

A national survey of the management of delirium in UK intensive care units

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Summary

Background: Delirium is an acute organ dysfunction common amongst patients treated in intensive care units. The associated morbidity and mortality are known to be substantial. Previous surveys have described which screening tools are used to diagnose delirium and which medications are used to treat delirium, but these data are not available for the United Kingdom.

Aim: This survey aimed to describe the UK management of delirium by consultant intensivists. Additionally, knowledge and attitudes towards management of delirium were sought. The results will inform future research in this area.

Methods: A national postal survey of members of the UK Intensive Care Society was performed. A concise two page questionnaire survey was sent, with a second round of surveys sent to non-respondents after 6 weeks. The questionnaire was in tick-box format.

Results: Six hundred and eighty-one replies were received from 1308 questionnaires sent, giving a response rate of 52%. Twenty-five percent of respondents routinely screen for delirium, but of these only 55% use a screening tool validated for use in intensive care. The majority (80%) of those using a validated instrument used the Confusion Assessment Method for the Intensive Care Unit. Hyperactive delirium is treated pharmacologically by 95%; hypoactive delirium is treated pharmacologically by 25%, with haloperidol the most common agent used in both. Over 80% of respondents agreed that delirium prolongs mechanical ventilation and hospital stay and requires active treatment.

Conclusions: This UK survey demonstrates screening for delirium is sporadic. Pharmacological treatment is usually with haloperidol in spite of the limited evidence to support this practice. Hypoactive delirium is infrequently treated pharmacologically.

Introduction

Delirium is a common, potentially preventable syndrome¹ that can be regarded as an acute brain dysfunction.² The reported incidence of delirium in mechanically ventilated patients treated in intensive care units (ICUs) is up to 67%.³ Delirium in ICU is associated with increased duration of mechanical ventilation,³ ICU length of stay⁴ and hospital stay.⁴ Furthermore, mortality in the 6 months following an episode of ICU delirium is increased 3-fold over those patients without delirium even after adjusting for severity of illness, and other potential confounding variables;³ long-term survival is also more than halved in cases of non-ICU delirium.⁵ A longer duration of delirium in ICU is associated with increased mortality.⁶ Additional non-ICU based studies have demonstrated that survivors of episodes of delirium suffer a more rapid functional decline,^{7,8} increased rates of admission to nursing homes⁸ and a greater risk of the subsequent development of cognitive impairment.⁹

The economic costs of delirium are significant. Each additional day spent with delirium is associated with a 20% increased risk of prolonged hospitalisation, translating to an average of over 10 additional hospital days.³ A UK intensive care bed cost between £1200 and £1800 per day in 2006–07.¹⁰ In the USA delirium is associated with a 39% increase in ICU costs, a 31% increase in hospital costs,¹¹ and an attributable Medicare bill estimated at \$6.9 billion annually.¹²

Delirium exists in three forms, a hyperactive form manifest as agitation, a hypoactive form characterised by a withdrawn, quiet state and a mixed form which fluctuates between the hyperactive and hypoactive forms.¹³ Without the use of a screening tool, ~65% of patient days with delirium in the ICU are missed.¹⁴ The routine use of a validated tool for diagnosing delirium in mechanically ventilated patients has been specifically recommended in critical care guidelines.¹⁵ Six screening tools have been reported for use in the ICU¹⁶ but the only validated tools are the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU),^{17,18} the Intensive Care Delirium Screening Checklist (ICDSC)¹⁹ and the NEECHAM confusion scale.²⁰

