Poster P224

Expert Consensus Recommendations on Seizure Emergencies Suitable for Rapid and Early Seizure Termination (REST) and Timing of Intervention[1]

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Overview

QUESTION

Which types of patients with epilepsy could benefit from Rapid and Early Seizure Termination (REST) medication and/or Acute Cluster Treatment (ACT), and when should they be advised to administer outpatient treatment?

INVESTIGATION

A working group formed by 12 international experts in the field of epilepsy developed a series of consensus recommendations using a multi-step modified Delphi approach, consisting of three anonymous electronic questionnaires and a hybrid face-to-face/online working session. Consensus was reached when ≥75% (9/12) of experts voted 'strongly agree' or 'agree' on a statement or recommendation.

RESULTS

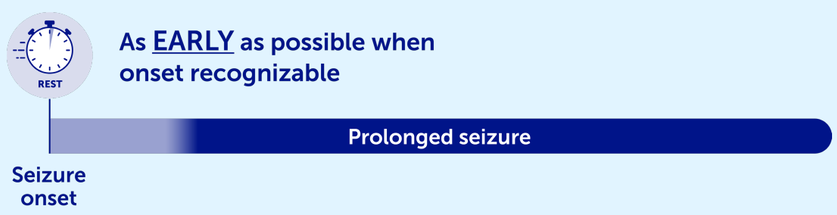
All patients who have previously experienced:

a prolonged seizure should be offered **a REST medication**

a seizure cluster should be offered **an ACT**

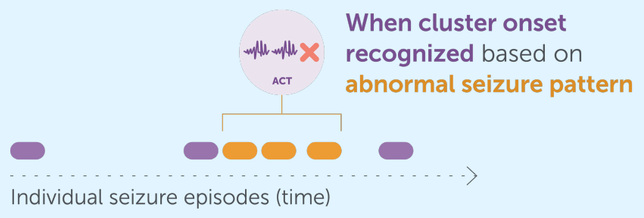
Advice to patients and caregivers regarding when to use REST medication and/or ACT

Patients with a history of **prolonged seizures of any type**



There are currently no approved outpatient medications that can achieve REST

Patients with a history of **seizure clusters**



ACT, acute cluster treatment; REST, Rapid and Early Seizure Termination.

CONCLUSIONS

High levels of agreement were reached on which patients with epilepsy could benefit from REST to stop an ongoing seizure in as short a time as possible, and the advice which should be provided to patients and caregivers regarding when to use REST medication and/or ACT. In patients with a history of PS who have a recognizable pattern of onset, REST medication should be administered as early as possible; and in patients with a history of SC, ACT should be administered when their pattern of onset has been recognized, according to their individual seizure history/pattern.

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Background

- While most seizures will self-terminate within a short time, any seizure is at risk of becoming prolonged or progressing to a tonic–clonic phase[2,3]
- Such seizures have a significant impact on the quality of life of patients and caregivers, and increase the risk of injury, seizure recurrence and progression to status epilepticus (SE)[3]
- While there is international guidance on the definitions and treatment of SE, the management of prolonged seizures (PS) and seizure clusters (SC) is impeded by the lack of international, evidence-based recommendations[4–6]

