Predictors of Outcome in Children with Status Epilepticus during Resuscitation in Pediatric Emergency Department: A Retrospective Observational Study

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Abstract

Objectives: To study the clinical profile and predictors of outcome in children with status epilepticus (SE) during resuscitation in pediatric emergency department. Materials and Methods: This retrospective study was carried out in a tertiary care teaching hospital. Admission and resuscitation data of children, aged between 1 month and 12 years, treated for SE, between September 2013 and August 2014, were extracted using a standard data collection form. Our SE management protocol had employed a modified pediatric assessment triangle to recognize and treat acute respiratory failure, cardiovascular dysfunction (CD), and subtle SE until all parameters resolved. Continuous positive airway pressure, fluid boluses based on shock etiology, inotropes, and cardiac safe anticonvulsants were the other modifications. Risk factors predicting mortality during resuscitation were analyzed using univariate and penalized logistic regression. Results: Among 610 who were enrolled, 582 (95.4%) survived and 28 (4.6%) succumbed. Grunt odds ratio (OR): 3.747 (95% CI: 1.035–13.560), retractions OR: 2.429 (95% CI: 1.036–5.698), rales OR: 10.145 (95% CI: 4.027–25.560), prolonged capillary refill time OR: 3.352 (95% CI: 1.339–8.388), and shock requiring >60 mL/kg fluids OR: 2.439 (95% CI: 1.040–5.721) were associated with 2–3 times rise in mortality. Inappropriate prehospital treatment and CD were the significant predictors of mortality OR: 7.82 (95% CI: 2.10–29.06) and 738.71 (95% CI: 97.11–999), respectively. Resolution of CD was associated with improved survival OR: 0.02 (95% CI: 0.003–0.17). Conclusion: Appropriate prehospital management and treatment protocol targeting resolution of CD during resuscitation could reduce mortality in children with SE.

Keywords: Cardiovascular dysfunction, Pediatric assessment triangle, prehospital care, status epilepticus

Introduction

Prehospital emergency care is still in its infancy in India. Although nationwide ambulance services were established in 2009, most children with status epilepticus (SE) reaching our hospital had not received protocol-based care. Children were reaching late with respiratory failure and shock.[1] Most children presented with features of acute respiratory failure (ARF) and cardiovascular dysfunction (CD), low systolic blood pressure, and low mean arterial pressure (MAP). These children with SE may develop neurogenic pulmonary edema (PO), characterized by the acute onset of PO following significant central nervous system injury.[2] Described as secondary to a catecholamine surge that changes cardiopulmonary hemodynamics and Starling forces, the clinical patterns impact diagnosis, cardiac evaluation, fluid management, and choice of inotropic or vasoactive substances.[3,4]

An academic 837-bedded public hospital, our institution provides free care to over 700,000 children who registered at the outpatient department every year. Around 7000–8000 patients were critically ill on arrival. Blood gas analysis and invasive monitoring were unavailable in emergency room settings.

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Post-resuscitation access to mechanical ventilation was also scarce.[5] Hence, the conventional SE protocol was modified to recognize and resolve ARF and CD.[5] Implementation of this modified SE protocol consistently reduced hospital mortality to 2%–6% since 2006 [Table 1]. This study aimed to study the clinical profile and predictors of outcome in children with SE during resuscitation in pediatric emergency department.

**MATERIALS AND METHODS**

Children with seizures lasting for more than 5 min in duration and children with subtle signs such as eye deviation, roving eye movements, or focal or multifocal face or limb motor movements with altered mental status following overt seizures were included in the study. Retrospective data of children with SE, aged between 1 month and 12 years, admitted to the PED between September 2013 and August 2014, were entered in a predesigned proforma. Children with abnormal movements other than SE were excluded from the study. Our objectives were to describe the clinical profile of children resuscitated for SE in the PED and second, to find the predictors of outcome in these children during resuscitation. Institutional review board approval was obtained.

