The MISSED score, a new scoring system to predict Mortality In Severe Sepsis in the Emergency Department: a derivation and validation study

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Introduction

- it is important to identify patients with severe sepsis and septic shock→ for resuscitate in a timely manner
- Those patients who receive early aggressive resuscitation having a decreased mortality rate

Introduction

- The criteria used for recognized patients who need early goal-directed therapy (EGDT) recently:
  - after a 20–30 ml/kg fluid bolus or a lactate of 4 mmol/l→ SBP < 90mmHg or MAP < 65mmHg
- Many patients do not meet these criteria, yet have a high mortality rate
- Those at highest risk of death must be identified in the ED, for aggressive resuscitation beneficial to these patients

Introduction

- Aims of this investigation
  - derive independent prognostic factors associated with mortality rate
  - develop a new clinical prediction rule, MISSED score(The Mortality In Severe Sepsis in the Emergency Department) to identify patients with severe sepsis who have a high mortality rate

Patients and methods

- Study design and setting
  - This is a retrospective study
  - collected data from December 2005 to December 2011 in a university teaching hospital
  - Patients were identified from the ED clinical record

Patients and methods

- Included:
  adults presenting with sepsis, and admitted to the ICU within 7 days of hospital admission, and those patients who received EGDT in the ED
- excluded:
  - interhospital transfers,
  - those with bowel obstruction or bowel infarction,
  - those who were known to have active malignancy or who were diagnosed with active malignancy

Patients and methods

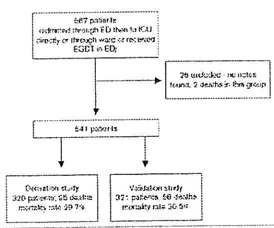
- Selection of predictor variables:
  - practical availability at ED
  - Including the vital signs and blood results that are available within an hour of the patient's attendance
- Comparison with current standards
  - compared the MISSED score with the EGDT inclusion criteria, severe sepsis criteria and the APACHE II score, in predicting mortality performance

Results

- A total of 667 patients satisfying the inclusion and exclusion criteria over the study period
- 26 patients were excluded as their ED notes could not be found. Two of the 26 are known to have died
- The remaining 641 patients had mortality rate of 30.1% (193 deaths)

Results

- The 641 patients were placed in chronological order; the first 320 forming the derivation study population and the remaining 321 forming the validation study population



Results

Derivation study

- The median age was 64 years and 52.5% were men
- Excluded whose INR, lactate and serum albumin were missing, as were patients on warfarin

  → excluding a total of 111 patients, leaving 209 patients in the derivation population, included 67 death

- The variables on which the univariate analysis was conducted is shown

Table 1 Univariate analysis of variables in the derivation data using the Mann-Whitney *U*-test comparing medians in survivors and nonsurvivors, together with percentage data missing for each variable and χ^2 analysis of comorbidities ($n = 320$)

