Prophylactic antiepileptic treatment of seizures for patients with primary brain tumors or brain metastasis when oral and intravenous access is not possible - a literature review.

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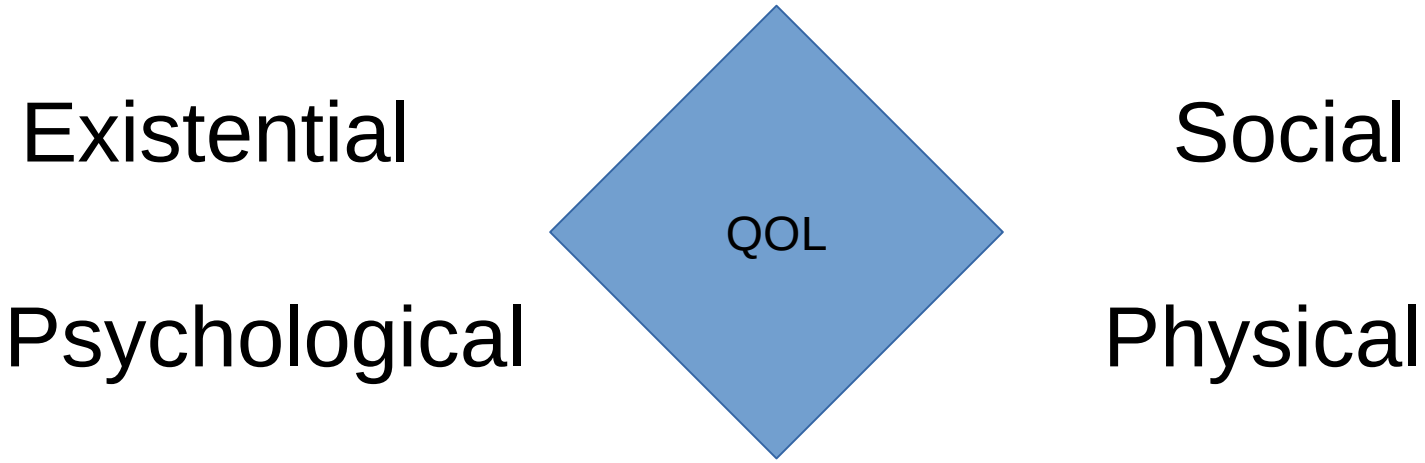
Disposition

- Background
- Aims and objectives
- Methods
- Results
- Discussion
- Conclusion

Background



Background

- **Classification of seizures:**
  - Generalized seizures and partial or focal seizures
- **Reasons for seizures:**
  - Systemic causes:
    - Primary tumours, metastases
    - Abscesses
    - Hemorrhage
    - Radiation necrosis
  - Structural damage:
    - Hypoxia,
    - Metabolic encephalopaties: hypo/hyperglycaemia, hypo/hypernatremia, hypomagnesium, hypo/hypercalcemia, uremia, hepatic failure, antipsychotics, medications
    - Abstinence

Background

- **When do we start prophylactic antiepileptic treatment?**
  - We need to have excluded reversible causes
  - Treatment is required if the pt. has had one generalized seizure in the control periode

Background

- **Antiepileptic treatments:**

  - Different drugs old/new
  - Sideeffects
  - Interactions
  - Monitoring (bloodtest)

Background

Occurrence of seizures among brain tumor patients:

- In general: 30-70%
- In EOL: 6-56%

High risk: Slow growing tumors

- Low-grade atrocytomas, oligodendrogliomas and gangliogliomas (70-100%)

Low risk:

Anaplastic glioma (30-50%)

Glioblastoma multiforme (10-20%)

Brain metastasis (15-20%)

Dysphagia:

- **Prevalence:** Up to 40% last 3 mdr. of life and increase up to 85% in the last weeks of life.

Aims and objectives

Seizures at the end of life:

- Management challenge
- Leads to family and patient distress and negative impact on QOL
- Antiepileptic drugs pros and cons
- Management of seizures relies on expert opinion rather than standardised approach

Aims and objectives

Aim of the project:

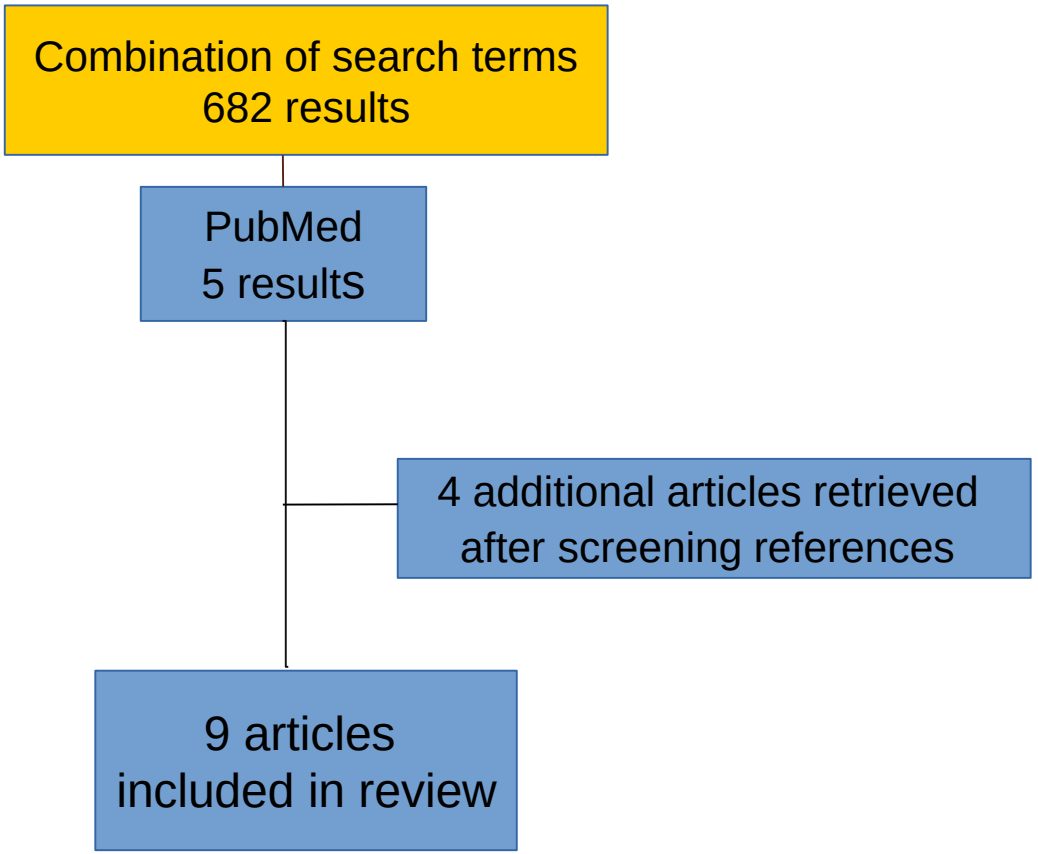
- To provide an overview of the possibilities described in the literature for prophylactic antiepileptic treatment of seizures for patients with primary brain tumors or brain metastasis when oral and intravenous access is not possible
- To contribute to the preparation of a local instruction/guideline based on our literature review

Methods

Keywords: (medical) *preparations, epilepsy, prophylactic, administration*.