**Modified status epilepticus protocol**

On arrival, of the convulsing child, a focused history was elicited while addressing the airway and breathing. Duration of seizure activity was computed based on the time of onset and distance traveled to reach the hospital. We hypothesized that risk of ARF/CD was high if seizures lasted for more than 30 min, or if altered level of consciousness (ALOC) was noted between precipitating events (fever, focus of infection, breathlessness, or diarrhea) and generalized tonic–clonic seizures (GTCS). ALOC between the precipitating event and GTCS was presumed as secondary to severe hypoxia or shock carrying increased risk of ARF and CD. SE that occurred suddenly was less prone to ARF/CD. Developmental status, history of epilepsy, antiepileptic drugs, and nature of prehospital management were also reviewed. The second responder, concurrently, performed the rapid cardiopulmonary cerebral assessment. Clinical signs of ARF and cardiac dysfunction and signs of subtle SE (SSE) were incorporated into the modified pediatric assessment triangle (PAT) to enable decision-making.[5]

Intravenous or intraosseous access was established simultaneously. Blood and tissue fluids were collected for appropriate testing. An initial bolus of 10 mL/kg normal saline was administered if shock was recognized. Hypoglycemia and dyselectrolytemia were corrected. Antipyretic was administered if needed. The rapid cardiopulmonary cerebral assessment was repeated after each intervention and incorporated into the PAT, thereby guiding therapy until therapeutic goals were achieved.[5] Fluid boluses were interrupted, inotrope infusion was initiated, and intubation was performed if signs of ARF or CD were unmasked during shock correction.[5] SE requiring phenobarbitone or raised intracranial pressure was other indications for intubation. Shock was managed appropriately with inotropes. Following inotrope infusion and intubation, if shock persisted, further fluids were given based on etiology. If septic, hypovolemic, or anaphylactic shock was identified, large volumes (>60 mL/kg) of fluid boluses were planned.[5] If severe traumatic brain injury, submersion injury, envenomation, or toxin ingestion had preceded SE, the total volume of fluids needed to correct shock was restricted to 20–30 mL/kg.[5]

Ceftriaxone was initiated in PED as per hospital infection control policy, if septic shock was associated with leukocytosis. If malaria, scrub, leptospirosis, H1N1, or herpes simplex was suspected, the appropriate antimicrobial drug was administered in the PED. Anticonvulsants were administered simultaneously during resuscitation as per our PED protocol shown in Figure 1.[5] Phenytoin and fosphenytoin were avoided if duration of SE was more than 30 min, history suggestive of septic shock or evidence of PO or vasodilatory shock was noted during resuscitation. Alternatively, levetiracetam (60 mg/kg) was initiated after benzodiazepines, followed by sodium valproate (20–40 mg/kg) if seizures were refractory. Airway positioning, provision of continuous positive airway pressure (CPAP), bag valve mask ventilation/intubation, fluid boluses, inotropes, and anticonvulsants were continued until PO, shock, convulsive SE, or SSE were corrected.[5]

Sample characteristics were analyzed using descriptive statistics. The predictive association of different variables for mortality was analyzed using univariate logistic regression with constant in all the analyses. Variables, which were clinically significant, were analyzed using penalized logistic regression analyses. Analyses were performed using SPSS (version 21) and MedCalc (version 12.2.1.0). Penalized logistic regression was analyzed using R 3.1.2.

### RESULTS

Of 610 children who were resuscitated for SE, 582 (95.4%) survived and 28 children (4.6%) succumbed. Baseline history and characteristics of our cohort are shown in Tables 2 and 3. Mean duration of SE before reaching our PED was 2.51 h, while mean distance traveled was 39 km. Although 195 (31.9%) had

**Table 1: Incidence and mortality for children presenting with status epilepticus to our pediatric emergency department between 2006 and 2010 (medical records department data from ICH and HC)**

| Year | Number of children presenting with SE to the PED | Mortality, n (%) |
|------|--------------------------------------------------|-----------------|
| 2006 | 656                                              | 36 (5.48)       |
| 2007 | 653                                              | 17 (2.60)       |
| 2008 | 744                                              | 25 (3.36)       |
| 2009 | 756                                              | 14 (1.85)       |
| 2010 | 571                                              | 10 (1.75)       |

SE = Status epilepticus, PED = Pediatric Emergency Department, ICH = Institute of Child Health, HC = Hospital for Children
received prehospital care, only twenty (3.2%) had received oxygen and six (0.9%) had been intubated. Prehospital diazepam and phenytoin had been administered to 123 (20.1%) and 63 (10.3%), respectively. However, route of administration had not been documented in 93 (15.2), whereas dose was not mentioned in 103 (16.8) patients.