Variables	All median (IQR)	Survivor's median (IQR)	Nonsurvivor's median (IQR)	P value	Percentage data missing
Age (years)	64 (48.25–76.75)	60 (43–73)	71 (61–81)	<0.001	0
Initial systolic BP (mmHg)	113 (93.25–135)	114 (96–135)	113 (90–131)	0.237	0
Initial diastolic BP (mmHg)	65.5 (54–79)	66 (56–79)	65 (53.5–78)	0.591	0
Initial heart rate (beats/min)	109 (90–127)	109 (92–127)	105 (84.3–125.8)	0.426	0
Initial MAP (mmHg)	83 (68.08–97.8)	84 (69.7–98)	79.3 (66.7–98.3)	0.440	0
Initial shock index	0.94 (0.7–1.23)	0.94 (0.7–1.2)	1 (0.8–1.2)	0.704	0
Temperature (°C)	37.5 (36.4–38.5)	37.9 (36.7–38.9)	36.7 (36–37.8)	<0.001	4.7
Respiratory rate (breaths/min)	26 (20–32)	26 (20–32)	28 (23–35)	0.139	<0.1
$PaCO_2$ (kPa)	4.09 (3.39–4.9)	4.07 (3.4–4.9)	4.2 (3.4–5.3)	0.575	13.7
PaO_2 (kPa)	10.8 (8.6–15.7)	10.7 (8.7–15.5)	10.9 (8.6–16.2)	0.611	12.9
PaO_2/FiO_2	36.7 (24–49.6)	38.05 (25.9–50)	34.3 (22.5–40.5)	0.150	13.2
Lactate (mmol/l)	2.6 (1.4–4.56)	2.3 (1.3–4.2)	3.6 (1.65–6.7)	0.004	5.9
Base excess (mmol/l)	−3.7 (−8.45 to −0.1)	−3.4 (−7.8 to −0.07)	−4.8 (−10.2 to −1.05)	0.199	8.4
Bicarbonate (mmol/l)	22 (19–25)	22 (19–25)	21 (16.6–23.5)	0.041	1.6
pH	7.4 (7.31–7.46)	7.4 (7.33–7.46)	7.36 (7.25–7.46)	0.051	13.1
Sodium (mmol/l)	135 (131–138)	135 (132–138)	135 (129.5–139)	0.805	0
Potassium (mmol/l)	4.1 (3.6–4.7)	4.1 (3.5–4.6)	4.3 (3.75–5)	0.08	<0.01
Urea (mmol/l)	10 (6.45–18.3)	9.23 (5.6–6.4)	14.4 (8.1–26.5)	<0.001	<0.01
Creatinine (µmol/l)	147.5 (94.3–256)	135 (87–227)	167 (104–265)	0.082	0
Phosphate (mmol/l)	1.26 (0.87–1.6)	1.24 (0.86–1.63)	1.4 (0.87–1.94)	0.193	44.1
Albumin (g/l)	28 (22.5–33.5)	29 (24–34)	25 (21–31)	<0.001	1.9
Bilirubin (µmol/l)	15 (9–24)	14.5 (8–23)	15 (9–32.3)	0.126	3.1
Glucose (mmol/l)	7.7 (5–10.4)	8 (6.2–10.45)	7.3 (5.8–10)	0.594	5.3
C-reactive protein (mg/l)	209 (89.5–324)	210 (88–316)	195 (102–343)	0.857	3.8
Troponin (µg/l)	70 (30–210)	0.07 (0.03–0.2)	0.07 (0.04–0.21)	0.951	45
Lowest systolic BP (mmHg)	93 (78–113)	97 (80.5–114)	87 (74–110.5)	0.037	0
Lowest diastolic BP (mmHg)	50 (40–60.25)	52 (42–62)	44 (35.5–56)	0.001	0
Highest HR	120 (102–135)	120 (102–133)	120 (100–135)	0.939	0
Lowest MAP	65 (55–78)	67 (56–79.5)	60 (54.5–75.5)	0.01	0
Highest shock index	1.1 (0.9–1.4)	1.1 (0.9–1.3)	1.2 (1.1–1.4)	0.158	0
Haemoglobin (g/dl)	12.8 (11.1–14.6)	12.9 (11.1–14.7)	12.7 (11.1–14.1)	0.337	0
WCC $\times 10^9$/l	15.2 (9.6–21.6)	15.1 (9.9–21.4)	15.6 (8.8–22.55)	0.927	0
Platelets $\times 10^9$/l	266 (189–366)	269 (191–361)	259 (186–372)	0.996	3.1
HcT	0.39 (0.33–0.43)	0.38 (0.33–0.43)	0.38 (0.34–0.42)	0.626	1.6
INR*	1.2 (1.1–1.48)	1.2 (1.1–1.4)	1.3 (1.2–1.6)	0.001	21.9

Results

- ~~Multivariate regression analysis identified only~~ age, albumin, INR and temperature to be independent variables associated with mortality
- But temperature
  - cut-off point was 37.2'C,
  - influenced by the timing of measurement, antipyretics, and the body area is measured

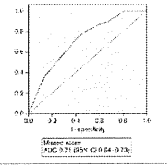
  Therefore, temperature was removed from further analysis

