The weekend effect in status epilepticus: a national cohort study

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Summary

Higher mortality following admission to hospital at the weekend has been reported for several conditions. It is unclear whether this variation is due to differences in patients or their care. Status epilepticus mandates hospital admission and usually critical care: its study might provide new insights into the nature of any weekend effect. We studied 20,922 adults admitted to UK critical care with status epilepticus from 2010 to 2015. We used multiple logistic regression to evaluate the association between weekend admission and in-hospital mortality, comparing university hospitals with other hospital. There were 2462 in-hospital deaths (12%). There was no difference in mortality after weekend admission to university hospitals, adjusted odds ratio (95% CI) 0.99 (0.84-1.16), p = 0.89. Mortality was less after weekend admission than after admissions Monday to Friday in hospitals not associated with a university, adjusted odds ratio (95% CI) 0.74 (0.64-0.87), p = 0.0001. There is no evidence that adults admitted to UK critical care in status epileptic are more likely to die than similar patients admitted during the week.

Introduction

Status epilepticus (SE) is a life-threatening syndrome of prolonged seizure activity. There are 10-16 episodes per 100,000 persons in Europe and 18-41 episodes per 100,000 persons in the United States [1, 2]. Death accompanies status epilepticus in 10%-33% cases and it is followed by permanent disability in more than half the survivors [1, 3, 4].

Differences in outcome after admissions at the weekend, compared with admissions Monday through Friday, have been described for general hospital admissions [5, 6], intensive care unit admissions [7] and after trauma [8], myocardial infarction [9], stroke [10], emergency surgery [11] and cardiac arrest [12]. The inference that variation in outcome was caused by variation in provision of services led to proposals to make weekend clinical services the same as services Monday through Friday [6, 13–15]. However, a number of studies suggest that variation in outcomes are due to variation in patients rather than their care, in part due to inconsistent coding of clinical events [16–20]. The absolute magnitude of the reported association is extremely small and thus vulnerable to small violations of the assumption of no confounding [21]. A number of recent studies have failed to show any evidence of a weekend effect [22], including one in UK intensive care units [23], while others found no evidence to support increasing the weekend provision of services [24, 25]. This remains a topic of considerable clinical and political interest.

Status epilepticus is a useful condition to study the weekend effect for several reasons. Firstly, status epilepticus requires rapid seizure control and treatment of precipitants. Secondly, optimal care requires specialist multi-disciplinary input, as well as rapid access to advanced diagnostic and therapeutic tools that may be less available at weekends. Importantly, early specialist care may be less available in some hospitals at weekends than others, particularly in smaller, non-academic centres: we would expect a 'weekend effect' to be more pronounced or perhaps exclusively present in smaller, non-specialist centres.

We therefore evaluated the association between weekend critical care unit admission and in-hospital mortality in patients presenting with status epilepticus, comparing hospitals we categorised more or less likely to have full seven-day services. We studied a comprehensive nationwide cohort of critical care unit admissions in the United Kingdom over a six-year period.

Methods

We studied adults ($\geq$ 16 years) admitted to UK critical care with a primary or secondary diagnosis of 'status epilepticus or prolonged seizure', from 1st January 2010 to 31st December 2015. We included only the first of multiple admissions. We did not study patients transferred from or to other units. We defined critical care as an intensive care unit (general or neurological) or high dependency unit, 90% of which contribute to the Case Mix Programme of the Intensive Care National Audit and Research Centre (ICNARC), which we analysed [26]. Data access and analyses were approved under section 251 of the NHS Act 2006 (approval PIAG 2-10(f)/2005) and ICNARC's Independent Data Access Advisory Group approved the protocol.

The primary outcome was in-hospital mortality. We assessed the association of mortality with when patients were admitted to critical care; midnight Friday to midnight Sunday (the weekend) versus any other time (weekdays). We assessed the interaction of this association with category of hospital, which might determine weekend availability of specialist services; university hospitals versus others.

