Introducing a new sedation policy in a large district general hospital: before and after cohort analysis

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Abstract

Background: The management of pain, agitation and sedation for ventilated patients who are admitted to intensive care is an essential part of their care. The introduction of sedation protocols is associated with improved patient outcomes.

Methods: We conducted an observational cohort study among mechanically ventilated patients in a 16-bed ICU over a two-year period. We retrospectively examined data from two patient populations, namely those before and after the introduction of a new sedation protocol in July 2015. The primary outcome was the duration of mechanical ventilation in both groups.

Results: After the implementation of the new sedation protocol, there was a significant decrease in the mean duration of mechanical ventilation (1.45 days). Furthermore, we observed a non-significant reduction in the mean duration of ICU stay.

Conclusion: The new protocol was associated with outcome improvements including: decreased mean duration of mechanical ventilation and a reduced number of ventilated days; and increased patient throughput with a slight increase in the length of vasopressor support. Moreover, the use of a structure-process-outcome model of quality improvement was associated with significant improvements in process measures of quality.

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The administration of sedative and analgesic therapeutic agents has long been viewed as fundamental to the successful management and treatment of mechanically ventilated patients in the intensive care unit (ICU) in order to facilitate necessary, but painful interventions [1].

Notwithstanding the almost universal utilisation of sedatives in critical care, the optimal strategy for sedating mechanically ventilated patients is still the subject of much debate and research [2].

It has been shown in numerous studies that the excessive use of sedative medications has significant disadvantages in critically ill patients, including but not limited to: unpredictable pharmacokinetics and pharmacodynamics caused by liver or renal dysfunction; excessive testing for altered mental status; prolonged mechanical ventilation; ventilator-associated pneumonia and delirium [3, 4].

Despite the potential benefits of reduced sedative use, many critically ill patients continue to be managed without daily sedative interruptions worldwide [5]. These findings are due, in part, to an assumption that severely ill patients require deep sedation, along with other barriers encountered when attempting to change practice [6].

With the increasing evidence of suboptimal outcomes caused by benzodiazepine-based sedation protocols and those that lacked goal-oriented sedation, we decided to alter substantially the "usual care" protocol of our unit as part of an ICU-wide, structured quality improvement (QI) project to change routine medical and nursing care of the

patients requiring sedation [1, 4]. The new sedation protocol was heavily influenced by the 2013 Society of Critical Care Medicine (SCCM) guidelines and peer-reviewed articles pertaining to best practice sedation in critical care patients [1].

METHODS

The QI project attempted to change the standard ICU practice in three ways, namely: 1) changing the first line analgesic/sedative agents from morphine and midazolam to alfentanil and propofol; 2) the introduction of the Richmond Agitation Sedation Scale (RASS) with a requirement to record RASS scores every 4 hours and target RASS between −2 and 0; 3) the systematic assessment of delirium using the Confusion Assessment Method-ICU (CAM-ICU) on each shift. Changes in practice were implemented using a structured QI process, using a "4Es" framework (engage, educate, execute, and evaluate) [7] as outlined below.

Engagement and education: before the implementation of the new protocol, our multidisciplinary team piloted, educated, and sought feedback on the management protocols for the systematic assessment and management of sedation, and delirium. The QI team focused on three groups of clinicians (day and night nursing staff; junior medical; and consultant staff) in order to inform them of the rationale for changing practice and importance of screening, preventing, and treating delirium. The QI team educated these groups regarding the new sedation protocol, RASS and CAM-ICU tools, and the common methods for preventing and treating delirium. The roll-out involved sequential teaching and competency-based assessment of all nursing and medical staff over a six-week period. Nurses were introduced to the sedation protocol by an ICU nurse educator and a protocol "super user". Medical staff were educated by two physicians from the QI team (JW and CW), both during their ICU orientation the weekly teaching programme.

