Acidosis, non-invasive ventilation and mortality in hospitalised COPD exacerbations

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ABSTRACT

Background Reports of non-invasive ventilation (NIV) use in clinical practice reveal higher mortality rates than in corresponding randomised clinical trials.

Aim To explore factors related to chronic obstructive pulmonary disease (COPD) admissions and NIV use that may explain some of the previously reported high mortality rates.

Methods National UK audit of clinical care of consecutive COPD admissions from March to May 2008. Retrospective case note audit with prospective case ascertainment. Participating units completed a web-based audit proforma of process and outcomes of clinical care.

Results 232 hospital units collected data on 9716 patients, mean age 73, 50% male. 1678 (20%) of those with gases recorded on admission were acidotic and another 6% became acidotic later. 1077 patients received NIV, 55% had a pH<7.26 and 49% (305/618) had or were still receiving high flow oxygen. 30% (136/453) patients with persisting respiratory acidosis did not receive NIV while 11% (15/131) of acidotic admissions had a pure metabolic acidosis and did. Hospital mortality was 25% (270/1077) for patients receiving NIV but 39% (86/219) for those with late onset acidosis and was higher in all acidotic groups receiving NIV than those treated without. Only 4% of patients receiving NIV who died had invasive mechanical ventilation.

Conclusions COPD admissions treated with NIV in usual clinical practice were severely ill, many with mixed metabolic acidosis. Some eligible patients failed to receive NIV, others received it inappropriately. NIV appears to be often used as a ceiling of treatment including patient groups in whom efficacy of NIV is uncertain. The audit raises concerns that challenge the respiratory community to lead appropriate clinical improvements across the acute sector.

BACKGROUND

Non-invasive ventilation (NIV) is an evidence-based treatment recommended for acute respiratory acidosis for defined patients admitted with exacerbations of chronic obstructive pulmonary disease (COPD).[1 2] A synthesis of the relevant randomised controlled trials (RCTs) has been used to produce national guidelines outlining the indications and practical issues around its use by acute hospital units.[3 4] The 2003 UK national COPD audit included data collection on the use of NIV in usual clinical practice and described survival rates significantly below those reported in RCTs used as a basis for the national recommendations.[5] Questions were raised about the appropriate application of NIV outside controlled trial conditions. While the 2003 audit data were unable to provide adequate explanations for the high mortality, the authors of the paper suggested 'confounding factors', unidentified factors and poor patient selection as probable reasons for the observed outcomes.

In 2008, the Royal College of Physicians (RCP), British Thoracic Society and the British Lung Foundation undertook a further round of national audit of the acute care of COPD patients admitted to hospital and included additional data items to further explore issues raised by the 2003 audit. This paper reports the findings of the 2008 national audit with reference to the use of NIV in COPD patients admitted with an exacerbation.

METHODS

The 2008 audit collected data in five different areas of COPD care and details can be viewed at http://www.rcplondon.ac.uk/clinical-standards/ceeu/Currentwork/ncrop/Pages/audit.aspx. All UK and island Trusts admitting COPD exacerbation patients were invited to participate in the audit programme and to collect data as acute units. The term 'unit' was used to describe each participating organisation and was defined as 'a hospital that admits acute unselected emergency admissions'. Thus, where a whole Trust participated in the audit, the term 'unit' refers to that Trust. Where a hospital participated as part of a Trust, the term 'unit' refers only to that hospital within the Trust. Participants were asked to define 'units' in terms of the functionality of their Respiratory Medicine Departments.

Units completed a retrospective case note audit of up to 60 consecutive patients with admissions identified prospectively between March and May 2008. An admission for COPD was defined as a senior physician made diagnosis on the post take ward round. The lead audit physician in each unit was encouraged to validate diagnoses at discharge and exclude cases where the diagnosis had subsequently been changed and to exclude cases where an admission diagnosis was not COPD but had subsequently been changed to COPD. Cases with radiological changes were included in the audit if the senior admitting physician defined the admission as exacerbation of COPD as the primary diagnosis. The audit collected items relating to process of care and clinical outcomes within 90 days of the index admission. Data were entered onto a bespoke web-based programme and collated centrally at the RCP. Patients were divided into

subgroups for purposes of analysis according to arterial blood gas pH measurements and whether they received NIV.