Table 2 Independent variables with their cut-off points, odds ratios, 95% confidence interval of the odds ratio (P-value and the score attributed to each variable)

Variables	Cut-off point	Odds ratio for death	95% confidence interval	P-value	Score attributed
Age	≥ 65 years	2.6	1.42–4.7	0.002	2.5
Albumin	≤ 27 g/l	2.78	1.49–5.1	0.001	3
INR	≥ 1.2	3.5	1.76–6.99	<0.0001	3.5

Scores	Number of cases	Number of deaths	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
a) MISSED score and associated mortality rates in derivation and validation data						
Derivation study (n = 209; 67 deaths)						
0	27	0	0 (0–8.7)	81 (73.7–86.9)	0 (0–15.5)	83.2 (55.7–95)
> 0 (any variable present)	182	67	100 (93.2–100)	19 (13.1–26.6)	36.8 (29.6–44.3)	100 (84.5–100)
< 5.5 (up to one variable present)	93	15	22.4 (13.5–34.5)	45.1 (36.8–53.6)	16.1 (9.6–25.5)	55.1 (45.7–64.3)
≥ 5.5 (minimum two variables present)	116	52	77.6 (65.5–86.5)	54.9 (46.4–63.2)	44.8 (35.7–54.3)	83.6 (74.5–90.4)
≥ half 3 variables present	45	24	35.8 (24.7–48.5)	86.6 (79.6–91.5)	53.81 (40–70.6)	74.1 (65.6–80.4)

- The area under the curve (AUC) for the MISSED score was 0.712 with a cut-off point at 5.5 or more



Results

Validation study

- consisted of 321 patients including 98 deaths. The median age: 68 years, 44.2% were men
- Excluded: whose data missing (age, albumin and INR) as were patients on warfarin
  - →105 were excluded leaving 216 patients in the validation population, which included 62 deaths

Scores	Number of cases	Number of deaths	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Validation study (n = 216; 62 deaths)						
0	27	3	3.2 (0.5–12.2)	89.8 (78.8–96)	7.4 (1.3–25.7)	68.3 (61–74.7)
> 0	189	60	96.8 (87.8–99.4)	16.2 (11–23.2)	31.7 (25.3–39)	92.6 (74.2–98.7)
< 5.5	111	19	30.6 (19.9–43.6)	40.5 (32.5–48.5)	17.1 (10.9–25.7)	59 (49–68.4)
≥ 5.5	105	43	69.4 (56.5–80.1)	59.7 (51.5–67.5)	41 (31.6–51)	82.9 (74.9–88.1)
0	35	22	35.5 (24–48.7)	91.6 (85.7–95.2)	62.9 (45–78)	77.9 (71–83.6)

Results

- The addition of the criterion of a MISSED score of at least 5.5 to the EGDT criteria increased the sensitivity for identifying death from 46.8 to 83%

Scores	Number of cases	Number of deaths	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
b) Comparison of mortality prediction using MISSED score and EGDT criteria (n = 158; 47 deaths)						
EGDT criteria met	56	22	46.8 (32.3–61.7)	69.4 (59.8–77.8)	39.3 (26.6–53.2)	75.5 (65.6–83.2)
EGDT criteria not met	102	25	53.2 (38.2–67.8)	30.6 (22.4–40.2)	24.5 (16.8–34.2)	69.7 (59.7–78.2)
MISSED score ≥ 5.5	74	31	66 (50.6–78.7)	61.2 (51.5–70.2)	41.9 (30.7–53.9)	81 (70.6–88.4)
MISSED score < 5.5	84	16	34 (21.3–49.4)	38.7 (29.8–48.5)	19 (11.6–29.4)	58.1 (46.1–69.3)
Per EGDT criteria or MISSED score ≥ 5.5	103	39	83 (68.7–91.9)	42.9 (33.1–52.1)	37.9 (28.4–48)	85.5 (72.8–93.1)
EGDT criteria met and MISSED score ≥ 5.5	27	14	29.8 (17.8–45)	88.2 (80.5–93.4)	51.9 (32.4–70.8)	74.8 (66.3–81.6)
EGDT criteria met and MISSED score 0	12	3	19.1 (9.6–33.7)	97.3 (91.7–99.3)	75 (42.8–93.3)	74 (65.9–80.7)