Execution: On July 1, 2015, the old sedation protocol was removed from the ICU and replaced by the new protocol, and RASS and CAM-ICU assessments were introduced. Super-users were present during day and night shifts to answer questions about the new sedation strategy, as well as RASS and CAM-ICU assessments. On morning rounds, bedside nurses reported each patient's target and actual RASS score, as well as CAM-ICU status. This information was incorporated into medical decision making. Following the ward rounds, RASS and CAM-ICU assessments were nurse-led, as was the titration of the sedative agents. Nursing team leaders, the ICU pharmacist and the consultants on the ICU supported the more junior members throughout the roll-out period. The important change in processes was communicated and explained to the wider multidisciplinary team of physiotherapists and dieticians, in order to enable them to plan their activities with the critically ill patients. During both control and QI periods, the 16-bed ICU had no changes in the type of patients referred and admitted, or staffing structure. The 16 critical care beds were used flexibly, with a maximum of 12 ventilated patients at any given time due to physical constrains on the intensive care unit.

Evaluation: After execution, the QI team continued meeting monthly to identify and resolve barriers to successful implementation. Furthermore, a formal audit and feedback was conducted regarding adherence to the new sedation protocol. Nursing staff were surveyed regarding their experience with the delirium education and assessment process, which helped one to anonymously identify concerns and focus additional educational efforts. Furthermore, during daily bedside rounds, the ICU pharmacist (J.H.) reviewed sedation and delirium practices and reminded clinicians regarding the sedation protocol, as well as delirium screening and management.

We conducted a formal evaluation of the effects of the QI project on important patient-centred outcomes before and after the implementation of the new sedation protocol. We performed an observational cohort study over a two-year period from 1/07/2014 until 01/07/2016. We retrospectively analysed data for all mechanically ventilated patients admitted to the ICU twelve months prior to the protocol change and twelve months after.

We extracted data for both groups from the local Intensive Care National Audit & Research Centre (ICNARC) database collected in WardWatcher™, including as follows: basic demographics; baseline characteristics such as APACHE II scores and acute physiology scores developed by ICNARC (ICNARC score; 0–100 scale derived from multiple acute physiological variables, calibrated for the UK ICU population); organ support days; along with ICU and hospital mortality [8]. We performed the statistical analysis using Microsoft Excel. Continuous variables were compared with Student's-t test while categorical variables were analysed using the Chi-square and Fisher's exact tests. A two-sided P-value of less than 0.05 was considered statistically significant. Our evaluation was classed as an audit and, as we only used anonymised data, the Research and Development Department's Risk Review Group indicated that external Ethics Committee approval was deemed unnecessary.

The primary outcome of the study was the duration of mechanical ventilation. Furthermore, we assessed if there were any statistically significant differences among the secondary endpoints which were as follows: total length of ICU stay; duration of vasopressor support; ICU mortality; and sedative agent cost. We calculated patient throughput defined by the number of patients admitted per bed in the ICU during the two periods.

Table 1. Baseline characteristics of ventilated patients

	Before (n = 359)	After (n = 355)	P-value
Age (years)	60 ± 16	59 ± 16	0.402
Male/Female (n)	197/162	219/136	0.053
Admission source:			0.340*
ED (n)	117	123	
Recovery (n)	124	112	
Ward (n)	107	113	
Other (n)	11	7	
Admission type			0.410*
Medical (n)	229	230	
Surgical (n)	130	125	
APACHE II score	16±8	18±9	0.010
ICNARC score	24±9	23±9	0.284

Data presented as mean ± SD as appropriate. Groups were compared using Student's t-test or Chi-square test. *P-value depicts multiple comparisons between the two groups using Chi-square tests; ED: Emergency Department; ICNARC score: Acute physiology score developed by the Intensive Care National Audit & Research Centre, UK

Table 2. Clinical outcomes comparing the two sedation protocol phases

	Before (n = 359)	After (n = 355)	P-value
Length of mechanical ventilation (days)	6.6 ± 10.5	5.1 ± 7.3	0.030
Total number of ventilated days	2366	1822	0.034
Length of ICU stay (days)	10.0 ± 15.8	8.3 ± 12.1	0.114
Length of vasopressor support (days)	0.1 ± 0.6	0.2 ± 0.9	0.024
Length of renal support (days)	1.5 ± 4.5	1.3 ± 3.2	0.226
ICU mortality (%)	33.2%	32.3%	0.777
Hospital mortality (%)	39.9%	37.1%	0.054