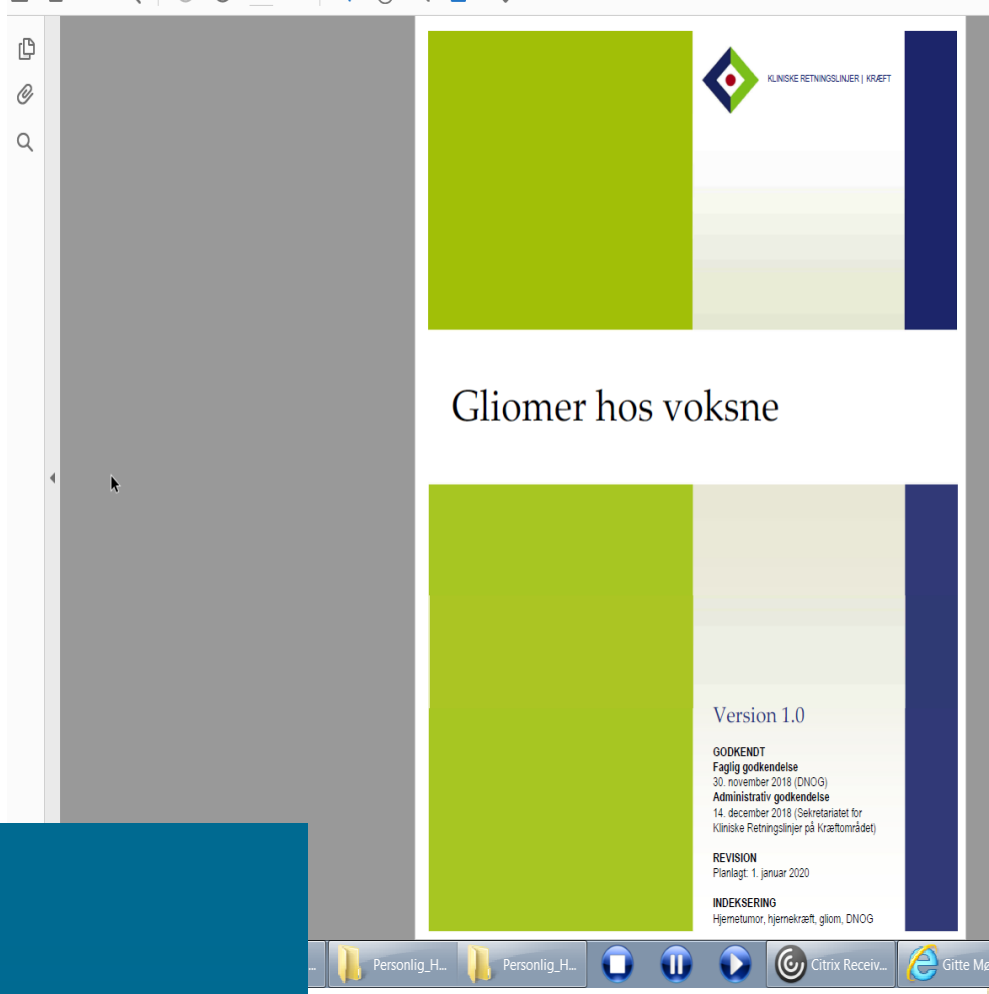
Search string: ((((((((((((((((((("Valproic Acid"[Mesh]) OR "Phenobarbital"[Mesh]) OR "etiracetam" [Supplementary Concept]) OR "Clonazepam"[Mesh]) OR "Midazolam"[Mesh]) OR "Diazepam"[Mesh]) OR "Carbamazepine"[Mesh]) OR valproate[Text Word]) OR delepsine[Text Word]) OR orfiril[Text Word]) OR phenobarbital[Text Word]) OR fenemal[Text Word]) OR levetiracetam[Text Word]) OR keppra[Text Word]) OR clonazepam[Text Word]) OR midazolam[Text Word]) OR diazepam[Text Word]) OR carbamazepine[Text Word])) AND ((("Epilepsy"[Mesh]) OR "Seizures"[Mesh]) OR epilep*[Text Word]) OR seizur*[Text Word])) AND ((((("Anticonvulsants"[Mesh]) OR (("prevention and control" [Subheading]))) OR "Anticonvulsants" [Pharmacological Action]) OR prophylactic*[Text Word]) OR prevent*[Text Word]) OR reduc*[Text Word])) AND ((((("Administration, Rectal"[Mesh]) OR "Injections, Intramuscular"[Mesh]) OR "Injections, Subcutaneous"[Mesh]) OR rectal*[Text Word]) OR subcutaneous*[Text Word]) OR intramuscular[Text Word])

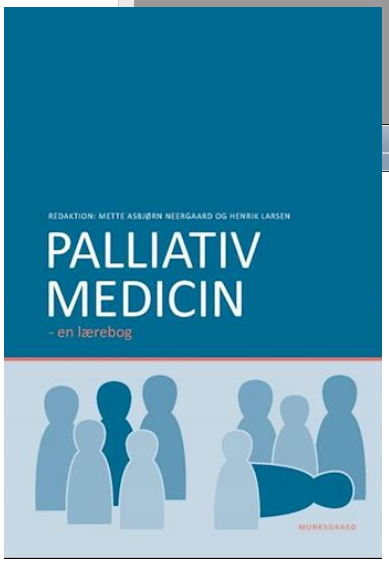
Methods


Combination of search terms
682 results
PubMed
5 results
4 additional articles retrieved
after screening references
9 articles
included in review

Methods


Klinisk vejledning for almen praksis
Palliation
Dansk Selskab for Almen Medicin
2014


KLINISKE RETNINGSLINJER | KRÆFT
Gliomer hos voksne
Version 1.0
GODKENDT
Faglig godkendelse
30. november 2018 (DNOG)
Administrativ godkendelse
14. december 2018 (Sekretariatet for Kliniske Retningslinjer på Kræftområdet)
REVISION
Planlagt: 1. januar 2020
INDEKSERING
Hjernetumor, hjernekræft, gliom, DNOG


REDAKTION: METTE ASBJØRN NEERGAARD OG HENRIK LARSEN
PALLIATIV MEDICIN
- en lærebog
MUNKSGAARD

Methods

Questionnaire among our colleagues at NSCPM:

You are consulted regarding one of your patients home. The patient is having problems taking his medicine orally and intravenous medicine is not an option.
The patient has had several seizures and has been on prophylactic antiepileptic medicine.

How would you now treat the patient regarding prophylactic antiepileptic treatment?