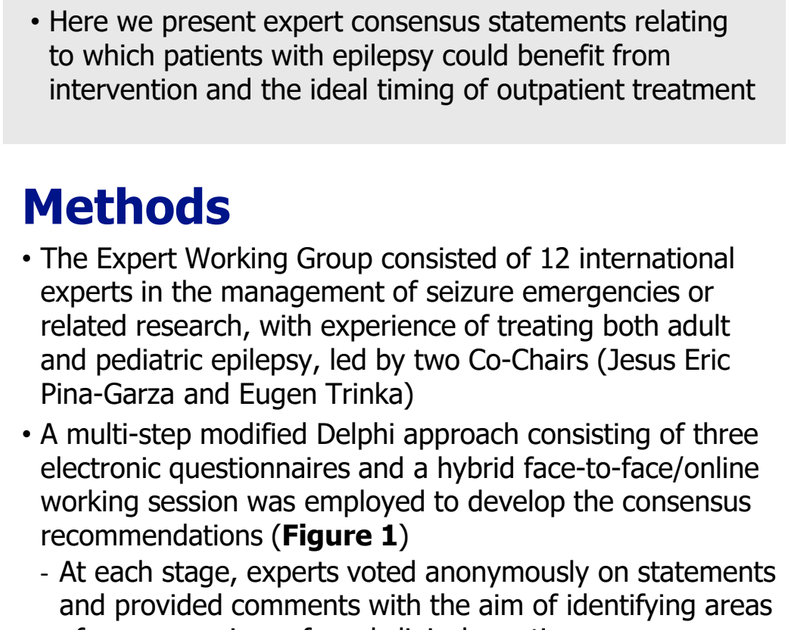
Objective

- The Seizure Termination Project was established to develop expert consensus recommendations for the rapid and early termination of certain PS and SC, to prevent progression to more severe types or seizure emergency
- Our group has previously reported consensus recommendations on definitions of different types of PS and SC, and terminology to describe treatments to prevent progression to more severe types or seizure emergency:[7]
  - Rapid and early seizure termination (REST) medication has the ability to terminate an ongoing seizure
  - Acute cluster treatment (ACT) is a medication with the ability to prevent the next or further seizures in a cluster of seizures
- Here we present expert consensus statements relating to which patients with epilepsy could benefit from intervention and the ideal timing of outpatient treatment

Methods

- The Expert Working Group consisted of 12 international experts in the management of seizure emergencies or related research, with experience of treating both adult and pediatric epilepsy, led by two Co-Chairs (Jesus Eric Pina-Garza and Eugen Trinka)
- A multi-step modified Delphi approach consisting of three electronic questionnaires and a hybrid face-to-face/online working session was employed to develop the consensus recommendations (**Figure 1**)
  - At each stage, experts voted anonymously on statements and provided comments with the aim of identifying areas of consensus in preferred clinical practice
  - Consensus was reached when ≥75% (9/12) of experts voted 'strongly agree' or 'agree'
  - Statements that did not reach consensus, or that Expert Working Group members felt could be improved, were modified based on discussion and feedback, and then revoted on

Figure 1. Overview of the modified Delphi consensus process



*Expert Working Group members were blinded to individual votes. Respondents could select 'unable to answer' if they felt they were not able to provide an informed opinion.

Table 1. Consensus statements and level of agreement on which types of patient should be offered a REST medication and/or ACT

EXPERT WORKING GROUP (N=12) VOTES, n (%)	STRONGLY AGREE	AGREE	DISAGREE	STRONGLY DISAGREE	UNABLE TO ANSWER
All patients who have experienced a prolonged seizure should be offered a REST medication	10 (83)	2 (17)	0	0	0
All patients who have experienced a seizure cluster should be offered an ACT	10 (83)	2 (17)	0	0	0
All patients who have experienced status epilepticus should be offered a REST medication	7 (58)	4 (33)	1 (8)	0	0
Patients who have a **history of myoclonic or absence seizures that progress to generalized tonic–clonic seizures** should be offered ACT or REST medication	10 (83)	2 (17)	0	0	0
Patients who experience focal seizures should be offered REST medication when they have a **history of focal seizures without impaired awareness that progress to focal seizures with impaired awareness**	5 (42)	7 (58)	0	0	0
Patients who experience focal seizures should be offered REST medication when they have a **history of focal seizures without impaired awareness that progress to bilateral tonic–clonic seizures**	9 (75)	2 (17)	0	0	1 (8)
REST medication may be considered for patients with a history of debilitating post-ictal symptoms (excluding sedation) irrespective of seizure duration	6 (50)	5 (42)	1 (8)	0	0
REST medication may be considered for patients when an anti-seizure medication is being reduced or discontinued	4 (33)	7 (58)	1 (8)	0	0
ACT and/or REST medication should be offered with caution to patients who are at high risk of severe adverse events such as respiratory depression	6 (50)	6 (50)	0	0	0
ACT and/or REST medication should be offered with caution to patients who are at risk of medication abuse or have suspected drug addiction, as this can be mitigated by limited supply	1 (8)	9 (75)	1 (8)	0	1 (8)
ACT and/or REST medication should be offered with caution to patients who are taking opioid medication	2 (17)	8 (67)	1 (8)	0	1 (8)

