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CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Vitamin and Mineral Supplements for Mild Traumatic Brain Injury: Clinical Effectiveness

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Research Questions

1. What is the clinical effectiveness of nutritional supplementation as a prophylactic treatment for mild traumatic brain injury?
2. What is the clinical effectiveness of nutritional supplementation as treatment for mild traumatic brain injury?

Key Findings

One non-randomized study was identified regarding the clinical effectiveness of nutritional supplementation as a treatment for mild traumatic brain injury. No studies were identified regarding the clinical effectiveness of nutritional supplementation as a prophylactic treatment for mild traumatic brain injury.

Methods

A limited literature search was conducted by an information specialist on key resources including Medline, Embase, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were mTBI and specific vitamin or mineral supplements (Vitamin D_3, Vitamin C, Vitamin E, Magnesium or Zinc). No filters were applied to limit retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2005 and March 19, 2020. Internet links were provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Q1: People of all ages, at risk for mild traumatic brain injury Q2: People of all ages, with suspected or diagnosed mild traumatic brain injury
Intervention	The following nutritional supplements, either as single ingredients or in combination preparations: • Cholecalciferol (Vitamin D3) • Vitamin E

	• Ascorbic acid (vitamin C) • Magnesium • Zinc
Comparator	Q1,2: Placebo or usual diet
Outcomes	Q1,2: Clinical effectiveness (e.g., severity of signs and symptoms [e.g., nausea, headache, dizziness], duration of hospitalization, mental status [e.g., level of consciousness, memory], structural brain lesions, neurologic disability, performance measures) and harms (e.g., morbidity, mortality, adverse drug reactions, side effects)
Study Designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, and systematic reviews are presented first and are followed by randomized controlled trials, and non-randomized studies.

One non-randomized study[1] was identified regarding the clinical effectiveness of nutritional supplementation as a treatment for mild traumatic brain injury. No relevant health technology assessments, systematic reviews, or randomized controlled trials were identified. Additionally, no studies were identified regarding the clinical effectiveness of nutritional supplementation as a prophylactic treatment for mild traumatic brain injury.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

One non-randomized study[1] was identified regarding the clinical effectiveness of nutritional supplementation as a treatment for mild traumatic brain injury (TBI). The authors of this study investigated the acute and long-term effects of vitamin D supplementation in patients recovering from traumatic brain injury.[1] The authors found that the group receiving vitamin D supplementation had significantly improved cognitive outcomes and scores on the extended Glasgow Outcomes Scale from the first week of TBI to 3 months post-TBI.[1] Therefore, the authors concluded that the administration of vitamin D supplements during the acute phase of injury for patients with mild to moderate TBI with significant vitamin D deficiency, may improve long-term performance and cognitive outcomes.[1]

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

No literature identified.

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

1. Lee JM, Jeong SW, Kim MY, Park JB, Kim MS. The Effect of Vitamin D Supplementation in Patients with Acute Traumatic Brain injury. *World Neurosurg*. 2019 June;126:e1421-e1426.
PubMed: PM2001807482

Appendix — Further Information

Previous CADTH Reports

2. Amino Acids and Related Supplements for Mild Traumatic Brain Injury: Clinical Effectiveness. (CADTH Rapid response report: summary of abstracts). Ottawa (ON): CADTH; 2020: https://www.cadth.ca/amino-acids-and-related-supplements-mild-traumatic-brain-injury-clinical-effectiveness

3. Lipids and Related Supplements for Mild Traumatic Brain Injury: Clinical Effectiveness. (CADTH Rapid response report: summary of abstracts). Ottawa (ON): CADTH; 2020: https://www.cadth.ca/lipids-and-related-supplements-mild-traumatic-brain-injury-clinical-effectiveness-0

4. Vitamin Supplementation for Hospitalized Adults: Clinical Evidence and Guidelines. (CADTH Rapid response report: summary of abstracts). Ottawa (ON): CADTH; 2014. https://www.cadth.ca/vitamin-supplementation-hospitalized-adults-clinical-evidence-and-guidelines

Systematic Reviews and Meta-Analyses – Alternative Population

5. Lyons MWH, Blackshaw WJ. Does magnesium sulfate have a role in the management of severe traumatic brain injury in civilian and military populations? A systematic review and meta-analysis. *J R Army Med Corps*. 2018 01 Nov;164(6):442-449. PubMed: 29666199

