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Research Article

**LONG-TERM CONSEQUENCE OF REFRACTORY STATUS
EPILEPTICUS IN ADULTS: A RETROSPECTIVE
POPULATION-BASED STUDY****¹Dr. Zainab Farooq, ²Dr. Sadia Noureen, ³Dr. Muhammad Naeem Saleem**¹Dental Surgeon, DHQ Hospital, Jhelum.²WMO, BHU 34 SB, Sargodha.³MO, BHU 490GB Tandlianwala, Faisalabad.**Abstract:**

RSE (Refractory Status Epilepticus) is basically a neurological emergency with substantial mortality and morbidity. We intended to assess the long-term results of ICU (intensive care unit) preserved both RSE and SRSE (Super-refractory status epilepticus) patients in a population-based group.

A reflective study of ICU and RSE patients with anesthesia-treatment in hospitals has been controlled in the period of Jan. 2010 to Dec. 2012. With huge population coverage, five hospitals were included in our study and we comprise all sequential adult RSE (from sixteen years or older) patients, which admitted in partaking Intensive Care Units in the period of three years but omitted postanoxic etiologies' patients. We consumed an mRS (modified Rankin Scale) with one-year measurement of results into two categories: good (mRS 0-3, baseline function recovery) or poor (mRS 4-6, death or major functional discrepancy).

Our study found 75 ICU and RSE patients, with anesthesia-treatment, consistent with the yearly incidence of 3.0 (with 95% CI (confidence interval) (2.4-3.8)). SRSE classified patients were 21%, with yearly incidence being 0.6/100000 (95% confidence interval (0.4-1.0)).

Accordingly, for RSE, the mortality of ICU was 0%, the mortality of hospital was 7% (95% confidence interval 1.2%-12.8%) (n=5), and 12 months mortality was 23% (95% confidence interval 13.4%-32.5%) (n=17). RSE recovered to baseline patients 48% (n=36), and 29% (n=22) represented neurological discrepancy in one year. (mRS 4-6) or poor outcome was founded for 52% (n=39).

In the period of one year follow up, RSE, ICE treated 50% patients have been improved to baseline function, while new functional defects were 30% and died 20%. SRSE does not seem poorer result but the result is poorer in older patients along with those patients who have fatal etiologies. SE must be considered with generalized anesthesia on in the cases of refractory.

Keywords: RSE, SR, Epilepsy, Incidence, Mortality, Risk Factor, Etiology, LAE,

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1.0INTRODUCTION:

SE (Status Epilepticus) is fundamentally a condition subsequent from the breakdown of the responsible mechanisms for seizure closure or from mechanisms initiation which may further lead to abnormally extended seizures. The mortality and morbidity of Status Epilepticus associate with epileptic activity duration, SE cause identification and comorbidity and age of the patients. Status Epilepticus develops refractory status epilepticus (RSE) when AEDs of first and second line treatment fails to control and terminate the seizure. More seriously when SE continues more than one day (24 hours) it becomes SRSE (super refractory status epilepticus), specifically after the general anesthesia first administration (Aranda et al., 2010).

The essential SE etiology is reflected the most important analytical aspect determining the inclusive

result. Experimental data and clinical studies have represented that if the SE duration is longer, before the treatment initiation, and managing SE need time then prognosis will be worse (Betjemann, 2015).

Age is another major factor in the SE outcome as best results seen in young patients, while the worst ones in older patients. Therefore, it is not clear that whether age is etiology independent factor. Patients for whom age is more than 65 years, having no history of seizure, particular types of seizure and lessened realization; seen to forecast a worse result. Furthermore, predictors of other negative results are the acute brain lesion presence, the condition of respiratory failure, infections, or in electroencephalogram signals, discharges of postictal periodic epileptiform (Cooper, Britton and Rabinstein, 2009).