Given the incidence and associated morbidity of this condition, there is a surprising paucity of evidence to guide treatment. Although haloperidol is recommended in the Society of Critical Care Medicine (SCCM) guideline¹⁵ the evidence for this is limited. A retrospective observational study demonstrated an improvement in mortality in mechanically ventilated patients treated with haloperidol.²¹ Studies in non-critically ill patients have

also reported positive findings. A prospective study in patients undergoing general surgery showed haloperidol to be effective in reducing the incidence of post-operative delirium.²² Additionally, a prospective study of patients after hip fracture showed that although haloperidol was ineffective in preventing delirium, it reduced the duration and severity of the condition.²³ Evidence from outside the ICU setting has also accumulated against the use of haloperidol. A recent meta-analysis in patients with dementia found an association between the chronic use of antipsychotics and premature death.²⁴ Two community based retrospective cohort studies also identified an association between the chronic use of antipsychotics and the risk of pneumonia and death, although these studies did not correct for confounding risk factors.^{25,26} Adding to this uncertainty, a very recent study has report no increased risk with either atypical or typical antipsychotic medications in the management of elderly patients with dementia.²⁷ This lack of data to inform the management of delirium is reflected in recent Cochrane systematic reviews on delirium which have concluded data on the effectiveness of pharmacological therapy to prevent and treat delirium were limited and that further studies in the prevention and treatment of delirium were needed.^{28,29} A separate Cochrane review recommends not using benzodiazepines for the management of hyperactive delirium.³⁰

Against this background of an under diagnosed condition with an associated heavy burden of morbidity and mortality, and treatments with uncertain efficacy and safety, the aim of this survey was to define the current management of delirium in ICUs in the UK to inform future research into the prevention and treatment of delirium in ICU.

Methods

A postal survey (Appendix 1) was mailed to all members of the UK Intensive Care Society in June 2008. The questionnaire consisted of three sections. The first section determined the type of ICU the member worked in, and which screening tools were routinely used in that unit to detect delirium. The second section described two clinical vignettes, one of hyperactive delirium and the other of hypoactive delirium. The first vignette described a 60-year-old female receiving mechanical ventilation for pneumonia. She developed hyperactive delirium which hindered weaning and placed her at risk of self harm. The second vignette described a 56-year-old spontaneously ventilating male with a fractured pelvis who developed hypoactive delirium. Respondents were asked which medication,

or medications, they would use as first and second line pharmacological treatments. The dose, route and frequency of administration were also sought. The third section consisted of five statements regarding delirium with which the respondents were asked to rate their agreement with on a five point Likert item. A score of 1 equalled a strong disagreement, 3 was a neutral view and 5 was a strong agreement. The questionnaire was in tick-box format, with an open-text section to allow recording of prescribing practice for the management of the delirium vignettes.

Each questionnaire had a unique identifier number to allow responses to be tracked but was otherwise anonymous. A prepaid addressed envelope was attached to facilitate ease of reply. A second round of questionnaire surveys was posted to non-respondents 6 weeks later. When two replies were received from the same respondent, only the first round questionnaire was analysed. As only medical practitioners prescribe pharmacological treatments and because consultants determine ICU treatment policies and protocols, in the first instance it was decided to investigate consultant practice only.

Results

A total of 1308 questionnaires were sent to consultants and 681 replies were received, giving a response rate of 52%. Six hundred and seventy (51%) replies were analysable. Non-analysable responses were predominantly received from retired intensivists and clinicians no longer working in intensive care.

The majority of intensivists worked in general ICUs (89%), with smaller numbers working in specialty-specific units. Many respondents worked in more than one ICU. Fourteen percent worked in neuroscience ICUs, 7.5% in cardiac surgical ICUs, 4% in burns ICUs and 3% worked only in high dependency units.

Seventy-five percent of respondents did not use a delirium screening tool. Thirteen different tools were used to screen for the presence of delirium. Fourteen percent of respondents used a tool validated for intensive care. Of those who used a validated screening tool, 80% reported using CAM-ICU (Table 1). Other non-validated tools reported to be used in ICU as means of detecting delirium included the Mini-Mental State Examination, Delirium Rating Scale, Richmond Agitation-Sedation Scale, Ramsay Sedation Score and clinical assessment.