6. Li W, Bai YA, Li YJ, et al. Magnesium sulfate for acute traumatic brain injury. *J Craniofac Surg*. 2015;26(2):393-398. PubMed: PM607510274

7. Arango MF, Mejia-Mantilla JH. Magnesium for acute traumatic brain injury. *Cochrane Database Syst Rev*. 2006;(4):CD005400. PubMed: PM46841259

Randomized Controlled Trials

Upcoming Trials

8. University of Canterbury, Department of Psychology. UTN: U1111-1230-3860 Micronutrients and traumatic brain injury: a feasibility study Australian New Zealand Clinical Trials Registry (ANZCTR). Camperdown (AU): NHMRC Clinical Trials Centre; 2019: http://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=377609.

Alternative Population

9. Abdoli A, Rahimi-Bashar F, Torabian S, Sohrabi S, Makarchian HR. Efficacy of simultaneous administration of nimodipine, progesterone, and magnesium sulfate in patients with severe traumatic brain injury: A randomized controlled trial. *Bull Emerg Trauma*. 2019 April;7(2):124-129. PubMed: PM2001954043

10. Khazdouz M, Mazidi M, Ehsaei MR, Ferns G, Kengne AP, Norouzy AR. Impact of Zinc Supplementation on the Clinical Outcomes of Patients with Severe Head Trauma: A

Double-Blind Randomized Clinical Trial. *J Diet Suppl*. 2018 02 Jan;15(1):1-10.
PubMed: 28467150

11. Natale JE, Guerguerian AM, Joseph JG, et al. Pilot study to determine the hemodynamic safety and feasibility of magnesium sulfate infusion in children with severe traumatic brain injury. *Pediatr Crit Care Med*. 2007 January;8(1):1-9.
PubMed: PM46168350

12. Temkin NR, Anderson GD, Winn HR, et al. Magnesium sulfate for neuroprotection after traumatic brain injury: a randomised controlled trial. *Lancet Neurol*. 2007 January;6(1):29-38.
PubMed: PM44880259

Alternative Population

13. He BX, Ding L, Zhang ZF, et al. Clinical study on routine-dose magnesium sulfate treatment in patients with severe traumatic brain injury. [Chinese]. *Journal of Xi'an Jiaotong University (Medical Sciences)*. 2011;32(2):226-229.
http://yxxb.xjtu.edu.cn/en/oa/DArticle.aspx?type=view&id=201102022

Review Articles

14. Rawson ES, Miles MP, Larson-Meyer DE. Dietary supplements for health, adaptation, and recovery in athletes. *Int J Sport Nutr Exerc Metab*. 2018 March;28(2):188-199.
PubMed: PM621726717

15. Lawrence DW, Sharma B. A review of the neuroprotective role of vitamin D in traumatic brain injury with implications for supplementation post-concussion. *Brain Inj*. 2016 02 Jul;30(8):960-968.
PubMed: PM611272478

16. Vonder Haar C, Peterson TC, Martens KM, Hoane MR. Vitamins and nutrients as primary treatments in experimental brain injury: Clinical implications for nutraceutical therapies. *Brain Res*. 2016;1640:114-129.
PubMed: PM607644387

17. Scrimgeour AG, Condlin ML. Nutritional treatment for traumatic brain injury. *J Neurotrauma*. 2014 01 Jun;31(11):989-999.
PubMed: PM373247619

18. Morris DR, Levenson CW. Zinc in traumatic brain injury: From neuroprotection to neurotoxicity. *Curr Opin Clin Nutr Metab Care*. 2013 November;16(6):708-711.
PubMed: PM52731409

19. Cope EC, Morris DR, Levenson CW. Improving treatments and outcomes: An emerging role for zinc in traumatic brain injury. *Nutr Rev*. 2012 July;70(7):410-413.
PubMed: PM365154100

20. McConeghy KW, Hatton J, Hughes L, Cook AM. A review of neuroprotection pharmacology and therapies in patients with acute traumatic brain injury. *CNS Drugs*. 2012;26(7):613-636.
PubMed: PM365045261