The severity of many illnesses may be different at the weekend, but we think that this confounding factor is less likely to apply to status epilepticus. Nevertheless, we adjusted for some potential confounders: age; sex; calendar year; admission source; number of days from hospital admission to critical care admission; acute illness severity [26]; prolonged seizure as primary versus secondary diagnosis; severe co-morbidities; and functional status. We categorised admission source as: ward; emergency department; operating theatre; or other critical care area, for instance coronary care. We categorised duration of hospital stay, before critical care admission, as: ≤ 1 day; 2-7 days; or more than 7 days. We adjusted comorbidities: severe cirrhotic liver disease, dialysis-dependant kidney disease; NYHA functional class 4 heart disease; severe respiratory disease; metastatic cancer; haematological malignancy; or immunological dysfunction. We categorised functional status before hospital admission as independent, partly dependent or total dependent for activities of daily living.

We used Stata 15.1 (StataCorp, College Station, Texas) for analyses. We used multiple logistic regression to analyse the association between weekend admission to critical care and in-hospital mortality. We tested whether this association interacted with category of hospital, in the absence of which we pooled results for all hospitals. We modelled all variables as categorical, except age and ICNARC-predicted mortality, for which we used restricted cubic splines with four knots (5^{th}, 35^{th}, 65^{th} and 95^{th} centile). We clustered patients by hospital, using generalised estimating equations with an exchangeable working correlation structure and robust standard errors. We used marginal standardisation to produce adjusted risks and risk differences to aid interpretation of adjusted odds ratios (95% CI) [27].

We performed two sensitivity analyses. We first excluded patients admitted to critical care from an operating theatre, as the rate and type of operations might differ between weekends and weekdays. We also analysed interactions with markers of illness severity in the first 24 h after critical care admission: mechanical ventilation; sedation; neuromuscular blockade; and the lowest Glasgow

Coma Scale score. We decided not to include these in the primary analysis as they may be due to different practices on weekdays and at the weekend, potentially causing over-adjustment bias (Appendix) [28].

We performed two secondary analyses; seven days of the week as the exposure variable, to explore day-by-day variations in mortality; duration of hospital stay among survivors as an outcome, using negative binomial regression and the same exposure variables as the primary analysis. We considered two-sided p < 0.05 statistically significant. No sample size calculation was performed.

Results

There were 24,716 critical care admissions with status epilepticus to 277 units in 237 hospitals, of which 21,086 admissions met our inclusion criteria. We did not study: 1433 (6%) transfers from other hospitals; 957 (4%) children; 806 (3%) transfers to other critical care units;, 471 (2%) readmissions to critical care without discharge from hospital; or 58 (0.2%) with missing transfer information. We analysed 20,922 patients (99.2%) with complete data as the primary analysis.

Table 1 Characteristics of patients admitted to critical care with status epilepticus between 2010 and 2015. Values are mean (SD) or numbers (proportion).

Characteristic	Total (n = 20,922)	Weekday (n = 15,163)	Weekend (n = 5759)	p value
Daily admissions; n	9.6 (3.5)	9.7 (3.5)	9.2 (3.5)	$< 10^{-16}$
Age; y	51.0 (18.9)	51.1 (18.8)	50.7 (19.2)	
Male sex	11,563 (55%)	8338 (55%)	3225 (56%)	0.19
ICNARC predicted mortality; %	11.9 (17.0)	11.9 (17.1)	12.0 (16.9)	
≥ one severe comorbidity[a]	2110 (10%)	1566 (10%)	544 (9%)	0.061
Dependency for ADL				
None	14,413 (69%)	10,408 (69%)	4005 (70%)	
Partially	5703 (27%)	4159 (27%)	1544 (27%)	0.38
Completely	806 (4%)	596 (4%)	210 (4%)	
University hospital	11,744 (56%)	8626 (57%)	3118 (54%)	0.00035
Admission source				$< 10^{-34}$
Ward	5857 (28.0%)	4272 (28.2%)	1585 (27.5%)	
Emergency department	12,852 (61.4%)	9097 (60.0%)	3755 (65.2%)	
Other critical care area	1176 (5.6%)	871 (5.7%)	305 (5.3%)	
Operating theatre	1037 (5.0%)	923 (6.1%)	114 (2.0%)	
Second diagnosis recorded	9953 (48%)	7254 (48%)	2699 (47%)	0.21
In-hospital mortality	2462 (12%)	1822 (12%)	640 (11%)	0.072

a. Severe comorbidity was any one of cirrhotic liver disease, dialysis-dependant kidney disease, NYHA functional class 4 heart disease, severe respiratory disease, metastatic cancer, haematological malignancy, or immunological dysfunction.