Hyperactive delirium was managed pharmacologically by 95% of respondents. The commonest

first choice pharmacological treatment for hyperactive delirium was haloperidol which was used by 74% of respondents; 49% on an as required basis and 25% on a regular dosing basis (Figure 1a). Four-hundred and ninety-eight respondents chose

Table 1 Screening tools used for detecting delirium

None Used	75%
Confusion Assessment Method-ICU	11%
Mini-Mental State Examination	7.9%
Delirium Rating Scale	3.7%
Intensive Care Delirium Screening Checklist	2.7%
Neecham Confusion Scale	0%
Other	2.2%
Not answered	0.75%

Percentages are for the number of intensivists who would use that particular screening tool, regardless of whether they would also consider using a different tool.

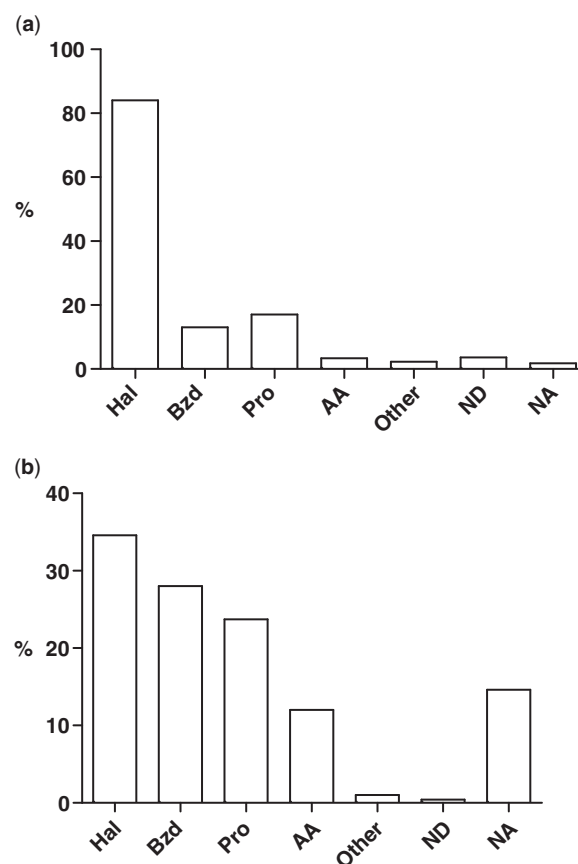


Figure 1. First line (a) and second line (b) treatment for hyperactive delirium. As some respondents used more than one medication values refer to the percentage of intensivists who used that particular medication. Hal, haloperidol; Bzd, benzodiazepine; Pro, propofol; AA, atypical antipsychotic; ND, no drugs; NA, not answered.

haloperidol as their first treatment for hyperactive delirium. Of this total, 321 (64%) specified a starting dose for haloperidol with 268 (83%) using a dose of 5 mg or less (Table 2). Haloperidol was also the most popular second line agent for the treatment of hyperactive delirium, although benzodiazepines, propofol and no pharmacological treatment were also commonly used therapeutic options (Figure 1b). Many respondents chose haloperidol on an as required basis as their first choice, but scheduled it regularly as their second choice, or vice versa. Of the 232 respondents who chose haloperidol as their second line agent, 117 (50%) specified a starting dose. Ninety-five (81%) again started with a dose of 5 mg or less.

In the management of hypoactive delirium 73% would not use medications as first line therapy. Haloperidol was over 5-fold more commonly prescribed than the next most frequent agent, atypical antipsychotics (Figure 2a). Haloperidol remained the most common pharmacological therapy as second line treatment, but was used by only 13% who replied to the question (Figure 2b). Again, the majority of haloperidol prescribers would use a starting dose of 5 mg or less for hypoactive delirium (Table 2).

The majority of respondents agreed or strongly agreed that delirium requires active treatment, prolongs both mechanical ventilation and hospital stay, and is associated with increased mortality. A minority consider delirium to be a risk factor for the subsequent development of dementia (Table 3).