Univariate logistic regression and penalized logistic regression analysis of five important factors that had a significant association with mortality are shown in Tables 4 and 5, respectively. Distance of >50 km was associated with 3-fold risk of mortality odds ratio (OR): 3.359 (95% confidence interval [CI]: 1.525−7.401). In addition, prehospital resuscitation was associated with 4.8-fold risk of mortality OR: 4.870 (95% CI: 2.161−10.976). Both prehospital benzodiazepines OR: 2.715 (95% CI 1.237−5.959) and phenytoin OR: 3.13 (95% CI: 1.275−7.691) were associated with a 2.3-fold risk of fatality. Penalized logistic regression showed that inappropriate prehospital care resulted in a 7-fold increased risk of mortality OR: 7.82 (95% CI: 952.10−29.06). CD was also associated with increased risk of mortality OR: 7.38 (95% CI: 97.11−999) and its resolution was associated with improved survival OR: 0.02 (95% CI: 0.003−0.17).

**DISCUSSION**

The overall mortality in our cohort was 4.6%. This compares favorably with other centers in India that report mortality ranging between 30% to 31.4%.[6,7] The mean age in our study population was 37.8 months (3.1 years), whereas in other Indian studies, the reported mean age varied between 56.6 and 71.28 months.[6,7] Although our study did not demonstrate an association between age and mortality, an Indian study had found that risk was higher in age <36 months, whereas other studies have demonstrated that older ages were at greater risk.[7−9] Our study demonstrated that SE was more in boys than girls. An analysis of population-based data from Europe and United States had revealed male preponderance in most studies.[10] Mortality in our study was greater in males than females (58.1% vs. 41.9%) although no significant association was noted between mortality and gender.

The higher incidence of SSE (66%) in our cohort was probably due to a focused history that probed for failure to regain baseline sensorium and the meticulous examination for eye signs on arrival and during every step in the protocol. SE precipitated by fever, diarrhea, breathlessness, and toxin
Table 2: Baseline characteristics of children with status epilepticus presenting to pediatric emergency department

| Variables                                      | Results       |
|------------------------------------------------|---------------|
| Age (mean±SD), months                         | 37.8±35.9     |
| Gender, n (%)                                 |               |
| Male                                           | 356 (58.4)    |
| Female                                         | 254 (41.6)    |
| Duration of seizures before reaching hospital (mean±SD), min | 171.5±410.0  |
| Distance traveled to reach hospital (mean±SD), km | 39.2±76.7    |
| Prehospital care, n (%)                        |               |
| Prehospital treatment                          | 195 (31.9)    |
| Prehospital oxygen                             | 20 (3.2)      |
| Prehospital intubation                         | 6 (0.9)       |
| Prehospital benzodiazepines                    | 123 (20.1)    |
| Prehospital phenytoin                          | 63 (10.3)     |
| Route of administration, n (%)                 |               |
| Not mentioned                                  | 93 (15.2)     |
| Appropriate                                    | 94 (15.4)     |
| Inappropriate                                  | 8 (1.3)       |
| Dose, n (%)                                    |               |
| Not mentioned                                  | 103 (16.8)    |
| Appropriate                                    | 83 (13.6)     |
| Inappropriate                                  | 9 (1.4)       |
| Precipitating events before SE, n (%)          |               |
| Precipitating events preceding GTCS            | 437 (71.6)    |
| Altered level of consciousness before seizures | 524 (85.9)    |
| Co-morbid conditions, n (%)                    |               |
| Developmental delay                            | 184 (30.2)    |
| Past history of seizures                       | 248 (40.5)    |
| On anti-epileptic drugs                        | 224 (36.7)    |

SD = Standard deviation, GTCS = Generalized tonic-clonic seizures, SE = Status epilepticus

exposure was predictive of mortality wherein fever and breathlessness emerged as independent risk factors. ALOC between the febrile illness or respiratory distress was noted in 86% of SE episodes.