There were 2,462 deaths (12%) in hospital. More patients with status epilepticus were admitted to critical care on weekdays, particularly in university hospitals (Table 1). Patient transfer to intensive care from the emergency department constituted a smaller proportion of admissions in university hospitals, during the week and weekend (Supplementary Information Table S1). University hospitals more often recorded a secondary diagnosis (Supplementary Information Table S1).

Patients were less likely to die after weekend admission to critical care than after admission during the week, but only in hospitals not associated with universities, odds ratio (95% CI): 0.78 (0.67-0.90), p = 0.001 (adjusting for age and sex); and 0.74 (0.64-0.87), p = 0.0001 (adjusting for all variables). The mortality (95% CI) was 2.1% (1.0%-3.2%) less after weekend admission. The equivalent odds ratios (95% CI) after weekend admission to university critical care were 1.03 (0.91-1.17), p = 0.66 and 0.99 (0.84-1.16), p = 0.89, respectively. The mortality (95% CI) was 0.8% less (1.3% less to 1.1% more) after weekend admission to university hospitals. Mortality was lower after weekend admission in sensitivity analyses, again only in hospitals not associated with universities, odds ratio (95%) 0.75 (0.64-0.87), p = 0.0003 (for both analyses). The odds ratios (95% CI) for mortality after weekend admissions to university hospitals, after excluding surgical admissions and after adjusting for illness severity, were 1.00 (0.86-1.17), p = 1, and 0.99 (0.85-1.16), p = 0.91, respectively.

Table 2 The association of the day 20,922 patients were admitted to critical care in status epilepticus with in-hospital mortality. Values are odds ratio (95% CI).

Day of the week	Critical care		p value
	University	Other	
Monday (reference)	1.00	1.00	
Tuesday	0.88 (0.70-1.08)	1.01 (0.76-1.34)	0.42
Wednesday	0.94 (0.76-1.16)	1.00 (0.76-1.30)	0.72
Thursday	0.81 (0.64-1.01)	1.03 (0.79-1.35)	0.18
Friday	0.91 (0.73-1.14)	0.92 (0.70-1.22)	0.99
Saturday	0.93 (0.74-1.16)	0.79 (0.61-1.02)	0.35
Sunday	0.87 (0.70-1.08)	0.69 (0.52-0.91)	0.21
Test for trend (p-value)	0.42	0.001	

The mortality was similar Monday to Thursday in hospitals not associated with universities and fell on Friday, reaching a nadir on Sunday (Table 2). In a further secondary analysis, there was no association between weekend admission and hospital length of stay among survivors, with a relative difference in duration of stay (95% CI) of 0.96 (0.90-1.03) in non-university ICUs and 0.99 (0.93-1.05) in university ICUs.

Discussion

We found no evidence of increased mortality after weekend critical care admission in patients with status epilepticus. Mortality was lower after weekend admission in hospitals not associated with a university.

The absence of harm following weekend admission is consistent with existing literature [16-19, 23]. The lower mortality after weekend admission compared with weekday admisison in some hospitals might be due to unmeasured differences in patients presenting at weekends. For example, prolonged seizures secondary to intoxication may be more common at weekends. Mortality may be less after intoxication than when seizures are triggered by other causes. Intoxication may precipitate a smaller proportion of admissions to hospitals associated with universities, which are more likely to admit patients with complex underlying neurological conditions. A lower proportion of patients admitted to critical care from the emergency department in university hospitals is consistent with this hypothesis. Although secondary reasons for admission are recorded in our dataset, it is possible that underlying causes such as intoxication are not consistently recorded as they are not themselves considered a reason for admission. Indeed, we found that non-university hospital ICUs were less likely to record a secondary reason for admission, creating a potential for residual confounding by such factors.