Data presented as mean ± SD as appropriate. Groups were compared using Student's t-test, or Chi-square test. Mechanical ventilation: invasive mechanical ventilation via endotracheal or tracheostomy tube; ICU: Intensive Care Unit; Renal support: use of renal replacement therapy

RESULTS

A total number of 775 patients were admitted to the ICU in the 12 months prior to the sedation protocol change, with 359 patients mechanically ventilated, whereas 986 patients were admitted to the ICU in the 12 months after introduction of the new protocol, with 355 patients mechanically ventilated. There was no difference in the baseline characteristics of the ventilated patient population (Table 1). Although the APACHE II scores were significantly higher in the propofol and alfentanil cohort as age and the more detailed physiology-based ICNARC scores did not differ, this is likely to be a sampling anomaly.

Following the introduction of the new sedation protocol there was a significant decrease in the mean duration of mechanical ventilation, with a reduction of 1.45 days observed (95% CI, 0.5–2.74; P = 0.034) (Table 2). The total number of ventilated days decreased by 544 days post protocol change. Furthermore, a non-significant reduction in the mean duration of ICU stay was observed (1.6 days; P = 0.117), with an increase in ICU throughput from 48 patients/bed to 62 patients/bed. There was no significant change in the ICU or hospital mortality (odds ratio, 0.95; 95% CI, 0.69–1.30; P = 0.77), despite a numerically small, but statistically significant increase in the number of vasopressor support days following the introduction of the protocol.

The drug usage details for the two phases are provided in Table 3.

Table 3. Use of sedation, analgesia and antipsychotic drugs during the two phases

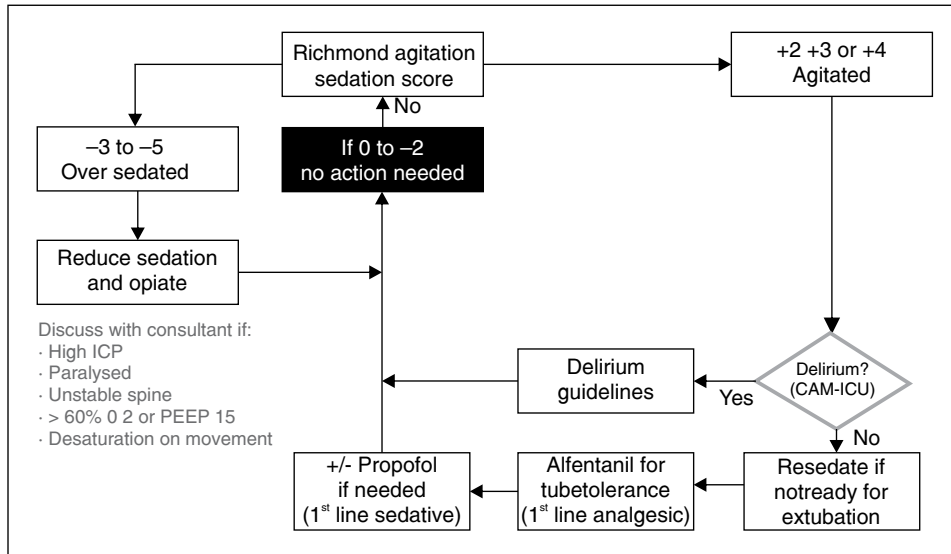|	Before (n = 359)	After (n = 355)
Midazolam (50 mg vials) (n)	1029	377
Morphine (60 mg vials) (n)	112	129
Propofol (100mg vials) (n)	4270	3545
Alfentanil (5 mg vials) (n)	892	9170
Clonidine (750 mcg vials) (n)	1575	907
Dexmedetomidine (200 mcg vials) (n)	95	780
Haloperidol (5 mg vials) (n)	280	320
Quetiapine (25 mg tablets) (n)	5820	6600
Sedation costs (total)	£30,051	£38,911

Figure 1. Flowchart for the new sedation guidelines introduced in the ICU. Sedative agents are stopped daily at 8am unless a contraindication exists

Total sedation costs increased by almost £9,000. However, this increase can be fully explained by the increased use of dexmedetomidine (£1,785 vs. £14,657).

