



## Review

## Pharmacological interventions in traumatic brain injury: Can we rely on systematic reviews for evidence?



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## ABSTRACT

**Introduction:** Providing current, reliable and evidence based information for clinicians and researchers in a synthesised and summarised way can be challenging particularly in the area of traumatic brain injury where a vast number of reviews exists. These reviews vary in their methodological quality and are scattered across varying sources. In this paper, we present an overview of systematic reviews that evaluate the pharmacological interventions in traumatic brain injury (TBI). By doing this, we aim to evaluate the existing evidence for improved outcomes in TBI with pharmacological interventions, and to identify gaps in the literature to inform future research.

**Methods:** We searched the Neurotrauma Evidence Map on systematic reviews relating to pharmacological interventions for managing TBI in acute phase. Two reviewers independently screened search results and appraised each systematic review using the validated AMSTAR tool and extracted data from the review.

**Results:** A total of 288 systematic reviews relating to TBI were available on the Neurotrauma Evidence Map at the time of this study. We identified 19 systematic reviews on pharmacological management for acute TBI with publications dates ranging from 1998 to 2014. The studies were of varying methodological quality, with a mean AMSTAR score of 7.78 (range 2–11).

**Conclusion:** The evidence from high quality systematic reviews show that there is currently insufficient evidence for the use of magnesium, monoaminergic and dopamine agonists, progesterone, aminosteroids, excitatory amino acid inhibitors, haemostatic and antifibrinolytic drugs in TBI. Anti-convulsants are only effective in reducing early seizures with no significant difference between phenytoin and leviteracetam. There is no difference between propofol and midazolam for sedation in TBI patients and ketamine may not cause increased ICP. Overviews of systematic review provide informative and powerful summaries of evidence based research.

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## Contents

Introduction .....	517
Methods .....	517
Search strategy .....	517
Quality assessment .....	517
Data extraction and analysis .....	518
Results .....	518
Discussion .....	518
Summary of the evidence .....	518

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Magnesium . . . . .	518
Monoaminergic and dopamine agonists . . . . .	521
Haemostatic and antifibronolytic agents . . . . .	521
Aminosteroids . . . . .	521
Excitatory amino acid inhibitors . . . . .	521
Progesterone . . . . .	522
Anti-convulsants . . . . .	522
Sedatives . . . . .	522
Strength and limitations . . . . .	522
Conclusion . . . . .	523
Conflict of interest . . . . .	523
References . . . . .	523

## Introduction

Traumatic brain injury (TBI) is a significant public health problem worldwide [1]. The incidence of TBI varies across the world from 91 to 430 per 100,000 population per year [2]. Low and middle-income countries have the greatest burden due to the result of transport-related injuries [3]. Young adolescents and men have an increased risk of being affected. Head injury secondary to falls in the elderly is a major contributor to the higher incidence and mortality of TBI amongst this population group [4].

Currently, a vast amount of literature exists on the topic of TBI. Much progress has been reported in animal studies, but there is a question over translating these advancements to humans. Obtaining high quality information for the management of TBI is a challenge for healthcare providers. Systematic reviews are used to provide information to aid decision-making and advice on best practice in TBI management. Systematic reviews collate evidence that fits pre-specified eligibility criteria and therefore, when properly conducted, it is considered to minimise any bias when answering a specific research question.

Although systematic reviews are helpful in corroborating the literature, it can be problematic for clinicians to not only access the reviews but also keep up to date with the increasing number of published systematic reviews. Furthermore, existing systematic reviews vary in quality, complexity and length and are published in a range of sources. This information needs to be synthesised and summarised in order to provide health care providers with current, accurate and accessible evidence for decision-making.

Overviews of systematic reviews provide a solution to this issue. They collate the best available evidence in a single source to provide comprehensive and collective statements that synthesise the current evidence on the effectiveness of certain interventions. These overviews also provide clinicians with the necessary evidence-based information to aid decision making, improve patient care and identify areas for future research.

In this paper, we present an overview of systematic reviews in pharmacological management of TBI. Our aim was to evaluate the existing evidence for improved outcomes in TBI with various pharmacological interventions, and to identify gaps in the literature to inform future research.

## Methods

### Search strategy

We searched the Neurotrauma Evidence Map [5] (an up-to-date, quality assessed repository of neuro-trauma systematic reviews) for published systematic reviews on pharmacological management of acute TBI. The database is current to 31st June, 2014.

The Neurotrauma Evidence Map includes systematic reviews relating to TBI or spinal cord injury, either alone or in conjunction with other injuries. The definitions of TBI used to identify eligible reviews are as per the World Health Organization (1995) [6] as follows:

TBI: traumatic injury to the head resulting in one of the following:

- alteration of consciousness or amnesia or;
- neurological or neuropsychological changes or;
- diagnoses of skull fracture or intracranial lesions;
- death due to the sequence of conditions resulted from TBI.

The following databases are searched by the Neurotrauma Evidence Map for English language systematic reviews relating and included in the database:

- Medline (OVID)
- Embase (OVID)
- Cinahl Plus (EBSCO Host)
- Cochrane Library (Wiley)

The Neurotrauma Evidence Map excludes systematic reviews on:

- Guidelines;
- Educational and other strategies aimed at preventing TBI/SCI, including legislation, for example road safety campaign, bicycle helmet laws;
- Animal studies;
- Laboratory and physiological studies not involving clinical application;
- Studies using simulated patients or simulated training programs;
- Cadaver studies;
- Overviews, summaries protocols of systematic reviews;
- Conference proceedings or posters.

At the review level, systematic reviews are categorised relating to traumatic brain injury according to its phases of care. These phases included pre-hospital, acute care, rehabilitation and long-term care, epidemiology and prognosis. The systematic reviews relating within these groups are then further categorised according to topics.

### Quality assessment

Two reviewers (RG and LP) independently assessed the methodological quality of all systematic reviews involving pharmacological management of TBI with the 'Assessment of Multiple Systematic Reviews' (AMSTAR) tool [7]. This validated measurement tool provides an overall quality rating on a scale of

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