Results

Articles	Study design	Location	1)Recommandation 2)Guidelines 3)Given drug	Conclusion
Krouwer, Minnesoda, 2000	Literature review		2)Rectal Valproat, Rectal Carbamazepin or Rectal or sc. Phenobarbital	Guidelines are based on pharmacological and clinical studies on pediatric and adult epilepsy pt. because no specific data on dying patients These guidelines are appropriate for pt. whose seizures are caused by diseases other than brain tumors
López-saca, Spain, 2013*	Case report	Hospital	3)Levetiracetam sc.	Levetiracetam is feasible in exceptional situations where other routes cannot be used
Tradovnsky, Canada, 2013	Literature review	Hospice	Many options listed -no recommandations	Proper management of seizures for the sake of pt. and familiy. -Check reversible causes -Remember a prescription of future seizures

Results

Articles	Study design	Location	1)Recommandation 2)Guidelines 3)Given drog	Conclusion
Remi, Germany, 2014*	Literature review	In and out patient setting	Levetiracetam sc.	Levetiracetam is effective treatment an well tolerated in palliative setting
Koekkoek, Netherland, 2014	Literature review	Out of hospital setting	1) Buccal Clonazepam or sc. Phenobarbital or sc. Midazolam (pal. Sedation -last option)	Treatment decision are dependent on experts opinion, standard approach for treating seizures in the EOL stage is lacking. Due to the lact of evidens it is too limited to recommend the use of certain AEDs
Koekkoek, Netherland, 2015	Observertional study	Out of hospital setting	2) Buccal Clonazepam (prophylactic) 2) Intranasal Midazolam (acute seizures	No intolerable side effects It is possible to treat these pt.in out of hospictal setting. Contribute to a more dignified death

Results

Articles	Study design	Location	1)Recommandation 2)Guidelines 3)Given drog	Conclusion
Wells, UK, 2016	Case report	Hospital	3)Continous sc. levetiracetam	Should be considered when limited adm. routes. Seizures controlled and well tolerated. Could communicate until death and this contribute to a more dignified death
Sutherlan dUK, 2017	Literature review	Hospitals/ hospices	Levetiracetam sc.	It may have a role in the management of these pt.s. Randomised trials are urgently needed to establish the efficacy and tolerability of sc Levetiracetam adm.
Murray-Brown, UK 2018	Case report	Hospice	3)Syringe (sc.) Levetiracetam + Oxycodon + Metocloopramid	Mixing Leveracetam with other drugs without data regarding compatibility carries risk (sideeffect, less effective) Limited data. Refering to article Remi and López-saca (*)

Results

Danish group for General Medicine (DSAM)

- Recommendations:
  - Prophylactic antiepileptic treatment should be started in collaboration with a neurologist
  - Untill this is possible, the following treatment can be started:
  - • Lamotrigen (Lamictal®): 50 mg × 1, slowly increasing to 200 mg or
  - • Levetiracetam (Keppra®): Startdosis
  - is 250 mg × 2, Increasing to 500 mg × 2

Results

- **Danish Neuro-oncologic group (DNOG)**
- Recommendations:
  - When pt.s cannot take tablets many drugs can be given iv, sc or rectally (valproat, levetiracetam, lacosamid)
  - Supplementary treatment in the terminal phase, both prophylactic treatment and acute seizure treament occur in the form of Benzodiazepines, of which there is best evidence for the use of diazepam (sc/iv/im, rect) and Midazolam (sc/iv/nasal/gingival)

Results from questionnaire

Answers:	Numbers:
Midazolam sc/syringe driver	19
Carbamazapine sup	7
Contact a neurologist	6
No prophylaxis	2
No prophylaxis but Benzodiazepine sup./sc./Buccal	6
Diazepam sc.	3
Other things / Uncertain answer	3
Nasogastric tupe/PEG to give AED	2
Levetiracetam sc./oral mixture	2
Phenobarbitone sc.	2
Diazepam sup	1
Valproat sup	1
Clonazepam	1

Discussion

- Is prophylactic antiepileptic treatment required in this patient group?
- Lack of knowledge regarding pharmacokinetics and pharmacodynamics
- Different drug availability in different countries
- A need for more studies

Discussion

- Levetiracetam s.c. - future possibility?

Discussion

...and what about the local clinical guideline?

Conclusion

- Seizures in palliative care patients present a management challenge
- Only low evidence articles on this topic, and a need for further research
- Our research show a ”tendency” for using s.c. levetiracetam for this particular patient group

Thanks to

- Our tutor Jon Kroll Bjerregaard
- Librarians Karin Velbæk og Henrik Laursen
- Neurologist Kåre Severinsen
- Dagny Renata Faksvåg Haugen for kindly giving feedback on the abstract
- Our Scandinavian colleagues

Results

- Local guideline on antiepileptic treatment among pt.s with braintumors in the terminal phase when they can no longer take per oral medication:
- 1. choice: Valproat (delepsine) sup.
- Start dosis 600 mg x 1, increase to 600 mg x 2 if no effect. Higher dose is not recommended
- 2. choice or 1. combination treatment:
- Midazolam or Diazepam sup., sc.
- Dosis is individual
- 3. choice: Buccolam, but only if there is no risk of aspriation
- Start dosis: 10 mg x 1-2

- Otherwise contact a neurologist