The reliability of the clinical case data was assessed by asking units to double enter data on the first five cases using a different auditor. The levels of reliability for 952 submitted cases were generally good with κ values of 0.60 and higher dominating with many over 0.80 (very good), but the reporting of the administration of high flow oxygen before admission was less good (κ 0.48) with κ values of between 0.40 and 0.59 regarded as representing 'fair' agreement. Data were analysed using SPSS (SPSS Inc. V15). Missing data values affect patient denominators and results presented as percentages will vary in their denominators accordingly. Binary-level data were compared between patient subgroups using either Fisher's exact test (2 subgroups) or the χ^2 test (>2 subgroups); numerical data were compared using either the Mann–Whitney test (2 subgroups) or the Kruskal–Wallis test (>2 subgroups). We used random effects logistic regression (STAT8, Stata corporation) to adjust for site clustering to give NIV treatment ORs for mortality adjusted for independent predictors. Variables adjusted in the logistic regression comprised of age (<65, 65–74, 75–84, 85+), performance score (5 levels), lowest acidotic pH (quintiles), initial pH (<7.26, 7.26–7.34, 7.35+), blood urea (≤7.1, >7.1), serum albumin (<34, 34+), CXR cancer (Yes/No), weight (tertiles), peripheral oedema (Yes/No), PaCO2(≤6.0, 6.0+), PO2 (<7.3, 7.3–8.0, >8.0), BIC (<23, 23–30, >30), Creatinine (tertiles) and acidotic prognostic group (groups 1, 2 and 3 as defined in this paper). Missing values for covariates were coded to preserve the full sample size in the regression. Reliability of the parameter estimates were checked and confirmed using the quadchk command within Stata.

Ethics approval was given by the University College Hospital/University College London MREC.

RESULTS

Patient characteristics

Clinical data for 9716 patients were received from 232 units within 177 of 184 (96%) of all eligible acute Trusts. The median number of cases contributed by units was 46, inter-quartile range (IQR) 29–58. Overall mean (SD) patient age was 73 (10) years and half (4906) were male. The mean (SD) FEV_1% predicted was 42% (18%) for the 5199/9716 for whom it was recorded. Where indicated 98% (8681/8863) of patients were described as 'white'. Four per cent (429) lived in sheltered accommodation and 5% (503) in a residential home, while 90% (8784) lived alone or with someone else in a flat or house. Thirty-nine per cent (3784) received some form of personal care. In-hospital mortality was 7.7% (745/9716) and mortality within 90 days of the admission date was 13.9% (1289/9300).

Arterial blood gases (ABG)

NICE COPD guidelines recommend an arterial blood gas be taken on admission (NICE 2004). Whether or not ABG were taken at admission was recorded in 99% (9596) of cases and 87% (8340) had gases taken. Twenty per cent (1678/8215) were acidotic on admission. Acidotic patients had higher levels (all at p<0.001) of residential placement (8% vs 4.5%), of receiving some form of care (45% vs 38%), a poor performance status (11% vs 6% chair or bed bound) and a pre-admission MRC dyspnoea score of 5 (41% vs 29%) compared with non-acidotic patients. Mean (SD) FEV_1% predicted when known for 866/1678 acidotic cases was 34% (17%), as compared with 42% (19%) for 3628/6537 non-acidotic cases, p<0.001. Asian/British Asian patients presented with a higher level of acidosis (31% 28/91) in the audit than other patients with known ethnicity (20%, 1516/7407), p=0.02. Of the 1678 who were acidotic on admission 45% (750) received NIV and of these 76% (558/736) were recorded as having one or more co-morbidities with 18% (132/736) having three or more co-morbidities, similar to the 77% (7439/9716) and 19% (1865/9716), respectively, for all patients.

NICE guidelines recommend that the aim of oxygen therapy is to maintain adequate levels of oxygenation without precipitating respiratory acidosis or worsening hypercapnia (NICE 2004). Fifty per cent of patients (4864/9176) were receiving oxygen at the time of the initial blood gas and 30% of these (1385/4685) received more than 28% or 4 l by nasal cannulae at that time. Thirty per cent (1491/5052 recorded) had received >35% oxygen in the ambulance prior to admission and 35% (491/1385) were still receiving this when admission gases were taken. There was a strong relationship between the timing since high flow oxygen was received and the degree and prevalence of acidosis in the admission arterial blood gas (table 1). High flow oxygen was received by 49% (305/618) who received NIV, and by 57% (243/425) of patients who received NIV and who were acidotic on admission, p=0.01. High flow oxygen was associated with subsequent ventilatory support (22%, 331/1491 vs 9%, 336/3561, p<0.001) and with higher in-hospital mortality (11.1% 165/1491 vs 7.2%, 256/3561, p<0.001). Patients who were acidotic on admission having received high flow oxygen, however, had similar in-hospital mortality as patients who were acidotic on admission and did not receive high flow oxygen (16.9%, 88/522 vs 14.9%, 60/403, p=0.47).