Nearly 15% had traveled more than 50 km to reach our PED, a feature that was associated with a greater risk of mortality. Mean duration of seizures was long in our study cohort, a finding that is corroborated with data from other centers in India. A long duration of time lapse between the onset of seizures and treatment was observed in a retrospective data from developing country and a high mortality was reported in this study. Delorenzo et al. reported a higher mortality rate when SE lasted for more than 30 minutes. Referral bias and lack of transportation, causing prolonged SE, were considered contributory to increased mortality rate due to prolonged SE in another Indian study. Gulati et al. also had identified that a delay in initiation of treatment as a risk factor for immediate mortality. Nearly 40% had pre-existing seizures in our study group while 45% had been reported in a previous study. Also SE was reported in 10-25% of patients with epilepsy. Kang et al had found that nearly one-third of patients presenting with SE had pre-existing epilepsy and the risk of SE was also high in non-epileptic subjects.

Silbergleit observed that the risk of respiratory depression was not different when intramuscular midazolam or intravenous lorazepam was administered in the prehospital setting. In our study, however, prehospital benzodiazepines resulted in a 2-fold risk of mortality OR: 2.715 (95% CI 1.237–5.959). This, was perhaps, evidenced by the fact that <1% had received appropriate airway management. Among children who had received medications before arrival to our PED, only 83 (13.6%) had received the appropriate dose.

Prehospital use of phenytoin was associated with increased risk of mortality OR: 3.131 (95% CI 1.275–7.691). Intravenous administration of phenytoin is known to cause hypotension, decreased peripheral vascular resistance, bradycardia, complete atrioventricular block, ventricular tachycardia, ventricular fibrillation, and asystole. Discrete cardiac events due to intravenous phenytoin have been reported in literature. It could be accounted by high concentration or rapid infusion rate. Profound bradycardia and severe hypotension were reported even at slower infusion rates in healthy human volunteers. Most of the cardiac ill effects of phenytoin were traditionally attributed to the solvent-propylene glycol.
If propylene glycol was indeed responsible for causing cardiac side effects, the propylene-free derivative, fosphenytoin is expected to be safe for the heart. Data comparing intravenous phenytoin and fosphenytoin have shown that the latter also causes cardiotoxicity, suggesting that the solvent is not the culprit.[22,23] A consensus guideline recommended that intravenous phenytoin should be avoided in patients with cardiovascular disease or when symptoms of debilitating illness, emaciation, hyponatremia, peripheral vascular disease, hemodynamic instability, or sepsis coexist.[24] The increased mortality due to prehospital phenytoin might have resulted from failure to recognize these complications in our cohort. On the contrary, our study also demonstrates that cautious use of phenytoin in our PED, however, was associated with negative risk of death. This beneficial impact was probably due to judicious usage for seizures <30 min, without precipitating events and the absence of ARF and CD.

Our study demonstrates that retractions, grunt, and adventitious sounds at arrival were associated with 2–10-fold risk of mortality. It is possible that the ARF in our cohort could have resulted from neurogenic PO. Aspiration and septic shock could also present with respiratory failure and shock. Besides, ninety children required more than 60 mL/kg for shock resolution, increasing the risk of PO.

Prolonged capillary refill time, hypotension, low MAP, and shock requiring more than 60 mL/kg or inotrope were