Results

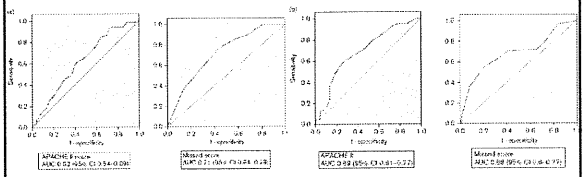
- Compare the MISSED score with the criteria defining severe sepsis :
  - The sensitivity of severe sepsis criteria was identical to that of a MISSED score > 0
  - The severe sepsis criteria missed two deaths in each of the derivation and validation populations. All four deaths had a MISSED score of at least 5.5

Results

- The mortality rate when none of the severe sepsis criteria were met remained at 28.6% (2/7) in the derivation population and 13.3% (2/15) in the validation population.
- The mortality rate for a MISSED score 0 was 0% and 7.3% in the derivation and validation populations

Results

- compare the MISSED score with the APACHE II score in predicting mortality:



Discussion

- Age factors (in particular age >65 years) has been found to be a significant independent variable in several studies
- Hypoalbuminaemia: recognized as being associated with critical illness and mortality, cut-off value we defined was albumin ≤ 27 g/l
- Coagulopathy, another well-recognized factor associated with severe sepsis
  - is usually associated with mortality when the INR >1.5
  - However, our finding of an INR ≥1.2 with mortality has not been reported previously

Discussion

- The MISSED score of 5.5 or more is equivalent to the EGDT inclusion criteria
- The MISSED score is also equivalent to the APACHE II score in predicting mortality, and is sensitive as the criteria defining severe sepsis
- When the MISSED score of 5.5 or more is used together with the EGDT criteria, the two methods complement each other, and the sensitivity improves to over 80%

Discussion

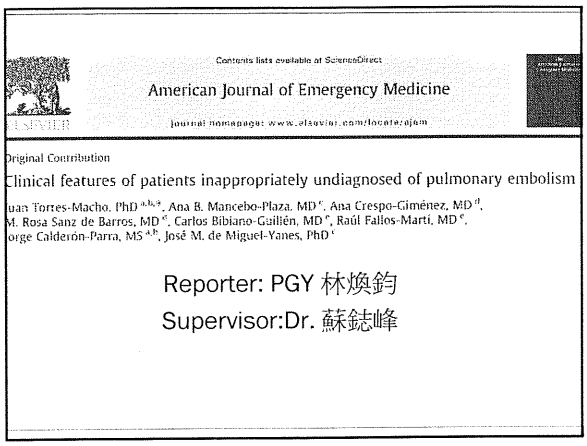
- Although a MISSED score is more specific when 5.5 or more, it is our view that the MISSED score should not be used as a decision tool to discharge a patient home from the ED
- When both EGDT inclusion criteria and the MISSED score ≥ 5.5 overlap, the mortality rate increases to above 50%

Discussion

- Limitation
  - it is a retrospective study of data collected in a single center
  - The cohort of patients studied, were those who were admitted to ICU→possibly overestimating the performance of the score when used prospectively
  - the exclusion of patients who were known or found to have active malignancy
  - Exclusion of patients who have not the full spectrum of blood tests

Conclusion

- The MISSED score should be used in the ED in addition to the criteria for EGDT to identify patients with sepsis who are at high risk of death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Original Contribution

Clinical features of patients inappropriately undiagnosed of pulmonary embolism

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Introduction

- Acute PE patients often have nonspecific symptoms, and as a result, the diagnosis is sometimes delayed
- Previous studies have reported that patients diagnosed within 48 hours of arrival at the emergency department (ED) had better outcomes

Introduction

- Factors associated with the timing of diagnosis have been reported,
  - but only in patients who were admitted to hospital
  - patients who were sent home with a wrong diagnosis have not been included
- Aim of the research:
  - identify the prevalence and clinical factors associated with a delayed diagnosis
  - analyzed whether patients with a delayed diagnosis showed more severe PE or worse outcomes