The arterial gas measurements recorded by the audit are summarised in table 2 in which 2143 patients with a recorded acidosis are also stratified into three groups. In the first group, 1225/2143 (57%) had their lowest pH on their initial admission ABG. In the second group of patients who also presented with acidosis, 453/2143 (21%), went on to have a lower pH recorded further into the admission. For this group, the median (IQR) time interval between initial blood gas and lowest blood gas pH was 5 h (2–24 h). The third group of patients 465/2143 (22%) had a normal range pH on admission, but became acidotic later in the admission. In this group, the median (IQR) time from admission to the lowest recorded pH was 24 h (7–72 h). These patients were no more likely to have co-morbidities recorded (79% vs 77%) and specifically no more likely to have diabetes (13% vs 11%) or cardiac disease (ischaemic heart disease 22% vs 26%; cardiac arrhythmia 9% vs 10%; other cardiovascular disease 18% vs 20%) recorded than patients admitted with a normal pH and who did not become acidotic later.

Table 1 Relationship between the interval since high flow oxygen was received and prevalence of acidosis and hypoxia in the admission arterial blood gas

	% with pH<7.35 on admission	% with PaO_2≤8.0 on admission
	% (N)	% (N)
Proportion of cases with:		
High flow oxygen not received before arterial gases taken	14 (403/2942)	38 (1143/2983)
Time interval between high flow oxygen stopped and blood gases taken:		
>60 min before gases	20 (107/537)	39 (211/538)
>15 but ≤60 min before gases	36 (127/350)	34 (120/352)
≤15 min before gases	52 (44/85)	33 (28/85)
χ^2 p value (comparing above three groups)	p<0.001	p=0.22
Still receiving high flow oxygen when gases taken	52 (244/471)	11 (53/479)

Table 2 Arterial blood gas results as recorded in the national audit for the three acidotic patient subgroups

		All cases on admission		ACIDOTIC on admission, this being the lowest pH (group 1)		ACIDOTIC on admission, later lowest pH ALSO ACIDOTIC (group 2)				NON-ACIDOTIC on admission, later lowest pH ACIDOTIC (group 3)			
						On admission		Later		On admission		Later	
pH			N=8215		N=1225		N=453		N=453		N=465		N=465
	<7.26	7%	557	35%	427	29%	130	60%	272	–	0	32%	151
	7.26–7.34	14%	1121	65%	798	71%	323	40%	181	–	0	68%	314
	7.35+	80%	6537	–	0	–	0	–	0	100%	465	–	0
	Median (IQR)	7.41 (7.36–7.45)		7.29 (7.22–7.32)		7.30 (7.25–7.32)		7.24 (7.18–7.27)		7.39 (7.36–7.41)		7.29 (7.23–7.32)	
Bic			N=7826		N=1144		N=438		N=432		N=452		N=445
	<23	14%	1096	16%	187	14%	61	17%	73	11%	48	23%	101
	23–30	65%	5104	51%	584	44%	191	39%	168	57%	256	46%	204
	>30	21%	1626	33%	373	42%	186	44%	191	33%	148	31%	140
	Median (IQR)	26 (24–30)		28 (24–32)		29 (25–34)		29 (24–35)		28 (25–32)		27 (23–32)	
PCO_2			N=8229		N=1197		N=453		N=452		N=462		N=465
	≤6.0	56%	4628	9%	107	5%	24	4%	16	39%	182	11%	49
	>6.0	44%	3601	91%	1090	95%	429	96%	436	61%	280	89%	416
	Median (IQR)	5.8 (4.9–7.2)		8.8 (7.3–10.9)		9.0 (7.6–10.5)		10.3 (8.7–12.4)		6.5 (5.4–7.6)		8.7 (7.3–10.1)	
PO_2			N=8231		N=1200		N=453		N=450		N=462		N=463
	<7.3	21%	1691	19%	230	35%	158	24%	109	38%	176	24%	113
	7.3–8.0	14%	1125	7%	87	9%	41	9%	39	13%	60	10%	47
	>8.0	66%	5415	74%	883	56%	254	67%	302	49%	226	65%	303
	Median (IQR)	8.9 (7.6–11.3)		10.4 (7.9–14.8)		8.6 (6.5–11.9)		9.3 (7.5–12.5)		8.0 (6.6–9.7)		9.1 (7.3–11.5)	

