	6 (13)	0 (0)	< 0.001
Mechanical ventilation, *n* (%)	29 (11)	22 (47)	7 (3)	< 0.001
Outcome				
Cardiac arrest, *n* (%)	5 (1.8)	3 (6.4)	2 (0.9)	0.037
Seizure, *n* (%)	14 (5.1)	4 (8.5)	10 (4.4)	0.272
Arrhythmia, *n* (%)	17 (6.2)	5 (10.6)	12 (5.3)	0.184
Death during hospitalisation, *n* (%)	7 (2.6)	2 (4.3)	5 (2.2)	0.346
Predicted hospital mortality (%)	0.7	1.1	0.6	< 0.001
Observer/expected ratio of mortality (95% CI)	3.8 (1.5, 7.7)	3.8 (0.5, 12.9)	3.8 (1.2, 8.7)	0.998
Length of stay in ICU, days, median (IQR)	1 (1–2)	1 (1–3)	1 (1–2)	0.025
Length of stay in hospital, days, median (IQR)	1 (1–3)	2 (1–7)	1 (1–3)	< 0.001

GCS, Glasgow Coma Scale score [14]; APACHE II, Acute Physiologic and Chronic Health Evaluation II [9]

Table 2 Predictors of aspiration pneumonitis in univariate and multivariate analyses

Variable	Odds ratio	95% Confidence interval	*p* Value
Univariate analysis			
GCS on admittance (continuous)	0.81	0.75–0.87	< 0.001
Opiate ingestion	4.58	2.24–9.33	< 0.001
APACHE II (continuous)	1.17	1.10–1.24	< 0.001
Heart rate on admittance (per minute) (continuous)	1.02	1.00–1.03	0.027
Serum sodium (mmol/l) (continuous)	0.94	0.88–1.00	0.039
Serum potassium (mmol/l) (continuous)	1.81	1.17–2.81	0.008
White blood cell count (10^9/l) (continuous)	1.11	1.04–1.19	0.002
Multivariate analysis			
GCS on admittance (continuous)	0.83	0.75–0.93	0.001
Opiate ingestion	4.50	1.74–11.60	0.002
White blood cell count (10^9/l) (continuous)	1.05	1.00–1.19	0.049

Continuous variables: odds ratios (OR) for each increase of one unit of the respective variable. For instance, a patient with a GCS of 15 on admittance has an OR of 0.81 for aspiration pneumonitis compared with a patient with a GCS of 14

Discussion

This study shows that clinically relevant AP is a frequent complication in an unselected cohort of consecutive overdose patients admitted to the ICU. In addition, AP was associated with an increased length of stay in the ICU and in hospital, and a higher incidence of cardiac arrest. GCS on admittance, ingestion of opiates, and WBC were identified as readily definable independent risk factors for AP.

The incidence of AP in our population is within the wide range found in previous studies. Differences in the types of drugs abused, ICU admission strategies, incidence of risk factors and definition of clinical significant AP seem to account for most of the difference in incidence. Isbister and colleagues reported a frequency of AP of 11% in unselected overdose patients admitted to the ICU in Australia [5]. In a study of the relation between GCS score and the incidence of AP, the rate of AP in overdose patients admitted to the ICU was 29% [11]. A GCS score of 14 or less was present in 85% of patients in that study, compared with 61% in our study. Since deeper unconsciousness as indicated by a lower GCS score is associated with a higher risk of aspiration, the difference in GCS score may well be responsible for the different incidence of AP in the two studies. Also, a high incidence of AP of 28% was found in a Finnish population [12]. In that cohort, 68% of patients were unconscious, with unconsciousness defined as a GCS score of 3–7. In contrast, only 26% of our patients had a GCS score of 3–7. Again, the difference in the level of consciousness between the two populations might account for the different frequency of AP.

In our study, AP was associated with significantly increased morbidity: patients with AP had longer LOS both in the ICU and in hospital. This finding is supported by recent data from Australia [5]. In addition, our study shows that patients with AP have a higher rate of cardiac arrest. Mortality overall was low in our cohort. Therefore we had limited statistical power to investigate the impact of AP on mortality. In our cohort, risk-adjusted mortality rates showed no differences between patients with AP and without. Isbister and colleagues reported significantly greater overall mortality in patients with AP than in patients without AP in a very large overdose population [5].

Given the clinically significant increased morbidity in patients with AP, it is mandatory to identify easily and rapidly assessable risk factors for AP. Our study clearly shows the important role of the GCS score, the ingestion of opiates and an increased WBC as independent predictors for AP. All three risk factors are easily available during the initial assessment in the ICU and therefore very useful in clinical practice. Differences in baseline patient characteristics, study setting, and definition of clinically significant AP may account for the difference in independent predictors found in previous studies [5, 12]. Additional prospective studies are necessary to validate the risk factors found in our study.

Several limitations apply to our study: firstly, our definition of AP may have included some patients with early aspiration pneumonia. Although the identification of secondary bacterial colonisation and infection is difficult, the rate of this complication was low, at most, as we included only patients with infiltration and respiratory dysfunction within 72 h after the admission. Infectious complications in general become clinically apparent only after several days of pulmonary aspiration. Secondly, it is possible that in our study some patients had other pulmonary complications of opiate intoxication rather than AP [2]. Particularly heroin can cause pulmonary oedema. Using a localised infiltrate on chest X-ray as inclusion criterion for AP should have excluded most cases of pulmonary oedema, since heroin-induced pulmonary oedema manifests typically as widespread, bilateral airspace consolidation on chest X-ray [13].

In conclusion, relevant AP is a frequent complication of overdose patients admitted to the ICU. Three readily assessable variables identify patients at risk for AP. This is clinically important, as AP is associated with increased morbidity.

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