Discussion

Although guidelines exist to assist management of delirium in the critically ill patient, the evidence is limited. This survey sought to determine current

management of this common condition in the UK. This survey demonstrates that UK intensivists, when prompted by written questions, appear to recognise delirium as a serious condition which is associated

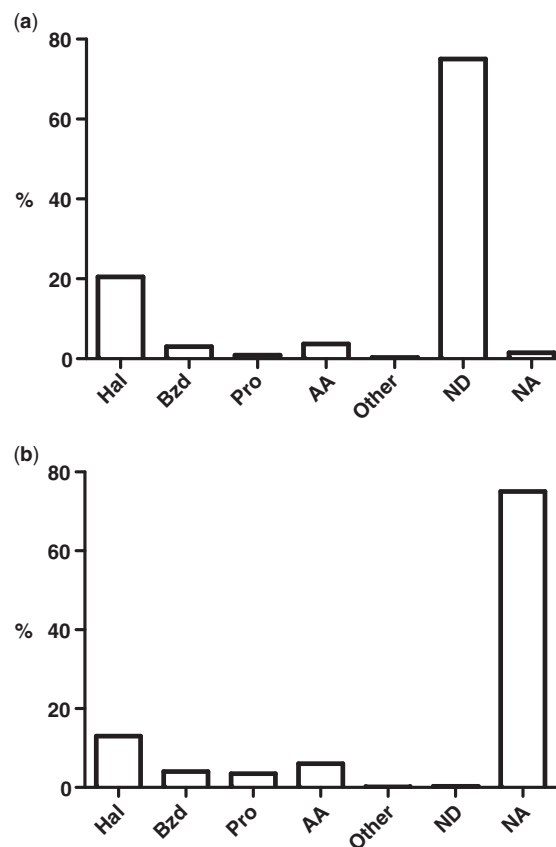


Figure 2. First line (a) and second line (b) treatment for hypoactive delirium. As some respondents used more than one medication values refer to the percentage of intensivists who used that particular medication. Hal, haloperidol; Bzd, benzodiazepine; Pro, propofol; AA, atypical antipsychotic; ND, no drugs; NA, not answered.

Table 2 Haloperidol dosing for delirium

	Hyperactive treatment		Hypoactive treatment	
	First line	Second line	First line	Second line
Respondents using haloperidol (n)	498 (74%)	232 (35%)	136 (20%)	88 (13%)
Respondents stating dose	321 (64%)	117 (50%)	79 (58%)	38 (43%)
Of those who specified a dose				
2.5 mg	61 (19%)	20 (17%)	20 (25%)	10 (26%)
5 mg	67 (21%)	21 (18%)	15 (19%)	5 (13%)
2.5–5 mg	91 (28%)	32 (27%)	21 (27%)	9 (24%)
Other doses <5 mg	49 (15%)	22 (19%)	13 (16%)	6 (16%)
>5 mg	53 (17%)	22 (19%)	10 (13%)	8 (21%)

Percentages are for the number of intensivists who would use that particular treatment, regardless of whether another treatment was also chosen.

Table 3 Respondents were asked to agree with each statement on a five point Likert item in response to five statements regarding delirium^a

Statement	Strongly disagree	Disagree	Neutral	Agree	Strongly agree	(%)
1. Delirium is a problem that requires active treatment	2	2	12	57	25	
2. Delirium is associated with prolonged mechanical ventilation	2	6	12	54	24	
3. Delirium in ICU is associated with prolonged hospital stay	1.5	3	10	56	27.5	
4. Delirium is associated with increased hospital mortality	2	5	27	47	17	
5. Delirium is a risk factor for subsequent dementia	4.5	24	53	13	3.5	

^aTwo percent of respondents did not answer this section. Values correspond to the total percentage of intensivists who felt that response most accurately reflected how much they agreed with each statement.