| Variables                          | Survivors, n (%) | Death, n (%) | Unadjusted OR | P      | 95% CI      |
|------------------------------------|------------------|--------------|---------------|--------|-------------|
| Precipitating event                | 412 (70.7)       | 25 (89.2)    | 3.439         | 0.046  | 1.205-11.540|
| Fever                              | 357 (61.3)       | 24 (85.7)    | 3.782         | 0.015  | 1.295-11.042|
| Breathlessness                     | 66 (11.3)        | 9 (32.1)     | 3.703         | 0.002  | 1.609-8.52  |
| Distance from hospital (>50 km)    | 94 (16.2)        | 11 (39.2)    | 3.359         | 0.003  | 1.525-7.401 |
| History of generalized tonic-clonic seizures | 475 (86.5)   | 16 (57.1)    | 0.300         | 0.002  | 0.138-0.653 |
| Prehospital treatment              | 176 (30.2)       | 19 (67.8)    | 4.870         | <0.001 | 2.161-10.976|
| Prehospital benzodiazepines        | 112 (19.2)       | 11 (39.2)    | 2.715         | 0.013  | 1.237-5.959 |
| Prehospital phenytoin              | 56 (9.6)         | 7 (25)       | 3.131         | 0.013  | 1.275-7.691 |
| Grunt                              | 18 (3)           | 3 (10.7)     | 3.747         | 0.044  | 1.035-13.560|
| Chest retraction                   | 82 (14)          | 8 (28.5)     | 2.429         | 0.041  | 1.036-5.698 |
| Rales                              | 22 (3.7)         | 8 (28.5)     | 10.145        | <0.001 | 4.027-25.560|
| Prolonged capillary refill time    | 303 (52)         | 22 (78.5)    | 3.352         | 0.010  | 1.339-8.388 |
| Abnormal blood pressure            | 181 (31.1)       | 21 (75)      | 6.613         | <0.001 | 2.762-15.837|
| Septic shock: Fluid bolus (>60 mL/kg) | 82 (14.1)      | 8 (28.5)     | 2.439         | 0.040  | 1.040-5.721 |
| Dopamine                           | 202 (34.7)       | 21 (75)      | 5.599         | <0.001 | 2.340-13.395|
| Norepinephrine                     | 92 (15.8)        | 12 (42.8)    | 3.170         | 0.001  | 1.818-8.669 |
| Epinephrine                        | 28 (4.8)         | 13 (46.4)    | 17.055        | <0.001 | 7.406-39.274|
| Dobutamine                         | 9 (1.5)          | 3 (10.7)     | 6.828         | 0.005  | 1.768-26.363|
| Lorazepam                          | 547 (93.9)       | 22 (78.5)    | 0.235         | 0.003  | 0.090-0.618 |
| Fosphenytoin                       | 205 (35.2)       | 3 (10.7)     | 0.219         | 0.014  | 0.065-0.734 |
| Levetiracetam                      | 349 (59.9)       | 23 (82.1)    | 4.101         | 0.010  | 1.404-11.974|
| Midazolam infusion                 | 30 (5.2)         | 17 (60.7)    | 7.722         | <0.001 | 2.993-19.927|
| Phenobarbitone                     | 119 (20.4)       | 13 (46.4)    | 5.179         | <0.001 | 2.378-11.278|
| Cardiovascular dysfunction         | 73 (12.5)        | 27 (96.4)    | 187.52        | <0.001 | 25.10-1400.86|
| Refractory seizures                | 81 (13.9)        | 11 (39.2)    | 3.978         | 0.001  | 1.798-8.800 |
| Shock corrected                    | 436 (74.9)       | 7 (25)       | 0.110         | <0.001 | 0.046-0.264 |
| Resolution of cardiovascular dysfunction | 184 (31.6)       | 3 (10.7)    | 0.258         | 0.028  | 0.077-0.866 |

OR = Odds ratio, CI = Confidence interval

If propylene glycol was indeed responsible for causing cardiac side effects, the propylene-free derivative, fosphenytoin is expected to be safe for the heart. Data comparing intravenous phenytoin and fosphenytoin have shown that the latter also causes cardiotoxicity, suggesting that the solvent is not the culprit.[22,23] A consensus guideline recommended that intravenous phenytoin should be avoided in patients with cardiovascular disease or when symptoms of debilitating illness, emaciation, hyponatremia, peripheral vascular disease, hemodynamic instability, or sepsis coexist.[24] The increased mortality due to prehospital phenytoin might have resulted from failure to recognize these complications in our cohort. On the contrary, our study also demonstrates that cautious use of phenytoin in our PED, however, was associated with negative risk of death. This beneficial impact was probably due to judicious usage for seizures <30 min, without precipitating events and the absence of ARF and CD.

