Pharmacological Treatment of Agitation and/or Aggression in Patients Suffering from Traumatic Brain Injury: A Systematic Review of Reviews

Elham Rahmani1, Anita Kablinger1

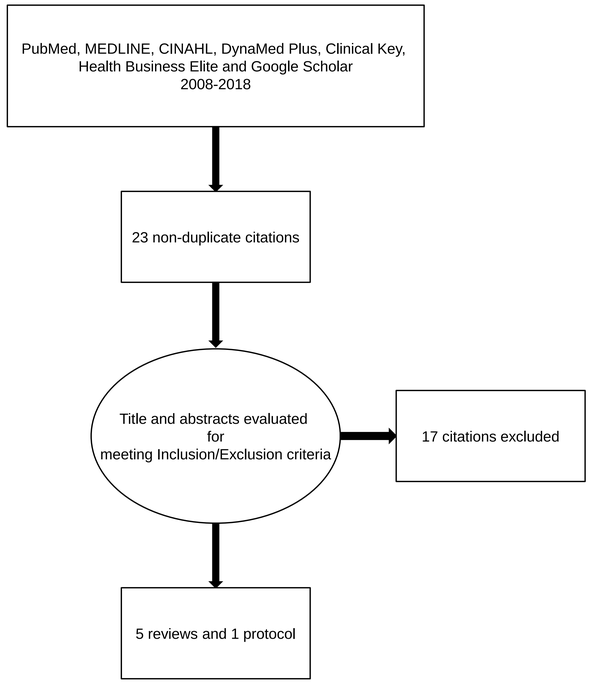
1.Virginia Tech Carilion School of Medicine, Department of Psychiatry and Behavioral Medicine, VA, USA

INTRODUCTION

Traumatic Brain Injury(TBI) is a major cause of disability and it has been associated with agitation and aggression (1,2). The treatment of these symptoms usually falls in an intera-disciplinary area and suffers from a lack of evidence and available guidelines. The aim of this study is to synthetize the available data and provide guidelines.

METHODS

A literature review of the following websites: PubMed, MEDLINE, CINAHL, DynaMed Plus, Clinical Key, Health Business Elite and Google Scholar, was performed looking for systematic reviews on the treatment of agitation and/or aggression among patients suffering from TBI. This search led to 23 reviews. The title and abstract of these articles were evaluated for meeting inclusion criteria and 5 published article and one review protocol were selected (3-8).



RESULTS

Before pharmacological management, first, medical reasons of agitation and behavioral measures need to be considered. After consideration of these methods, in cases of acute agitation, atypical antipsychotics have the best evidence for acute management (6,7). Benzodiazepines and typical antipsychotics may interfere with neurocognitive recovery and should be avoided (3-6). In addition to these concerns, the efficacy of typical antipsychotics and in particular haloperidol is questionable for patients with TBI (6,7). Amantadine, Beta Blockers, Valproate and Carbamazepine have the best evidence for long-term preventative treatment of episodes of agitation or aggression (3-7).

Article	Year	Main findings
Plantier et al.	2016	-Valproate and Carbamazepine can be used as first line treatment. -Propranolol can improve aggression. -No evidence of efficacy for neuroleptics, specifically for long-term use.
Luaute et al.	2016	-Neuroleptics should be limited to short-term use in cases of acute agitation with risk of harm to self or others. -Beta blockers, Valproate and Carbamazepine yield the most compelling evidence. -No articles found specifically evaluating benzodiazepines. Benzodiazepines are associated with risk of several side effects including paradoxical effect and inhibiting brain plasticity.
Bhatnagar et al.	2016	- Beta-Blockers can be used to reduce hyper-arousal. - Benzodiazepines and typical antipsychotics can hinder neurocognitive recovery.
Mohamed Ali et al.	2015	-Quetiapine is effective in reducing aggression in doses of 25 to 300 mg. -IM Droperidol is more effective and associated with less side effects when compared to IM Haloperidol.
Mehta et al.	2018	-Amantadine effectively reduces symptoms of agitation. -Haloperidol was not found to be effective in reducing agitation. -Quetiepine, Ziprasidone, Droperidol, methotrimeprazine and lithium carbonate were found to be effective but the latter three are associated with side effects. -Pindolol and Propranolol are effective in reducing the frequency and intensity of agitation respectively.
Williamson et al. (Protocol)	2016	-

General Recommendations for Pharmacological Treatment of Agitation and/or Aggression in Patient Suffering from TBI based on the results of this Systematic Review.
Acute Management
Recommend Against Benzodiazepines and Typical Antipsychotics (Specifically Haloperidol)
Recommend Atypical Antipsychotics (Quetiapine, Ziprasidone, Olanzapine)
Long-Term Preventative Management
Recommend Valproate, Carbamazepine, Amantadine and Beta-Blockers

CONCLUSIONS

Despite the paucity of data for treatment of agitation or aggression in TBI, some recommendations can be derived from available data to help inform clinical decisions. Further studies are required.

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