DISCUSSION

Using a structured QI process, we demonstrated a substantial reduction in the length of mechanical ventilation and an overall reduction in advanced respiratory support in patients with a high severity of illness. The QI process was implemented using a previously successful 4Es model (engaging, educating, executing, and evaluating) [7]. Central to this QI project was a new sedation protocol using short-acting non-benzodiazepine sedatives directing clinicians to target an "alert and calm" sedation goal in all patients whenever feasible. Furthermore, structured mandatory assessment of sedation and agitation, together with twice-daily delirium screening was added to existing nursing assessments.

Before the introduction of the new protocol, our unit had been an outlier compared with other UK critical care units, where propofol was used almost exclusively as a first line sedation agent in 2014 [9]. A recent observational study of sedation practice in Australia and New Zealand (Sedation Practice in Intensive Care Evaluation) found that clinicians used midazolam and propofol as the primary sedative with comparable frequency [10]. It also identified a high prevalence of deep sedation in the first 48 hours after initiation of mechanical ventilation which was found to independently predict delayed time to extubation and increased long-term mortality [11]. Two surveys carried out in the UK in 2014 suggested that almost 90% of the critical care units used the shorter-acting propofol as their first-line agent for sedation while 40% used alfentanil as a first-line agent
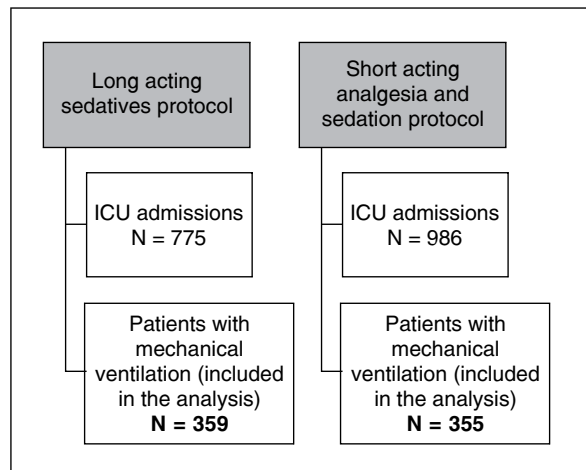

Figure 2. Number of patient admissions to the ICU before and after the sedation protocol change with the total number of patients mechanically ventilated for each group.

for analgesia [9, 12]. In contrast to this, in Eastern Europe and in the low and middle-income countries around the world the use of benzodiazepines and long-acting opioids for sedation and analgesia is common [5, 11]. In the pre-implementation period, despite using midazolam as a first-line sedative, our patients also received large quantities of propofol. Surprisingly, the change to propofol as a first-line sedative agent actually reduced its use. We attribute this to the more systematic and targeted sedation assessments following the introduction of the RASS scale. Similarly, the change from morphine to alfentanil as a first-line analgesic drug has moved our practice more in line with progressive critical care units in Western Europe [5]. It is important to note that the introduction of structured

assessment of sedation and delirium, whilst seen as a "gold standard", is far from universal, even in recent surveys conducted in Eastern Europe and, indeed, worldwide [5, 13]. Morandi *et al.* [5] reported that a more-than-once-daily delirium assessment is only conducted in 20% of European ICUs. Moreover, at the time of the introduction of our new sedation protocol, this was not common in the UK, with only 43% of critical care units reporting regular delirium assessment [12]. Therefore, in changing the whole "ethos" of our sedation practice we expected to improve clinical outcomes, as had been suggested by previous trials [4].

Process improvement is the mainstay of attaining improved ICU outcomes; this includes care bundles and measurable processes [14]. Our findings are in broad agreement with this principle as implementation of a short-acting sedation protocol coupled with a structure-process-outcome model of quality improvement was associated with significant improvements in the process measures of quality on our unit. A significant reduction in the duration of mechanical ventilation was observed post protocol change. While it is not possible to pin-point the precise mechanism for this reduced duration of mechanical ventilation, it is not unreasonable to assume that the combined effect of short-acting sedative agents, along with a concomitant introduction of structured, validated and mandatory assessments of agitation and delirium, were the key processes underpinning this reduction [1]. The 2013 SCCM guidelines strongly advocate the use non-benzodiazepine medications for sedation and the treatment of agitation, as they are associated with improved ICU patient outcomes, including as follows: a shortened duration of mechanical ventilation; decreased ICU stay; as well as reduced incidences of delirium, supported by data from randomised clinical trials and a recent propensity-matched analysis [1, 15, 16]. Although our results are in line with these studies, the mean reduction of length of mechanical ventilation was only 1.5 days vs. the 1.9 days reported by Fraser *et al.* [15] in their meta-analysis. This can very likely be explained by the dilution effect when interventions are applied outside of a randomised clinical trial, as there are numerous challenges in implementing a new sedation protocol [17].