Methods

Study design

- retrospective observational study at three University Hospitals in Madrid, Spain, from April 2008 to December 2011
- Review patients who were admitted to hospital with a diagnosis of acute symptomatic PE as confirmed by chest computed tomography (CT)

Methods

- Inclusion criteria: adult patients with symptoms compatible with acute PE who were diagnosed with chest CT
- Exclusion: patients with symptoms other than those mentioned above, and PE was incidentally diagnosed during evaluation

Methods

- Analyze the records in terms of age, gender, prior medical and accepted risk factors for PE, we also registered measurements related to PE severity
- "Time to diagnosis" was defined as the time (in hours) from first evaluation in the ED to chest CT diagnosis

Methods

- Categorized into three groups:
  - Group 1: PE was diagnosed by chest CT while the patient was still at the ED in the first visit
  - Group 2: PE was diagnosed by chest CT ordered during hospitalization after the patient had left the ED
  - group 3: patients who were sent home with a wrong alternative diagnosis and returned to the ED and were diagnosed of PE

Results

- enrolled a total of 452 adult patients with acute PE who were admitted to hospital
- 16 patients excluded: 10 diagnosis was not via chest CT, and 6 because PE did not have associated symptoms
- Thus, 436 patients were finally included
  - Mean age was 67.4±18.8 years,
  - 48.6% were male
  - 146 (33.5%) patients had a delayed diagnosis of PE: 94 (21.5%) belong to group 2 and 52 (11.9%) to group 3

Results

- Patients from group 2 showed a statistical significance compared to group 1
  - older age,
  - a higher prevalence of chronic diseases,
  - a higher incidence of cough
- Patients from group 3 showed a statistical significance compared to group 1
  - younger,
  - a higher proportion of pleuro-mechanical chest pain,
  - Hemoptysis,
  - a higher proportion of patients with a pulmonary infiltrate on chest x-ray

Results

Logistic regression analysis showing independent predictors of a delayed diagnosis of pulmonary embolism

Group 2			
Variables	OR	95% CI	*P*
COPD	4.3	2.2-8.6	.00
Asthma	3.4	1.2-9.7	.01
Cough	2.5	1.4-4.7	.002
Absence of Syncope	4.3	1.2-14.7	.02
Group 3			
Variables	OR	95% CI	*P*
Absence of dyspnea	2.3	1.1-4.8	.02
Pleuro-mechanic pain	3.6	1.3-9.5	.01
Fever	2.7	1.2-7.8	.04
Hemoptysis	5	1.4-9-17.1	.009
Pulmonary infiltrate	2.5	1.1-6.2	.04

Results

Wrong alternative initial diagnosis in patients from group 2 and 3

	Group 2	Group 3
Initial diagnosis (%)		
Pneumonia/RTI	34	41.3
Pleuritis	0	2.1
Mechanical chest pain	2.1	8.6
Asthma exacerbation	2.1	4.3
Heart failure	15.3	6.5
COPD exacerbation	16.4	4.3
Angina/ACS	5.4	0
Others	19.7	32.6

- Post hoc mean Geneva score: 5.6 ± 3, 5.3 ± 2.6, and 4.8 ± 2.2, no statistically significant differences between groups

Results

Table 4
Comparison of data associated with pulmonary embolism severity comparing group 1 to group 2 and 3

	Group 1	Group 2	Group 3
Troponin I (ng/mL)[a]	0.26 (0.5)	0.22 (0.3)	0.1 (0.1)[d]
D-Dimer (ng/mL)[b]	7131 (8021)	8440 (7300)	4920 (7760)[d]
RVD on TTE (%)[c]	30	29.6	25.7
Chest CT clot location (%)			
Proximal unilateral	16.9	23.9	17.6
Proximal bilateral	29	25.3	20.5
Distal unilateral	21.8	19.7	41.1[d]
Distal bilateral	32.1	30.9	20.5