NICE guidance recommends that ABG be repeated regularly according to the response to treatment (NICE 2004). A repeat blood gas was taken for 1635/2143 acidotic patients and the time interval to the repeat gas was categorised as <1 h (26%, 430), ≥1 but <2 h (28%, 454), 2–4 h (21%, 349) and >4 h (25%, 402).

Non-invasive ventilation

Guidelines recommend that NIV be commenced within 1 h of admission in all patients in whom a respiratory acidosis persists despite maximum medical therapy (RCP 2008). Twelve per cent (1168/9716) of all patients received ventilatory support of whom 1032 (88%) received NIV alone, 45 (4%) NIV with invasive and/or doxapram, 88 (8%) invasive alone and 3 (0.3%) doxapram alone. While 70% (317/453) of patients with both admission and subsequent lower acidotic ABGs received NIV, this means that nearly one third of those with the greatest evidence base for effectiveness did not. Only 35% (433/1225) of those with an initial acidosis but subsequent better pH did so, as did 47% (219/465) of those admitted with a normal pH but who later developed acidosis, p<0.001. The time interval from admission to receiving NIV is summarised in table 3. Eight per cent (131/1650) of acidotic patients on admission with a known PaCO2 had a normal PaCO2 implying a metabolic cause for the deranged pH. Of these, 11% (15/131) received NIV. For 76 patients becoming acidotic after admission (group 3) with a $PaCO_2 \leq 6.0$ kPa on admission 7% (5) received NIV within an hour, 9% (7) within 1–3 h, 32% (24) within 3–24 h and 53% (40) after 24 h. This was similar to the 142 group three patients with $PaCO_2 > 6.0$ kPa on admission with 5% (7) receiving NIV within an hour, 9% (13) within 1–3 h, 42% (60) within 3–24 h and 44% (62) after 24 h. All but 7 group 1 and 8 group 2 patients who were acidotic on admission and who received NIV had PaCO2 values of 6.0 and above on admission.

Of patients with pH<7.26 on admission 66% (370/557) received NIV, compared to 34% (380/1121) with pH 7.26–7.34 and 5% (297/6537) if non-acidotic. Of patients with lowest pH<7.26 at any time 68% (577/850) received NIV, compared with 30% (392/1293) with lowest pH 7.26–7.34 and 1% (78/6078) with non-acidotic lowest pH. Of all 1077 NIV patients, 1047 had gases recorded and 55% (577) had a lowest pH of <7.26 (median 7.19 IQR 7.13–7.22), 37% (392) a lowest pH of 7.26–7.34 and 7% (78) were non-acidotic.

Mortality

In-patient mortality for those receiving NIV was 25% (270/1077) overall, but was 39% for those with late onset acidosis and receiving NIV (table 4). Overall, both patients treated with or not receiving NIV had higher in-patient mortality when admission respiratory rate was 30 or above. For those on admission with a respiratory rate <20, 24% (25/104) and 4% (63/1541), respiratory rate 20–29, 23% (128/549) and 5% (266/5144), respiratory rate 30+, 29% (108/369) and 7% (98/1333). Patients treated with NIV with a low bicarbonate (<23 mmol/l) at time of lowest recorded acidotic pH had a higher mortality than those with a normal or high bicarbonate (>30 mmol/l): In hospital—38% (52/136) versus 22% (83/379) versus 25% (101/398), p=0.001; within 90 days—41% (56/135) versus 29% (103/356) versus 34% (131/386), p=0.03. This overall in-hospital mortality was 12% (152/1225) in those admitted with acidosis this being the lowest pH, 24% (109/453) in those admitted with acidosis that subsequently was worse and 33% (153/465) in those with normal pH at admission but later onset acidosis. Of these patients with low bicarbonate only 1 with a pH<7.26 had a paCO2<6 kPa suggesting that the vast majority of these