All N	Dead N	Functional deficit N	Recovery to baseline N	Status type
53	33	4	16	RSE
50	13	27	10	RSE
26	14	7	5	RSE
91	31	10	50	RSE
33	20	6	7	RSE
69	23	19	27	
322	134 (41%)	73 (23%)	115 (36%)	
4	1	1	2	SRSE
58	26	18	14	SRSE
11	4	2	5	SRSE
31	18	10	3	SRSE
70	46	12	12	SRSE
174	95 (55%)	43 (25%)	36 (20%)	

(Source: Aranda et al., 2010)

2.0 METHODS:

2.1 Patients

FICC (Finnish Intensive Care Consortium) database has been specifically analyzed for this study to recognize RSE patients with ICU treatment. This secondary level FICC data has been searching through ICD-10 codes, which was expressively associated with epilepsy, SE, and seizure (G40.x, R58.6, and G41.x) and APACHE (“Acute Physiology and Chronic Health Evaluation) and “seizure” diagnostic group to classify all ICU disorders seizure patients. The base of our data was adult (≥ 16 years) patients, particularly treated in an intensive care unit for at least forty-eight hours. Postanoxic etiologies patients were excluded and we also recognized those patients who meet the SRSE criteria (Beghi et al., 2010).

2.2 Clinical Factors

FICC is basically a coordinating body of the intensive care national benchmarking program. FICC database is capable to collect data from every regional intensive care units adult admission. All specific information on clinical characteristics, illness severity and final results are domestically validated in every intensive care unit before submitting to the main database. Accordingly, FICC delivered clinical data; we accomplished a retrospective review of medical record for SE kind, SE etiology, AESs of first and second line and any use of intravenous anesthetics with the classification of one year’s results. Patients’ gender and age attained from the same database. Seizure semiology and SE type were determined through medical records with the use of SE type’s clinical classification (Ferlisi et al., 2015).

2.3 Statistics

Overall population rate with a confidence interval of 95% was analyzed for the rate of single incidence. Both, Fischer’s exact test and the chi-square test were utilized to associate the categorical variables and test of non-parametric (“Man-Whitney U for median) were utilized with constant variables (Betjemann, 2015).

2.4 Patient Consents, Standard Protocol Approvals, and Registration

It is a retrospective investigational study based on medical reports and ICU registry on a national basis. The usage of medical registry data endorsement was approved by concerned regulatory authorities who are basically responsible for this data in Finland.

3.0 RESULTS:

3.1 Morbidity, Morality, and Incidence

Studied hospital data reflected that area intensive care units had 14,261 patients during the period of 2010-2012. While 0.5% of all ICU patients (75 in numbers) with RSE achieving the criteria were treated in intensive care units during Jan. 2010 to Dec. 2012. RSE annual incidence was 3.0/100000 (confidence interval 95%, 2.4-3.8) and SRSE 0.6/100000 (confidence interval 95%, 0.4-1.0) in local population (Holtkamp, 2017).

The mortality ICU for all group (RSE) was 0%, there was 7% hospital mortality (confidence interval 95%, 1.2% to 12.8%), accordingly there was 23% mortality (confidence interval 95%, 13.4% to 32.5%). The ratio of recovered patients to baseline were 36 of 75 (which was 48%), therefore 22 patients (29%) demonstrated the deficit of neurology at one year. There was poor result (mRS 4-6) was documented from 52% (39 out of 75) patients. SRSE hospital mortality patients was 6% (n=1), (confidence interval of 95%, 0%-17.6%) and one year mortality was (n=3) which is 19%, (confidence interval of 95%, 0%-38.2%) (Ferlisi et al., 2015).

3.2 Predictors and demographics by One Year RSE Outcome

Clinical predictors and demographics of patients for overall RSE group, specifically for one year functional result. The patient with middle age, like 56 years (from a range of 18-82), furthermore, older age was related with the poorer result with one year ($p=0.03$). Focal onset developing to convulsive bilateral Status Epilepticus was the most general type of seizure (with 75%, 56 out of 75) patients. Non-convulsive status epilepticus with 19% of coma accounted patients (number 14 out of 75). Baseline “Activities of Daily Living”, type of seizure, the category of etiology, STESS “Status Epilepticus Severity Score” or variables directing the status epilepticus duration did not forecast any result (Cooper, Britton and Rabinstein, 2009).