Results

- There were no statistical differences between the 3 groups in mortality rates, although a trend toward a higher mortality rate in group 3 as compared to groups 1 and 2 (P =0.07)
- Analyzing the patients who died, patients from group 3 were
  - older (86.8 ± 5.8 years vs 64.3 ± 7.2 and 71.1 ± 8.5,from groups 1 and 2 respectively)
  - with a higher prevalence of active neoplasia (80%) and heart failure (60%)

Discussion

- We found that when patients present with well-known risk factors for PE, physicians are more likely to make an expedited diagnosis
- In the previous study, the presence of transient risk factors (recent surgery, severe medical diseases, immobilization, pregnancy) was found to be significantly associated with an earlier diagnosis

Discussion

- When patients with the cardiopulmonary disease present with an acute PE, clinicians commonly attribute their symptoms to their known cardiopulmonary disease
- Smith et al found that patients older than 65 years or with coronary artery disease and heart failure had significant longer times from arrival to diagnosis
- several studies found that PE may be diagnosed less accurately in patients with coronary artery disease and COPD

Discussion

- Patients of group 3, showed a typical profile concerning the following issues:
  - (1) absence of risk factors for PE, like younger age, less comorbidities, or the absence of a history of previous major surgery
  - (2) without dyspnea but with symptoms and signs related to other clinical situations like respiratory tract infection or mechanical chest pain
  - (3) presence of a radiological infiltrate was an independent predictor of misdiagnosis

Discussion

- We found a trend toward a higher mortality rate in patients who were sent home, but not reach statistical significance
- Patients of group 3 who died during the subsequent admission, were older and showed a higher prevalence of coexisting comorbidities
- Therefore, this higher mortality is probably related to these comorbidities and not to a delayed diagnosis

Discussion

- Limitation
  - not include the Wells score because a retrospective review of charts may not be sufficiently accurate
  - it cannot be distinguish doctors delay from failure of the standardized diagnostic work-up, both situations was relevant in the reported patients
  - not include patients who were sent home with a wrong diagnosis and died before they arrived at the hospital or patients who where attended in other hospitals

Conclusion

- Conclusion
  - delay in diagnosis of acute PE is frequent despite current diagnostic strategies
  - Delay in diagnosis is not an independent predictor of a more severe disease or death
  - clinicians should be aware of these factors to provide expedited management of acute PE

Incidence and management of *N*-acetylcysteine-related anaphylactoid reactions during the management of acute paracetamol overdose

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Background

* Intravenous N-acetylcysteine (NAC) is the antidote for paracetamol poisoning
* NAC is effective in preventing paracetamol-related hepatotoxicity; however, it commonly causes adverse drug reactions (ADRs)

Background

* NAC-related ADRs have been classified previously as:
  * (i) minimal: no reaction or mild GI symptoms not requiring specific treatment;
  * (ii) moderate: GI symptoms requiring temporary cessation of NAC infusion, mild flushing, pruritus, mild chest pain, breathlessness, peak expiratory flow rate < 25–50% baseline
  * (iii) severe: severe flushing, respiratory distress, moderate to severe chest pain, >50% reduction in peak expiratory flow rate from baseline, hypotension with SBP < 90 mmHg or DBP < 50 mmHg, death has been reported but rare

Background

* Management guidelines for ADR to NAC have been proposed previously:
  * (a) stopping the NAC infusion temporarily;
  * (b) administering a H1antagonist (e.g. chlorphenamine) and/or H2 antagonist (e.g. cimetidine);
  * (c) administering nebulized salbutamol if bronchospasm is significant

  Corticosteroids are not recommended as first-line management

Background

* This study
  * a retrospective review of the incidence and management of ADR to intravenous NAC
  * at the emergency department in a large inner-city hospital
  * determine whether the management provided was in accordance with clinical guidelines

Patients and methods

* Data on all patients presenting with poisoning to our large inner-city ED have been entered onto a purpose-designed electronic clinical toxicology database(since 2005)
* retrospective search of the database, identify patients between February 2005 and June 2011 with paracetamol poisoning requiring treatment with NAC and those in whom an ADR to NAC treatment