with prolonged mechanical ventilation, prolonged hospital stay and increased hospital mortality. Respondents felt hyperactive delirium requires active pharmacological management; however, in contrast, most believed that hypoactive delirium did not require pharmacological treatment. Only 25% of intensivists routinely screen for delirium and just 14% use a tool validated in mechanically ventilated patients. This finding is not unique to the UK and has been replicated across the world. In Europe, only 7% of all Dutch ICUs use a validated screening tool.³¹ In Australia and New Zealand only 9% of ICUs use a screening tool,³² and in predominantly American samples only a minority routinely assessed for delirium with a specific tool.^{33,34} The mismatch between the high self-reported awareness of the problem, and the low screening tool use, suggests that clinicians may not attach the importance to delirium that their responses suggest. Alternatively, clinicians may not screen for delirium due to other reasons, including a lack of knowledge of available screening tools, a lack of evidence for current treatments or unavailability in the UK of medications such as dexmedetomidine. Despite only three delirium screening tools being validated for use in the ICU, the use of 13 different tools to identify delirium was reported. Of note some of these instruments are not designed to screen for delirium, suggesting that at least some clinicians who use screening tools may not be aware which instruments are optimal for delirium screening.

Hyperactive delirium, although easier to diagnose,³⁵ is much less common³⁶ and much more likely to be treated pharmacologically in this survey. In contrast, hypoactive delirium which is more common and also associated with a worse clinical outcome,³⁷ paradoxically is much less likely to be treated with medication in the UK. As potentially a large improvement in outcome might be seen with therapy in this hypoactive group, this is an area that requires investigation. It is possible that

hypoactive delirium is not treated pharmacologically due to a lack of efficacy data for haloperidol or other pharmacological treatments.

The SCCM guidelines¹⁵ recommend the use of haloperidol for the treatment of delirium on ICUs. When delirium is treated pharmacologically, haloperidol is the most commonly used agent for both hyperactive and hypoactive forms in this survey. Haloperidol has also been reported in other international surveys as the most popular choice for treating delirium.^{33,34} Given the increasing recognition of delirium,³⁴ it is likely that haloperidol will be more frequently prescribed. In light of non-ICU based studies suggesting an unfavorable safety profile with both typical and atypical antipsychotics^{24–26} the place of haloperidol in the prevention or treatment of delirium remains to be confirmed.

Positron emission tomography studies show the optimal degree of dopamine D2 receptor blockade to successfully treat episodes of first psychosis in schizophrenia is 65–70%^{38,39} and equates to a daily total dose of 2–5 mg haloperidol orally over a two-week period.³⁹ Higher daily doses are associated with an increase in D2 receptor blockade and resulting extrapyramidal symptoms.³⁹ The optimal dose of haloperidol in delirious critically ill patients is currently unknown. For the treatment of hyperactive delirium, 83% of respondents used a starting dose of 5 mg or less. The most commonly used dosing regime specified in this survey was 2.5–5 mg intravenously every 6 h, equating to a total daily dose of 10–20 mg. The recently completed MIND pilot study, although small, identified no serious adverse events with this haloperidol dosing regime in critically ill patients.⁴⁰ Studies comparing haloperidol with other therapies for the management of delirium in ICU have been performed. Extrapyramidal side effects were noted with haloperidol, but not with the atypical antipsychotic olanzapine, for the treatment of delirium.⁴¹ A pilot study suggests dexmedetomidine may be

superior to haloperidol for hyperactive delirious ICU patients, being associated with both decreased time to extubation and length of stay in ICU.⁴²

The response rate of 52% was similar to another postal survey of delirium in critical care (58%).⁴³ It has been shown that the average response for physician postal surveys is 61%⁴⁴ and our response rate is in line with this. The survey was designed using methods known to improve response rates such as the use of personally addressed letters, short questionnaires, prepaid self-addressed envelopes and providing non-respondents with a second copy of the questionnaire.⁴⁴ Our sample size of 670 is comparable with previous international critical care delirium survey samples of 912³³ and 130.⁴³ Clinical vignettes, which have been shown to be a valid tool for measuring clinical practice,⁴⁵ were used to assess treatment of hyper- and hypo-active delirium.

This survey has several limitations. It is possible the results may be confounded by a self-selected sampling bias. The tick box format of the questionnaire, designed to maximise response rate, led to a relatively closed selection choice possibly influencing responses. A proportion of respondents failed to provide full dosing specifications which limit the interpretation of the data in relation to the dosing regimen used. Finally, the reasons for not using a screening tool or for choosing not to treat delirium were not addressed in this survey.