Our study comprises one of the largest observational cohorts of patients with status epilepticus, in a dataset with careful local and central validation checks and quality control. We accounted for an extensive number of potential confounders, as well as potentially non-linear associations and data clustering by institution. Our study nevertheless has several limitations. As noted above, there may be residual confounding due to incomplete data on the precise nature and underlying cause of seizures in our patient population. In addition, we lacked data on the precise therapeutic interventions received by patients, which limits our ability to explain our findings in non-university centres. Finally, we lacked data on functional outcomes. More than half the patients who survive status epilepticus have severe functional impairment three months later[4].

In conclusion, there is no evidence for a harmful weekend effect for patients admitted to UK critical care with status epilepticus.

Acknowledgements and competing interests

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Supplementary Information

Additional confounders analysis

A sensitivity analysis was run with the following as additional potential confounder variables added to the main analytical model:

- Mechanical ventilation at admission or at any point during first 24 hours: modelled as a binary variable.
- Sedation or paralysis at admission or at any point during first 24 hours: modelled as a categorical variable (none, some period of sedation or paralysis, sedated for whole 24 hours, paralyzed for whole 24 hours).
- Lowest GCS in first 24 hours: modelled as linear variable. This variable was missing for 28% of subjects, thus missing values were imputed using multiple imputation using chained equations. The imputation model used predictive mean matching with 5 neighbors, with all the same exposure values as the main analysis as well as the outcome variable as predictors. 20 imputations were run.

Supplementary tables

Table S1.

Characteristics of ICU admissions with status epilepticus between 2010 and 2015, stratified by university hospital status. Values are numbers (%) unless otherwise noted.

	University hospital ICU		**Non-university hospital ICU**		**p value**[a]
Characteristic	**Weekday**	**Weekend**	**Weekday**	**Weekend**	
n	8626 (73%)	3118 (27%)	6537 (71%)	2641 (29%)	0.0003
Daily admissions, mean (SD)	5.6 (2.6)	5.0 (2.4)	4.3 (2.0)	4.3 (2.2)	$< 10^{-57}$
Age, mean (SD)	51 (19)	50 (19)	52 (19)	51 (19)	0.0009
Male sex	4797 (56%)	1773 (57%)	3541 (54%)	1452 (55%)	0.03
ICNARC predicted mortality risk	11.5%	11.9%	12.3%	12.2%	
≥1 severe comorbidity[a]	988 (11%)	339 (11%)	578 (9%)	205 (8%)	$< 10^{-11}$
Dependent for ADLs					0.008
Partially	2300 (27%)	823 (26%)	1859 (28%)	721 (27%)	
Completely	323 (4%)	107 (3%)	273 (4%)	103 (4%)	
Admission source, daily mean (%)					$< 10^{-67}$
Ward	1.6 (29%)	1.5 (29%)	1.1 (27%)	1.1 (26%)	
Emergency department	3.1 (56%)	3.1 (62%)	2.7 (65%)	2.9 (69%)	
Other critical care area	0.3 (6%)	0.3 (6%)	0.2 (5%)	0.2 (4%)	
Surgery	0.5 (9%)	0.1 (3%)	0.1 (3%)	0.04 (1%)	
Second diagnosis recorded	4287 (50%)	1539 (49%)	2967 (45%)	1160 (44%)	$< 10^{-10}$
In-hospital mortality	1822 (12%)	640 (11%)	825 (13%)	269 (10%)	0.55

a. Test of significance for difference between total values for university hospital ICUs vs. non-university hospital ICUs.

b. Severe co-morbidities were classified as for the Apache scoring system, including cirrhotic liver disease, dialysis-dependant kidney disease, NYHA functional class 4 heart disease, severe respiratory disease, metastatic cancer, haematological malignancy, or immunological dysfunction.
c. Included general and neuro-critical care units in university hospitals.