Patients and methods

- Data were collected
  - sex,
  - paracetamol concentration at the time of treat,
  - history of asthma or atopy,
  - symptoms developed after commencement of NAC treatment,
  - timing of ADR after treatment
  - any management(s) undertaken after development of the ADR

  These data were analysed to determine a correlation between the severity of symptoms and the presence of risk factors

Results

- total of 1648 cases of paracetamol poisoning presented to the hospital and 660 (40%) patients (total treated population) received treatment with NAC
  - 82 (12%) patients developed an ADR to NAC
  - 59 (72%) patients had complete case records available for review and were included
  - Of the 23 patients who were excluded from the study due to unobtainable or incomplete case records

Results

- population included 34 women (58%) and 25 men (42%), asthma history in 12 patients (20%)
- ADR occurred
  - 36 (61%) cases in the 15-min(150 mg/kg) infusion,
  - 22 (37%) in the 4-h (50 mg/kg) infusion,
  - one (2%) in the 16-h (100 mg/kg) infusion
- The time from starting NAC infusion to the onset of ADR ranged from 0 to 122 min (median 32.5 min)

Results

Table 2 Frequency of *N*-acteylcysteine-related adverse effects recorded during the treatment of acute paracetamol overdose

Adverse reactions	Number of patients	Frequency (%)
Vomiting	23	39.0
Nausea	19	32.2
Urticaria	16	27.1
Flushing	15	25.4
Breathlessness	14	23.7
Pruritus	12	20.3
Angiooedema	7	11.9
Chest pain	7	11.9
Bronchospasm	6	10.2
Tachycardia	6	10.2
Paraesthesiae	3	5.1
Abdominal pain	2	3.4
Respiratory distress	1	1.7
Hypotension	1	1.7
Headache	1	1.7

Results

- In patients with a history of asthma,
  - minimal symptoms in two patients (17%),
  - moderate in six patients(50%)
  - severe in four patients(33%)
- compared with patients without asthma
  - minimal in 14 (30%),
  - moderate in 20 (43%)
  - severe in 13 (28%)

No significant difference (P = 0.771)

Results

- female patients,
  - minimal symptoms in 11 patients (32%), moderate in 12 (35%) and
  - severe in 11 (32%),
- compared with male patients,
  - minimal symptoms in five (20%),
  - moderate in 14 (56%) and
  - severe in six (24%)

No significant difference (P = 0.330)

Results

- Management of the ADR included
  - stopping the NAC infusion (n = 32, 54%);
  - antiemetics (n = 36, 61%),
  - histamine H-1 antagonists (n = 26, 44%),
  - corticosteroids (n = 16, 27%, of these 10 had moderate and 6 had severe symptoms),
  - inhaled b 2 agonists (n = 6, 10%), intramuscular adrenaline (n = 4,8%),
  - nebulized adrenaline (n = 2, 4%) and
  - slowing of the NAC infusion (n = 1, 2%)

Discussion

- the clinical features seen in this series of patients were similar to those reported previously
- we did not find that a higher plasma paracetamol concentration was protective against ADR to NAC
- The mean paracetamol concentration was the highest in the minimal symptom group and the lowest in the moderate symptom group

Discussion

- History of asthma and female sex has been identified previously as a predisposing risk factor for NAC ADRs, but this was not seen in our study

Discussion

- The treatments administered largely followed the guidelines of TOXBASE
- One major exception was the use of corticosteroids, which were administered in 27% of cases.
- Despite the fact that corticosteroids are not one of the drugs used first line when treating anaphylactoid reactions and are not routinely recommended in the above guidelines

Discussion

- Limitation:
  - retrospective case note review, relies on documentation of an ADR in the notes and documentation of the exact symptoms experienced
  - recording of a history of atopy may not be as accurate as that of other past medical conditions such as asthma
  - a proportion of the patients included in our study population may have coingested one or more other substances

Conclusion

- This study has confirmed the clinical pattern of NAC-ADRs and management of these ADRs is generally appropriate
- However, corticosteroids continue to be used inappropriately
- There is a need for improved education of those managing NAC-related ADRs to ensure that optimal management is provided

Thanks for your attention!