From 75, nine patient (which is 12%) had the disease of cerebrovascular, eight out of nine had a poor result, 11/75 (15%) had recovered head injury and 7/11 (63%) had a poor result. Patients whose status epilepticus twirled out to developing fatal etiologies like CJD (“Creutzfeldt-Jakob disease is degenerative, rare, invariably brain disorder”), MELAS (“Mitochondrial Encephalomyopathy, lactic acidosis, and stroke-like episodes”), represents long-term poor prognosis (Ferlisi et al., 2015).

Thirteen out of seventy-five, 17% of patients represented alcohol-retreat-related status epilepticus” and 46% (6/13) represented poor results. Twenty-four out of seventy-five 32%, had pre-existent epilepsy, and 33% (8 out of 24) patient exhibited a poor outcome. The unfavorable results in patients with precluding epilepsy were associated with asymptomatic remote etiology like brain injury and stroke to a developing syndrome. All other no precluding epilepsy patients were left with minimum one AED after treatment and hence were identified as having further seizures risk (Leitinger et al., 2014).

3.3 EEG and AED adherence Strategies

In 69% of patients (49/75), “Diazepam” as the medication of first-line founded and in 84% (63/75) patients found the use of “fosphenytoin” as a first-line medication. Similarly, 80% (60/75) patients found “propofol” as first specified third line agent. Finnish “Status Epilepticus” instructions were recorded and followed accordingly in 90% patients and at the 93% of established status epilepticus phase. Sixty-eight of the seventy-five patients (which is 90%) had EEG diagnostic accessible and 93% (71 out of 75) patients have constant EEG monitoring of anesthesia period. EEG (electroencephalogram test) was also accomplished after medication in 93% (71 out of 75 patients). There are only two patients who had only clinical arbitration without any EEG diagnostic, with monitoring of electroencephalogram test or afterward of electroencephalogram test are 3% (Leitinger et al., 2014).

3.4 Epilepticus super-refractory status

Sixteen group RSE patients (which is 21%) categorized as patients of SRSE. At the median (51 years of age) range 18-71 from which 8 (50%) were male. The etiology was symptomatically isolated in (9 out of 16) 56% of prescribed cases. Overall 5 patients (which are 31%) had pre-lauding epilepsy. Evolving of focal onset to bilateral convulsive status epilepticus was the most general seizure type of 12 out of 16 patients, (which are 75%). The median stay length in the intensive care unit based on 8 days (ranging from 4-12) and inwards of a hospital for 17 days (from 8 to 45 days). Similarly, second “IV” anesthetic consumed was thiopental sodium (12 hours in 10/16) which is in 63% patients, the ratio of thiopental for (24 hours in 3/16) which is 19% and for propofol in 24 hours in 2/16, which is 13% (Merry, 2016).

4.0 RESULTS:

4.1 Findings

According to our best knowledge, this study of population-based retrospective ICE based with RSE of anesthesia-treated and of the patients of SRSE is one year’s functional outcome of the largest group, which is reported till date. The outcome of one year date approves the long-term mortality rates associated with most recent series were 26%-34% and with one to twelve months follow-up time’s variable with complete poor functional outcomes were 11-28% in prescribed patients.

Hence, we verify that even with anesthesia treated RSE in the intensive care unit, 50% patients represented functional growth over time and made recovery in one year. Fortunately, this outcome considered much better as compared with earlier published years from 1981-2011, where the rate of recovery was 30% (Shorvon, 2011).

The response and results of overall treatment were highly prompted by underlying etiology. According to our research, we could determine that putative etiology in 97% of patients and possibly recognize particular progressive etiologies in the process of treatment which would ultimately cause of poor outcome or death of the patient. In the research literature, etiology acute symptomatic is the most general and reported in 72% cases and furthermore, its reported outcome is worse as compared with other etiologies. According to this research series etiology, acute symptomatic was not concerned with poorer results as a cohort. The most obvious etiology acute symptomatic, specifically for RSE in our cohort was seizures related of alcohol-withdrawal and found in 17% patients, however on the SE other sides, it was only 3% to 13%. In general, alcohol-withdrawal-related RSE is identical prediction to RSE (Raspall-Chaure et al., 2007). It also describes that why etiology acute symptomatic was not completely related with poorer outcomes according to this study.

