Pharmacological treatment of agitation in the posttraumatic confusional state

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In general

- **Only if necessary**: the patients needs rest, safety issues.
- **Non-pharmacological interventions more important!**
- There is no evidence for any effect of medication on the confusion per se.
- Measure the problem, evaluate effects and document changes. Use validated instruments when possible.
- Try to be systematic. Have a plan.
- Aviod, if possible, drugs that may negatively affect plasticity or cognition (most….)

References

Review

Drugs for behavior disorders after traumatic brain injury: Systematic review and expert consensus leading to French recommendations for good practice

D. Plantier[a,*], J. Luauté[b,c], the SOFMER group

Annals of Physical and Rehabilitation Medicine 59 (2016) 42–57

Review

Care management of the agitation or aggressiveness crisis in patients with TBI. Systematic review of the literature and practice recommendations

Jacques Luauté[a,b,*], David Plantier[c], Laurent Wiart[d,e], Laurence Tell[a], the SOFMER group

Annals of Physical and Rehabilitation Medicine 59 (2016) 58–67

Sleep regulation

First choice: mianserin (Tolvon) start with 10 - 15 mg vesp, increase if needed. Max dose 60 mg

We do not usually recommend this in patients on antipsychotic medication, since they are also sedative.

Alimemazine (Vallergan) has anticholinergic effects. Should be avoided.

Zopiklone / zolpidem: binds to the same receptors as benzodiazepines. Especially zopiklone, which binds to both B1 and B2. Zopiklone should be avoided similarly as benzodiacepines.

Pharmacological treatment

First choice: Betablocker, lipofilic, non-selective: propanolol

Evidence: 4 older studies, in total 33 pas + survey doctors in USA.

Cochrane 2006 (Fleminger), based on two of the same: best evidence for betablockers.

Luauté: grade B. Gold standard if also high blood pressure.

Contraidications: Sick sinus, AV block grade 3, asthma and COLD

Check before start: Take ECG first (look for AV block, sick sinus)

Dosage: Start with10 mg x 3, can increase quickly to 20 mg x 3, and further increase every 2-3 days. Dosage higher than 40 mg x 3 seldom necessary, and do not og higher than 80 mg x 3.

(There may be genetic variants where so high doses are needed, but they are rare.)

Pharmacological treatment

Second choice : antiepileptic drugs

(Preferably) change to 2. choice, or add to 1. choice with caution (valproate only).

(carbamazepine best in monotherapy since carbamazepine will reduce concentration of propanolol and mianserin)

Evidence: complicated, few, older studies of (oxa-) carbamazepine, valproate, lamotrigine, miscellanious patient groups + survey among doctors in USA.

Luauté: weak evidence. Gold standard in severe TBI if cooccuring epilepsy or previous bipolar disorder.

Pharmacological treatment

Carbamazepine (Tegretol, Trimonil)

Contraindications: porphyri. Earlier bloodyscrasias/bone marrow depression. AV-block, hyponatremia.

Check before start: Haematological blood values, Se- Na, interactions with other drugs.

Disadvantage: powerful enzymeinductor. Check with the rest of the patient medication, check interactions.no., increase if necessary dosages of other drugs.

Dosage: start with 100 mg x 3, increase rather quickly up to total dose of 900 mg pr day.

(Oxcarbazepine (e.g Trileptal) more often causes hyponatremia, best to avoid.)

Valproic acid (Orfiril)

Contraindications: signs of disturbed liver function, bleeding diathesis, pregnancy.

Check before start: Blood tests of liver function, interactions with other drugs

Dosage: start with entero tablets 300 mg x 2, increase with 300 mg every 2.-3. dag mostly enough with 1200-1500 mg pr day. Enterotablets should be x 3 per day after initial dose.

Valproic acid more negative effect on cognition??? Some will say the opposite.

Pharmacological treatment

Third choice: antipsychotics

Evidence: small, open studies. No higher level of evidence than grade C and expert opinion.

Luauté: weak evidence, should be avoided. If forced: atypical.

Olanzapine (Zyprexa)/ quetiapine (Seroquel) / aripiprazole (Abilify):

Olanzapine first? Quetiapine?

Aripiprazole less sedating?

Olanzapine:

Contraindications: glaucoma, hypotension, bradycardia

Check before start: take ECG before start. Measure QT time if high doses are needed.

Dosage: 5 mg x 1, may be increased to 10 mg x 1 after 24 hours, and further to 20 mg x1.

NB! It is anticholinergic and has a D2-blocking effect

Quetiapine:

Contraindications and checking much the same.

Dosage: (with tablets, not depot): 25 mg x 2 day 1, 50 mg x 2 day 2, can be further increased to max 200 mg x 2.

Pharmacological treatment

Metylphenidate?

Evidence: no studies of this drug for this problem

Luauté: no evidence to support it’s place in a guideline yet.

Drugs to avoid

- Benzodiazepines /GABA-ergic drugs: affect plasticity.

  (Useful if recent alcohol abuse?)

Evidence: human and animal studies. (A.J.-P. Schwitzguebel 2016; Goldstein 1995,)

- zopiclone?
- clomethiazole ? (Heminevrin): no advantages over benzo, only more side effects and problems (http://tidsskriftet.no/sites/tidsskriftet.no/files/pdf2008--1182-4.pdf.)
- anticholinergic drugs: negative for cognition
- haloperidol and risperidone (also dopamin blocker).

Pharmacological treatment

Emergency

- First benzodiazepines (diazepam) for rapid sedation
- If needed: add olanzapine