Table 2. Consensus statements and level of agreement on advice to patients and caregivers regarding when to use REST medication and/or ACT

EXPERT WORKING GROUP (N=12) VOTES, n (%)	STRONGLY AGREE	AGREE	DISAGREE	STRONGLY DISAGREE	UNABLE TO ANSWER
When prescribing a REST medication and/or ACT, a seizure action plan should be agreed upon in consultation with the patient and caregiver	10 (83)	2 (17)	0	0	0
Patients with a history of stereotypical prolonged seizures (or their caregivers) are generally able to recognize onset of a prolonged seizure by an individual set of signs or symptoms	6 (50)	5 (42)	0	0	1 (8)
Patients with a history of prolonged seizures of any type who have a recognizable pattern of onset should be advised to administer REST medication as early as possible	8 (67)	3 (25)	1 (8)	0	0
Patients with a history of prolonged seizures of any type should be advised to administer REST medication as soon as the seizure becomes abnormally prolonged based on that patient's seizure pattern	7 (58)	4(33)	1 (8)	0	0
Patients with a history of prolonged bilateral tonic–clonic seizures should receive a REST medication as early as possible	7 (58)	5 (42)	0	0	0
When feasible, patients having a bilateral tonic–clonic seizure should receive a REST medication after 2 minutes of convulsive activity	3 (25)	7 (58)	1 (8)	0	1 (8)
Patients with a history of seizure clusters should be advised to administer REST medication and/or ACT when their pattern of onset has been recognized, according to their individual seizure history/pattern	9 (75)	3 (25)	0	0	0
In patients who have seizure clusters as their main seizure pattern, REST medication and/or ACT should be considered at onset of the first seizure	5 (42)	7 (58)	0	0	0

Results

PATIENTS WITH EPILEPSY WHO COULD BENEFIT FROM REST MEDICATION AND/OR ACT

- A high level of consensus was reached regarding which patients with specific seizure types should be offered a REST medication and/or ACT (**Table 1**)
- All Expert Working Group members strongly agreed or agreed that all patients who have previously experienced a PS should be offered a REST medication and all patients who have previously experienced a SC should be offered ACT
- The recommendation regarding patients with a history of severe post-ictal symptoms excludes cases of sedation, which could be either improved or worsened by REST medication or ACT

ADVICE ON TIMING OF TREATMENT INTERVENTION

- Consensus statements and level of agreement on advice to patients and caregivers regarding when to use outpatient REST medication and/or ACT are shown in **Table 2**
- All Expert Working Group members agreed that when prescribing REST medication or ACT, a seizure action plan should be agreed upon in consultation with the patient and caregiver
- Eleven out of twelve Expert Working Group members strongly agreed or agreed that patients with a history of PS of any type who have a recognizable pattern of onset should be advised to administer REST medication as early as possible
- All Expert Working Group members strongly agreed or agreed that REST medication and/or ACT should be considered at onset of the first seizure in patients who have SC as their main seizure pattern

Conclusions

- High level of agreement was reached on which patients with specific seizure types could benefit from:
  - Rapid and early seizure termination (REST) with the goal of terminating them in as short a time as possible
  - Acute cluster treatment (ACT) with the goal of preventing the next or further seizures in a cluster of seizures
- Expert consensus was also reached on advice to patients and caregivers regarding when to use outpatient treatments
- These expert consensus recommendations will provide clearer guidance to clinicians, patients and caregivers, and aid establishment of REST as a new paradigm for the management of prolonged seizures

References

1. Pina-Garza JE, et al. Epileptic Disord. 2024;00:1–14; 2. Meritam Larsen P, et al. Epilepsia. 2023;64(2):469–478; 3. Asnis-Alibozek A, Detynieckі K. Epilepsy Behav Rep. 2021;15:100409; 4. Trinka E, et al. Epilepsia. 2015;56:1515–1523; 5. Glauser T, et al. Epilepsy Curr.2016;16(1):48–61; 6. Samanta D. Neurol Sci. 2021;42(10):4017–4027; 7. Pina-Garza JE, et al. 35th IEC. 2023; Abstract 119.

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