Our study demonstrates that retractions, grunt, and adventitious sounds at arrival were associated with 2–10-fold risk of mortality. It is possible that the ARF in our cohort could have resulted from neurogenic PO. Aspiration and septic shock could also present with respiratory failure and shock. Besides, ninety children required more than 60 mL/kg for shock resolution, increasing the risk of PO.
associated with 3–6-fold increase in mortality. Need for epinephrine, used for hypotension or bradycardia, was associated with a 17-fold risk of mortality. CD carried the highest risk of mortality.

Our data show that SE responsive to lorazepam in the PED was a negative predictor of mortality OR: 0.235 (95% CI: 0.090–0.618). Concurrent provision of bag valve mask ventilation, or CPAP, might have contributed to improved survival. SE requiring levetiracetam, midazolam, or phenobarbitone was associated with 5–7-fold increased risk of mortality. This could be explained by the longer duration of SE predisposing to greater risk of PO, hypoxia, hypotension, bradycardia, stress cardiomyopathy, acidosis, hypoglycemia, and raised intracranial pressure.

Inappropriate prehospital care and the resultant CD have emerged as important predictors of mortality. In India, suboptimally organized prehospital services substantially hinder the evaluation, management, and transport of the acutely ill and/or injured child to an appropriate facility. Furthermore, the management of the ill child at the hospital level is often provided by overburdened providers who, by virtue of their training, lack experience in the skills required to effectively manage pediatric emergencies.[25] Indeed, Chin et al. had reported that if pre-pediatric intensive care treatment of SE is inadequate, appropriate modifications of standard guidelines may be required.[26]

Our data lend evidence for the need for strengthening prehospital care. In addition, it emphasizes that a modified protocol may be necessary to address the critically ill child whose heart and lungs are failing due to uncorrected hypoxia, shock secondary to SE. In the retrospective study design, failure to objectively assess for PO, hemodynamic status, and intracranial pressure during resuscitation are important limitations. Our stand for modification of the SE protocol is weakened due to the lack of documented PaO₂/FiO₂ ratio. Due to the lack of EEG facility in the emergency department, continuous EEG recording was not feasible in our study. Failure to include etiological data is another limitation as the data were collected from PED database. Despite these limitations, in settings lacking effective prehospital resuscitation, perhaps a SE protocol that aimed at resolution of CD can improve survival. More importantly, improved prehospital care can reduce the risk of CD in children presenting with SE.

Conclusion
We conclude that a modified SE protocol targeting resolution of CD in settings with inappropriate prehospital care improved survival. Our study emphasizes the need for a revised protocol and strengthening of prehospital care for the management of children with SE in resource-limited settings. Prospective studies in resource-limited settings analyzing the outcome in children with a modified SE protocol are needed in the future to support our observation.

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Conflicts of interest
There are no conflicts of interest.