Table 3 Time interval from admission to receiving NIV for patients

	ACIDOTIC on admission, this being the lowest pH (group 1)		ACIDOTIC on admission, later lowest pH ALSO ACIDOTIC (group 2)		NON-ACIDOTIC on admission, later lowest pH ACIDOTIC (group 3)	
	%	N=433	%	N=317	%	N=219
<30 min	17	75	7	23	2	5
30–60 min	20	86	14	44	4	8
1–3 h	32	140	31	98	9	20
3–24 h	25	109	38	119	38	84
Beyond 24 h	5	23	10	33	47	102

Table 4 Mortality

	Inpatient mortality:					90-day mortality*				
	For ALL Patients not receiving NIV		For ALL Patients receiving NIV		Fishers Exact test (NIV versus not NIV	For ALL Patients not receiving NIV		For ALL Patients receiving NIV		Fishers Exact test (NIV versus not NIV
	%	N	%	N		%	N	%	N	
ALL PATIENTS	5	475/8639	25	270/1077	<0.001	11	949/8269	33	340/1031	<0.001
Acidotic patients	14	165/1174	26	249/969	<0.001	22	246/1143	33	310/932	<0.001
Non-acidotic patients	4	246/5994	10	8/78	0.02	10	558/5727	21	15/73	0.005
No admission gases	4	64/1471	43	13/30	<0.001	10	145/1399	58	15/26	<0.001
ACIDOTIC on admission, this being the lowest pH (group 1)	9	70/792	19	82/433	<0.001	16	126/770	30	123/412	<0.001
ACIDOTIC on admission, later lowest pH ALSO ACIDOTIC (group 2)	21	28/136	26	81/317	0.28	32	42/133	31	95/305	0.99
NON-ACIDOTIC on admission, later lowest pH ACIDOTIC (group 3)	27	67/246	39	86/219	0.008	33	78/240	43	92/215	0.03
χ^2 p value (comparing above 3 groups)	p<0.001		p<0.001			p<0.001		p=0.003		

*Within 90 days from index admission.

cases were a mixed metabolic and respiratory acidosis. Patients with low bicarbonate had higher creatinine values (median 100 μmol/l, IQR 82–143, n=125) than other acidotic patients with a normal bicarbonate (median 85 μmol/l, IQR 66–112, n=358) or high bicarbonate (median 75 μmol/l, IQR 60–98, n=368), p<0.001.

In-patient mortality for patients with pH<7.26 on admission was 26% (98/370) for patients receiving NIV and 20% (38/187) if not receiving NIV, p=0.12; corresponding mortality for patients with pH 7.26–7.34 was 17% (65/380) with NIV and 8% (60/741), p<0.001. For patients in this pH range on admission with a persisting acidosis, 34% (110/323) did not receive NIV and of these 110 18% (20/110) died as an inpatient. For patients in this pH range on admission with a persisting acidosis who did receive NIV 21% (44/213) died as an inpatient. Of patients with acidosis at any time during admission in-patient mortality was 26% (249/969) with NIV and 14% (165/1174) without NIV, p<0.001, while 90-day mortality was 33% (310/932) and 22% (246/1143), respectively, p<0.001.

One thousand five hundred and thirty (16%) admissions had radiological changes described as consistent with pneumonia as did 223 (21%) of those who had received NIV. For each acidotic prognostic group mortality rates were higher for those with pneumonia, but there were no statistically significant differences. For all patients receiving NIV, in-patient mortality was 30% (67/223) with pneumonia and 24% (203/854) without pneumonia (p=0.06).

In the analysis of data from the 2003 national audit,[5] the main predictors of inpatient and 90-day mortality were age, performance score, lowest pH, initial pH, blood urea and serum albumin, oxygen saturation, CXR cancer, weight and peripheral oedema. Apart from oxygen saturation all these covariates were measured in the 2008 audit—and covariate adjustment for 2143 acidotic audit patients from the 2008 audit gave in-hospital and 90-day mortality odds for NIV treatment of 1.35 (95% CI 1.02 to 1.77) and 1.10 (95% CI 0.86 to 1.40), respectively. Adjusting further for acidotic prognostic group gave 1.29 (95% CI 0.98 to 1.71) and 1.09 (95% CI 0.85 to 1.40), respectively, and further for initial PaCO2, PO2, BIC and Creatinine gave 1.33 (95% CI 1.00 to 1.78) and 1.06 (95% CI 0.82 to 1.37).