Conclusion

UK consultant intensivists seem to recognise the significance of delirium in critically ill patients but despite this screening with validated tools is uncommon and hypoactive delirium is rarely treated. Haloperidol is the most common agent chosen to treat both hyper- and hypo-active delirium, in spite of concerns about side effects in non-ICU populations. This survey was undertaken to provide information on usual care of delirium in critically ill patients in the UK to help plan a multicentre placebo controlled effectiveness trial of haloperidol in the management of delirium in ICU, and suggests that, at least in patients with hypoactive delirium, such a trial could be undertaken. An adequately powered trial would clearly establish the incidence of delirium in the UK, determine whether delirium *per se* causes prolonged ICU stays and poor outcomes (attributable harm), establish the relative efficacy of haloperidol in hyper- and hypo-active delirium, and generate safety data. It is unlikely that more observational studies will significantly progress knowledge in this area.

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Appendix 1: Delirium Questionnaire, June 2008



DELIRIUM QUESTIONNAIRE JUNE 2008



About you and your ICU.....

Are you a?

☐ Consultant ☐ Trainee doctor ☐ SAS doctor ☐ Nurse ☐ Physiotherapist ☐ Other

Where do you regularly work? (tick all that apply)

☐ General ICU ☐ Neurosciences ICU ☐ Cardiothoracic ICU ☐ Burns ICU ☐ Discrete HDU

Does your unit use any of these tools routinely to screen for delirium? (tick all that apply)

☐ CAM-ICU ☐ Delirium rating scale ☐ Delirium screening checklist ☐ Mini Mental State Examination ☐ Other Specify:.....

About your practice.....

Two brief scenarios are presented, followed by a number of treatment options. For each scenario please indicate by ticking the appropriate box which treatment option would be your first and second choice. Assume all treatable causes (metabolic etc) of delirium have been corrected.

Scenario 1: A 60-year-old female patient ventilated for community acquired pneumonia develops acute agitated delirium. She is at risk of self harm and her weaning is hampered.

What would you (or the prescribers on your unit) do:

	First line	Second line	Please state which drug, usual dose used, route given and dose interval
Prescribe an atypical antipsychotic agent (risperidone or similar)?	<input type="checkbox"/>	<input type="checkbox"/>	
Prescribe PRN haloperidol?	<input type="checkbox"/>	<input type="checkbox"/>	
Prescribe regular haloperidol?	<input type="checkbox"/>	<input type="checkbox"/>	
Prescribe benzodiazepines?	<input type="checkbox"/>	<input type="checkbox"/>	
Prescribe propofol?	<input type="checkbox"/>	<input type="checkbox"/>	
Not use any drugs?	<input type="checkbox"/>		

Scenario 2: A 56-year-old spontaneously ventilating male patient with a fractured pelvis develops hypoactive delirium (Altered mental status with inattention plus disorganised thinking or reduced level of consciousness.) What would you (or the prescribers on your unit) do:

	First line	Second line	Please state which drug usual dose used, route given and dose interval
Prescribe an atypical antipsychotic agent (risperidone or similar)?	<input type="checkbox"/>	<input type="checkbox"/>	
Prescribe PRN haloperidol?	<input type="checkbox"/>	<input type="checkbox"/>	
Prescribe regular haloperidol?	<input type="checkbox"/>	<input type="checkbox"/>	
Prescribe benzodiazepines?	<input type="checkbox"/>	<input type="checkbox"/>	
Prescribe propofol?	<input type="checkbox"/>	<input type="checkbox"/>	
Not use any drugs?	<input type="checkbox"/>		

And finally, a bit about your opinions about delirium.....

How much do you agree or disagree with the following statements.....

	Strongly disagree	Disagree	Neither disagree or agree	Agree	Strongly agree
Delirium is a problem that requires active treatment:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Delirium is associated with prolonged mechanical ventilation:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Delirium in the ICU is associated with prolonged hospital stay:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Delirium is associated with increased hospital mortality:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Delirium in patients is a risk factor for subsequent dementia:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>