References
1. Santhanam I, Pai M, Kasturi K, Radhamani MP. Mortality after admission in the pediatric emergency department: A prospective study from a referral children’s hospital in Southern India. Pediatr Crit Care Med 2002;3:358-63.
2. Santhanam I, Sangareddi S, Venkataraman S, Kison N, Thiruvengadamudayan V, Kasthuri RK. A prospective randomized controlled study of two fluid regimens in the initial management of septic shock in the emergency department. Pediatr Emerg Care 2008;24:647-55.
3. Baumann A, Audibert G, McDonnell J, Merits PM. Neurogenic pulmonary edema. Acta Anaesthesiol Scand 2007;51:447-55.
4. Davison DL, Terek M, Chawla LS. Neurogenic pulmonary edema. Crit Care 2012;16:212.
5. Santhanam I, editors. Status epilepticus. In: Pediatric Emergency Medicine. 2nd ed., New Delhi: JAYPEE Brothers; 2013. p. 198-212.
6. Kamar M, Kumari R, Nairin NP. Clinical profile of status epilepticus (SE) in children in a tertiary care hospital in Bihar. J Clin Diagn Res 2014;8:PC14-7.
7. Gulati S, Kalra V, Sridhar MR. Status epilepticus in Indian children in a tertiary care center. Indian J Pediatr 2005;72:105-8.
8. DeLorenzo RJ, Towne AR, Pellock JM, Ko D. Status epilepticus in children, adults, and the elderly. Epilepsia 1992;33 Suppl 4:SI5-25.
9. Chin RF, Neville BG, Scott RC. A systematic review of the epidemiology of status epilepticus. Eur J Neurol 2004;11:800-10.
10. Logroscino G, Hedsorffer DC, Cascino G, Hauser WA, Coeytaux A, Galobardes B, et al. Mortality after a first episode of status epilepticus in the United States and Europe. Epilepsia 2005;46 Suppl 11:46-8.
11. Mboj I, Ndiaye M, Sene F, Salif Sow P, Sow HD, Diagana M, et al. Treatment of status epilepticus in a developing country. Neurophysiol Clin 2000;30:165-9.
12. DeLorenzo RJ, Garnett LK, Towne AR, Waterhouse EJ, Boggs JG, Morton L, et al. Comparison of status epilepticus with prolonged seizure episodes lasting from 10 to 29 minutes. Epilepsia 1999;40:164-9.
13. Shorvon S. The management of status epilepticus. J Neurol Neurosurg Psychiatry 2001;70 Suppl 2:II22-7.
14. Fountain NB. Status epilepticus: Risk factors and complications. Epilepsia 2000;41 Suppl 2:SS23-30.
15. Kang DC, Lee YM, Lee J, Kim HD, Coc E. Prognostic factors of status epilepticus in children. Yonsei Med J 2005;46:27-33.
16. Silbergie R, Durkslavi K, Lowenstein D, Conwit R, Pancioli A, Paleschi Y, et al. Intramuscular versus intravenous therapy for prehospital status epilepticus. N Engl J Med 2012;366:591-600.
17. Louis S, Kutt H, McDowell F. The cardiocirculatory changes caused by intravenous Dilantin and its solvent. Am Heart J 1967;74:523-9.
18. Cranford RE, Leppik IE, Patrick B, Anderson CB, Kostick B. Intravenous phenytoin: Clinical and pharmacokinetic aspects. Neurology 1978;28 (9 Pt 1):874-80.
19. York RC, Coleridge ST. Cardiopulmonary arrest following intravenous phenytoin loading. Am J Emerg Med 1988;6:255-9.
20. Earnest MP, Marx JA, Drury LR. Complications of intravenous phenytoin for acute treatment of seizures. Recommendations for usage. JAMA 1983;249:762-5.
21. Barron SA. Cardiac arrhythmias after small IV dose of phenytoin. N Engl J Med 1976;295:678.
22. Swadron SP, Rudis MI, Azimian K, Beringer P, Fort D, Orlinsky M. A comparison of phenytoin-loading techniques in the emergency department. Acad Emerg Med 2004;11:244-52.

23. Coplin WM, Rhoney DH, Rebuck JA, Clements EA, Cochran MS, O’Neil BJ. Randomized evaluation of adverse events and length-of-stay with routine emergency department use of phenytoin or fosphenytoin. Neurol Res 2002;24:842-8.

24. Meek PD, Davis SN, Collins DM, Gidal BE, Rutecki PA, Burstein AH, et al. Guidelines for nonemergency use of parenteral phenytoin products: Proceedings of an expert panel consensus process. Panel on Nonemergency Use of Parenteral Phenytoin Products. Arch Intern Med 1999;159:2639-44.

25. Mahajan P, Batra P, Shah BR, Saha A, Galwankar S, Aggrawal P, et al. The 2015 academic college of emergency experts in India’s INDO-US Joint Working Group white paper on establishing an academic department and training pediatric emergency medicine specialists in India. Indian Pediatr 2015;52:1061-71.

26. Chin RF, Verhulst L, Neville BG, Peters MJ, Scott RC. Inappropriate emergency management of status epilepticus in children contributes to need for intensive care. J Neurol Neurosurg Psychiatry 2004;75:1584-8.