Documentation of ventilatory plan

National guidelines recommend that a plan of action in the event of failure to respond to NIV be documented in the case notes (RCP 2008). For 60% (643/1077) of NIV patients a plan of what to do in the event of failure was documented, but for 12% (32/270) of those dying in hospital no plan was recorded. For 40% (431/1077) treated with NIV a Do Not Resuscitate order was signed, but for 30% (82/270) of NIV patients who died no order was evident. Fifty per cent (1079/2143) of patients with a recorded acidosis did not receive any form of ventilatory support. The reasons documented for not providing ventilatory support were: patient responded to medical therapy (60%, 648), medical decision not to escalate (14%, 149), patient refused NIV (4%, 38), no facilities available (3%, 30), failed (n=4). No apparent reason to withhold NIV or invasive ventilation could be discerned by auditors in 19% (210) of cases.

The 2008 NIV guidelines recommend that a decision not to escalate to invasive ventilatory support should be taken by a consultant (RCP 2008). For 11% (16) of the 149 cases where a medical decision was made not to escalate to NIV this decision was documented as being made by a Senior House Officer equivalent or more junior (Foundation Year 1[FY1]/Foundation Year 2[FY2]/Specialty Trainee year 1 or 2 [ST1/2] now Core Trainee year 1 [CT1/2]). In 50% (75/149), the decision was taken by a Specialist Registrar or ST 3–5. The following reasons were given for not escalating to NIV: poor pre-morbid functional status, multiple co-morbidities, malignant disease, patient's wishes, previously failed trial of NIV, metabolic acidosis.

Invasive mechanical ventilation (IMV)

NICE guidance states that patients with exacerbations of COPD should receive treatment on intensive care units, including invasive ventilation, when this is thought to be necessary (NICE 2004). Only 1% (122/9716) of patients in 91 of 232 units received IMV. Five per cent (110/2143) of all acidotic patients received it, as did 5% (38/745) of all inpatient deaths and 3% (44/1289) of all those who died within 90 days. Some 3.2% (34/1077) of all NIV patients went on to receive IMV including 3.3% (9/270) of NIV patients who died as an inpatient and 2.6% (9/340) of NIV patients who died within 90 days.

DISCUSSION

This study of the clinical care of 9716 patients admitted with COPD contains the largest group of prospectively identified patients treated with NIV in the literature. We report findings similar to those of the 7529 patients described in the 2003 National Audit.[5] In essence, patients treated in usual clinical practice with NIV appear to have much poorer outcomes than those reported in the RCTs on which the recommendations for

the use of NIV are based.[6–9] In fact the observed mortality in patients treated with NIV is higher than patients matched by arterial blood gas pH who do not receive NIV and is similar to that of the control group in the YONIV trial.[9] The data reported offer a number of explanations for these findings that in summary suggest that the patients treated in usual clinical practice are different from those included in the RCTs with many having severe acidosis with NIV used as the ceiling of care. It is also seen that some with metabolic acidosis receive NIV inappropriately while a proportion of patients who meet the RCT inclusion criteria of persisting respiratory acidosis do not receive NIV.

We have identified three groups of COPD patients defined by the timing of acidosis who have very different prognoses when managed by NIV. Those admitted with acidosis whose repeat gases improve have the best outcome followed by those who have two sets of acidotic gases. For these groups, the audit raises significant concerns about the standard of medical management. The first is the use of relatively high flow rates of oxygen prior to and after admission where there is not only a significant relationship with the degree of admission acidosis (table 1) but also adverse outcomes of need for ventilatory support and death. The second is the potential impact of delay in initiation of NIV after admission. National guidelines recommend the application of NIV if after 1 h of usual medical management ABG, patients fail to respond.[4] In those whose worse ABG was on admission less than a half of these patients received NIV within the first hour and 30% after at least 3 h had passed (table 3). While there may be concerns that NIV could be administered too quickly and unnecessarily in cases of oxygen poisoning the evidence here suggests delayed initiation. For those whose acidotic arterial pH deteriorated following admission less than a quarter received NIV in the first hour and 48% following at least a 3 h interval (table 3).