The hallmark of this SE treatment is performed dividing diagnostics protocol and the therapy to refractory, super-refractory, early and established stages. In the presented study, EEG use, the use of AEDs of first and second line and IV anesthetics was considered arrangement according to the national level guidelines. Specifically, in Finland, as some other European countries, the first-line treatment was initiated already out-of-hospital. On the contrary, according to individual cases, which represented a poorer outcome trend, and according to this poorer

trend, it is not clear whether the prescribed protocol was adopted or not and what AEDs were decided. The rate of lower mortality may also reproduce the entire precise observance to the protocol treatment in the locale, as sufficient basic treatment has been represented to be linked with highly rapid cessation of seizure. Recently, a new research found that the treatment of early and aggressive period have directed to proof decline death by SE, specifically in the UK in the period of 2001-2013 (Holtkamp, 2017).

5.0 CONCLUSIONS:

According to the period of twelve months of follow-up, anesthesia treated RSE and ICU recovered patients were 50% to baseline function. The 30% patients demonstrated new functional flaws, and 20% died. It is not necessary that SRSE holds poorer outcome, basically, the outcome is poorer in elderly patients and fatal etiologies affected patients. It is advised that SE should be handled through generalized anesthesia and only in cases of refractory with a proper prognosis of long-term and specifically after the seizure of properly used first and second AEDs line.

REFERENCES:

1. Aranda, A., Foucart, G., Ducassé, J., Grolleau, S., McGonigal, A. and Valton, L. (2010). Generalized convulsive status epilepticus management in adults: A cohort study with evaluation of professional practice. *Epilepsia*, 51(10), pp.2159-2167.
2. Beghi, E., Carpio, A., Forsgren, L., Hesdorffer, D., Malmgren, K., Sander, J., Tomson, T. and Hauser, W. (2010). Recommendation for a definition of acute symptomatic seizure. *Epilepsia*, 51(4), pp.671-675.
3. Betjemann, J. (2015). Current Trends in Treatment of Status Epilepticus and Refractory Status Epilepticus. *Seminars in Neurology*, 35(06), pp.621-628.
4. Cooper, A., Britton, J. and Rabinstein, A. (2009). Functional and Cognitive Outcome in Prolonged Refractory Status Epilepticus. *Archives of Neurology*, 66(12).
5. Ferlisi, M., Hocker, S., Grade, M., Trinka, E., Shorvon, S., Singh, G., Ercegovac, M., O'Brien, T., Cook, M., Yasiry, Z., Kumlien, E., Kramer, U., Kalviainen, R., Newton, C., Nabbout, R., Godoy, D., Groppa, S., Guecht, A. and Wu, T. (2015). Preliminary results of the global audit of treatment of refractory status epilepticus. *Epilepsy & Behavior*, 49, pp.318-324.
6. Holtkamp, M. (2017). Pharmacotherapy for Refractory and Super-Refractory Status Epilepticus in Adults. *Drugs*, 78(3), pp.307-326.
7. Kahriman, M., Minecan, D., Kutluay, E., Selwa, L. and Beydoun, A. (2003). Efficacy of Topiramate in Children with Refractory Status Epilepticus. *Epilepsia*, 44(10), pp.1353-1356.
8. Leitinger, M., Höller, Y., Kalss, G., Rohrer, A., Novak, H., Höfler, J., Dobesberger, J., Kuchukhidze, G. and Trinka, E. (2014). Epidemiology-Based Mortality Score in Status Epilepticus (EMSE). *Neurocritical Care*, 22(2), pp.273-282.
9. Merry, A. (2016). Merrif Syndrome and Refractory Status Epilepticus. *International Journal of Science and Research (IJSR)*, 5(4), pp.492-493.
10. Neligan, A. (2010). Frequency and Prognosis of Convulsive Status Epilepticus of Different Causes. *Archives of Neurology*, 67(8).
11. Raspall-Chaure, M., Chin, R., Neville, B., Bedford, H. and Scott, R. (2007). The Epidemiology of Convulsive Status Epilepticus: A Critical Review. *Epilepsia*, 48(9), pp.1652-1663.
12. Shorvon, S. (2011). Super-refractory status epilepticus: An approach to therapy in this difficult clinical situation. *Epilepsia*, 52, pp.53-56.