It is plausible, that the reduction in the duration of mechanical ventilation also contributed to increased unit throughput, as the earlier discontinuation of mechanical ventilation and the lower demand for one-to-one nursing care allowed us to use our resources more flexibly. Other studies have seen similar effects with the introduction of protocolised sedation [4, 18]. However, the effect is not universal, as demonstrated in an Australian ICU [19].

We observed higher vasopressor use after the introduction of the new protocol. This could be explained by the commonly observed vasodilatory effect of propofol,

reported as a side-effect in one of the first RCTs comparing midazolam vs. propofol for sedation in the critical care setting [20].

Despite the reduced length of mechanical ventilation, we observed an increase in the sedation costs after the introduction of the new protocol. Interestingly, this was solely related to the increased use of dexmedetomidine, a consultant-only prescription aimed at specific patient groups at a very high risk of delirium [21, 22]. Dexmedetomidine was used in only 14 patients, all of whom had had a significant history of alcohol or drug abuse and only as a rescue therapy following failure to achieve appropriate sedation with propofol and alfentanil.

There are several limitations to our study, due to retrospective data collection using the existing WardWatcher database for outcomes. This prevented us collecting detailed process measure compliance data following the implementation of the new sedation protocol with the RASS targets or the CAM-ICU scores. Interestingly, a recent cluster randomised study in the UK failed to show improved processes to optimise pain, sedation and delirium management in a similar setting to ours [23]. Due to our methodology and the lack of data from the pre-implementation period, we cannot be certain if the increase in the use of antipsychotics reflects better recognition and treatment of delirium, or a genuine increased incidence of delirium in our patients. Previous data including our own, suggests that the introduction of a structured assessment leads to better recognition of, not just delirium, but other ICU-acquired adverse events also [5, 24].

The introduction of and complete adherence to the ABCDEF bundle is associated with improved patient-centred outcomes, such, delirium and the use of physical restraints [5, 25]. One of the key elements of this bundle is structured screening for agitation, pain and delirium, similar to our efforts during this project [25]. As incidences of accidental self-extubation and the development of propofol-related hyperlipidaemia were not collected in our database, we cannot compare the two periods in this regard. It has been shown that up to 70% of self-extubations do not require re-intubation, with some arguing that a low incidence of self-extubation is a marker of the overuse of sedatives [26, 27]. A significant limitation of our present sedation protocol is its failure to assess pain systematically. As previously alluded to, pain is a key stressor in the ICU and, as such, its assessment and management is key to optimising ICU outcomes [6, 11, 16, 22, 25]. Although cognisant of this issue, it was felt that introducing a pain assessment tool, as well as RASS and CAM-ICU assessment tools simultaneously, would create an unmanageable workload for our nursing staff. Thus, it was decided to introduce a validated pain assessment tool at a later time point when the nursing staff was comfortable

with operating the current assessment tools. Throughout the study period, pain was assessed by the nursing staff using the numerical rating scale, in line with the majority of practices in European ICUs [5]. Since the development of the original protocol, we have identified several areas of improvement in order to address the findings of our large study on long-term outcomes of critical care survivors, namely: a) the introduction of the Behavioral Pain Scale as our validated tool in order to assess pain; b) increase the use of non-standard analogue-sedation such as clonidine and ketamine in selected cases; and c) the increased use of regional anaesthesia techniques, such as wound infiltration catheters and transdermal patches containing local and systemic analgesics in order to optimise pain control [28].

In conclusion, implementation of assessment-increasing, sedation-reducing, guideline-concordant protocols may be one way to improve the structure of ICUs, thereby improving the care processes that produce outcomes of importance to patients and their caregivers and thus enhancing the value of ICU care**.**Acknowledgements

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