The third group identified comprises those patients admitted without acidosis but who then develop this later in the admission. Their outcome is particularly poor with mortality rates approaching five times that reported in the RCTs and clinicians may be falsely reassured by a normal admission pH. It is likely from the blood gas analysis that some of these patients have a mixed metabolic/respiratory acidosis while a pure metabolic acidosis seems to be the exception. There is little in the NIV literature relevant to this group although Moretti[10] describes a group of late acidosis patients with a particularly poor prognosis if managed using NIV rather than IMV but these patients were admitted with acidosis and later relapsed after initial improvement on NIV. Patients with a low arterial blood bicarbonate level have worse outcomes. These patients are more likely to have renal impairment too but for most this is mild. It is important that physicians managing these patients do not over-rely on NIV to correct an acidosis that has an underlying metabolic component and arguably such patients when identified may be better managed on an HDU/ICU facility.

It appears that in clinical practice a range of severely acidotic patients are treated with NIV as the sole means of ventilatory support. In RCTs that have examined this approach as first line management intubation rates in severe acidotic COPD are over 50% and if accompanied by pneumonia as high as 100%.[11–14] Although subject numbers in prospective studies are small, the results of this clinical audit are consistent with the trials. It is clear that most patients receiving NIV have severe acidosis and a high mortality and for whom published guidelines suggest IMV should be considered sooner rather than later.[3 4] In the audit, only 1% of admissions and only 5% of all acidotic patients in only 91 of 232 secondary care centres received IMV. Only 3% of those with NIV and 3% of those managed initially with NIV but who subsequently died received IMV. We neither know how many of the NIV patients were managed in HDU and ICU beds where access to IMV was optimal[14] nor know the exact circumstances for the low rate of ventilatory support recorded. We can note the low IMV rates observed here compared against the higher ventilation rates recorded in the USA[15] the reported inconsistency in decision making within the UK that may deny patients life saving treatment[16 17] and COPD patient studies demonstrating preferences for ITU care and IMV.[18] What is known is that in 12% of cases managed with NIV who subsequently died there was no plan in the case notes of what the ceiling of treatment was in the event of failure of NIV. In 30% of cases who died following NIV a 'Do Not Resuscitate' order was not signed. Of those acidotic patients not given even NIV this decision was taken by a very junior trainee in 11% of cases and in a further 50% by a registrar grade doctor.

In contrast, the group of patients for whom there exists the strongest evidence base for the effectiveness of NIV, those with a pH range of 7.26<7.35, form only a minority of those overall receiving NIV. While case by case reasons for this are not known in detail, it was stated in 60% of acidotic patients who did not receive NIV that they had responded to medical therapy and the data concerning receipt of high flow oxygen therapy prior to admission give the cause for concern here. Some of these patients will improve simply by reducing oxygen flow while others may receive NIV inappropriately and this is to an extent justified by the better overall survival figures for this group (17% if treated with NIV and 8% if managed without if admission pH 7.26<7.35). However, 34% of patients with an admission pH in the 7.26<7.35 range but with a persisting acidosis where the indication for NIV is strongest did not receive NIV and 18% of these patients died. In addition, in 3% of acidotic admissions there were no NIV facilities available and in 19% of cases the auditors were unable to discern a documented reason for not offering NIV.

This report is limited in the conclusion that can be drawn as the details of decision making over individual cases are not available beyond the descriptions given above. This was not a prospective RCT but a survey of current clinical practice. In some instances data are missing specifically the FEV_1 in 46% cases to confirm the diagnosis of COPD. Audit reporting may contain inaccuracies particularly in the giving and timing of high flow oxygen pre-admission. This is, however, a comprehensive snapshot of care in nearly every UK secondary care unit and is based upon nearly 10 000 clinical cases of whom over a 1000 received NIV dwarfing the data of any existing prospective clinical trial. The data from this audit are entirely consistent with those collected from 7529 admissions in 2003[19] of whom 26% had acidosis recorded at some time in the admission and of whom 31% (529) received NIV with a 26% in-hospital mortality.[5]

This study has provided data that explain some of the high mortality observed among acidotic patients admitted to hospital and treated with NIV. It also raises concerns about the use of high flow oxygen, the timing of ABG and initiation of NIV and the management of acidosis in the presence of metabolic disturbance. Equally the report highlights a proportion of eligible patients with an arterial pH range demonstrated in randomised trials to benefit from NIV who do not go on to receive NIV in usual clinical practice. NIV appears to be used as the ceiling of treatment in very sick patients with an often poorly defined escalation pathway determined by junior medical staff. Acute physicians, general physicians and geriatricians on call, emergency staff, anaesthetists and intensivists all initiate and manage

COPD patients using or not using NIV. The challenge to the respiratory community is to respond to the audit findings by defining optimum care for the whole range of acidotic patients seen in clinical practice and to implement national standards fully leading by example.

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REFERENCES

1. **Ram FSF,** Picot J, Lightowler J, Wedzicha JA. Non-invasive positive pressure ventilation for treatment of respiratory failure due to exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2004;(3):CD004104.
2. **National Institute for Clinical Excellence (NICE).** Chronic obstructive pulmonary disease: national clinical guideline for management of chronic obstructive pulmonary disease in adults in primary and secondary care. *Thorax* 2004;**59**(Suppl 1):1—232.
3. **British Thoracic Society Standards of care committee.** Non-invasive ventilation in acute respiratory failure. *Thorax* 2002;**57**:192—212.
4. **Roberts CM,** Brown JL, Reinhardt AK, *et al*. Non-invasive ventilation in chronic obstructive pulmonary disease. Management of type 2 respiratory failure. *Clin Med* 2008;**8**:517—21.
5. **Kaul S,** Pearson MG, Coutts I, *et al*. Non-invasive ventilation (NIV) in the clinical management of acute COPD in 233 UK hospitals. Results from the RCP/BTS 2003 national COPD audit. *COPD* 2009;**6**:171—6.
6. **Brochard L,** Mancebo J, Wysocki M, *et al*. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med* 1995;**333**:817—22.
7. **Kramer N,** Meyer TJ, Meharg J, *et al*. Randomized prospective trial of noninvasive positive pressure ventilation in acute respiratory failure. *Am J Respir Crit Care Med* 1995;**151**:1799—806.
8. **Celikel T,** Sungur M, Ceyhan B, *et al*. Comparison of noninvasive positive pressure ventilation with standard medical therapy in hypercapnic respiratory failure. *Chest* 1998;**114**:1636—42.
9. **Plant PK,** Owen JL, Elliot MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomised controlled trial. *Lancet* 2000;**19**:1931—5.
10. **Moretti M,** Cilione C, Tampieri A, *et al*. Incidence and causes of non-invasive mechanical ventilation failure after initial success. *Thorax* 2000;**55**:819—25.
11. **Honrubia T,** Garcia Lopez FJ, Franco N, *et al*. Noninvasive vs conventional mechanical ventilation in acute respiratory failure: a multicenter, randomized controlled trial. *Chest* 2005;**128**:3916—24.
12. **Conti G,** Antonelli M, Navalesi P, *et al*. Noninvasive vs. conventional mechanical ventilation in patients with chronic obstructive pulmonary disease after failure of medical treatment in the ward: a randomized trial. *Intensive Care Med* 2002;**28**:1701—7.
13. **Phua J,** Kong K, Lee KH, *et al*. Non invasive ventilation in hypercapnic respiratory failure due to chronic obstructive pulmonary disease vs. other conditions: effectiveness and predictors of failure. *Intensive Care Med* 2005;**31**:533—9.
14. **Nava S,** Hill N. Non-invasive ventilation in acute respiratory failure. *Lancet* 2009;**374**:250—9.
15. **Cannon KT,** Sarrazin MV, Rosenthal GE, *et al*. Use of mechanical and noninvasive ventilation in black and white chronic obstructive pulmonary disease patients within the Veterans Administration health care system. *Med Care* 2009;**47**:1537—48.
16. **Wildman M,** O'Dea J, Kostopolou O, *et al*. Variation in intubation decisions for patients with chronic obstructive pulmonary disease in one critical care network. *QJM* 2003;**96**:583—91.
17. **Wildman MJ,** Sanderson CFB, Groves J, *et al*. Survival and quality of life for patients with COPD or asthma admitted to intensive care in a UK multicentre cohort: the COPD and Asthma Outcome Study (CAOS). *Thorax* 2009;**64**:128—32.
18. **Wildman M,** Sanderson C, Groves J, *et al*. Implications of prognostic pessimism in patients with chronic obstructive pulmonary disease (COPD) or asthma admitted to intensive care in the UK within the COPD and asthma outcome study (CAOS): multicentre observational cohort study. *BMJ* 2007;**355**:1132—5.
19. **Price LC,** Lowe D, Hosker H, *et al*. The UK national Audit 2003: impact of hospital resources and organisation of care on patient outcome following admission for acute COPD exacerbation. *Thorax* 2006;**61**:837—42.