THE EFFECTIVENESS AND HARMS OF PHARMACOLOGICAL INTERVENTIONS IN THE TREATMENT OF DELIRIUM IN ADULTS IN INTENSIVE CARE UNITS AFTER CARDIAC SURGERY: A SYSTEMATIC REVIEW

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**Definition**
- Delirium is defined as an acute alteration in consciousness, attention, cognition and perception that fluctuates in nature that is **often reversible** (Barr et al. 2013)

**Incidence**
- Those at a greater risk are postoperative patients who range between **10% - 40%** with postoperative cardiac patients ranging from **50% - 90%** (Balas et al 2012; Gosselt et al. 2015)

**Significance**
- Associated with poor patient outcomes for up to one year following the episode with **35% dying within six months** of the episode (van den Boogard et al. 2012)

**Risk Factors**
- Preoperative
- Intraoperative
- Postoperative (Balas et al. 2012)
Background: Converging Risk Factors

Preoperative Risk Factors
- Light Disturbances
- Noise

Intraoperative Risk Factors
- Windowless Rooms
- Single Occupancy Rooms

Postoperative Risk Factors
- Sleep Disturbances
The aim of this review was to synthesize the best available evidence about the **effectiveness** and **harms*** of pharmacological interventions in the **treatment of delirium** in adults identified with delirium treated in intensive care units (ICU) after cardiac surgery.

* **Definition of Harms**: “The totality of all possible adverse consequences of an intervention or therapy; they are the direct opposite of benefits, against which they must be compared.” (Ioannidis et al 2004 p. 782, Glossary in Better Reporting of Harms in Randomized Trials: An Extension of the Consolidation Standards of Reporting Trials (CONSORT) Statement)
Methods: Setting and Study Sample

Participants: Adults >16 years, admitted in a cardiothoracic intensive care unit (ICU), post cardiac surgery, identified as having delirium

Intervention: Any pharmacological intervention for treatment of delirium, regardless of dosage or frequency of administration

Comparator: Any two pharmacological interventions

Outcomes:
- Primary: mortality, duration, severity, quality of life, duration/severity of the aggressive episode, associated falls, severity of accidental self-harm, pharmacological harms.
- Secondary: ICU length of stay, hospital length of stay (post ICU), total hospital length of stay, need for additional intervention medication, need for rescue medication
Research Method

Quantitative conducted in accordance with the Joanna Briggs Institute and a *priori* protocol

(PROSPERO Registration Number: CRD42018100124)

Types of Studies:

First: randomised controlled trials
Second: non-randomised controlled trials and quasi experimental
Third: analytical observational studies
Search Strategy

Search to find both published and unpublished studies

For published studies, a three step approach was taken:

1. Initial search of PubMed and CINAHL with the development of search terms and key words
2. Full search across seven databases using the developed search terms and key words
3. Search of reference lists of the final potential studies being considered for inclusion

Unpublished studies were searched from clinical trial registries and ProQuest using broad key words

A hand search of five relevant journals, spanning the last five years was conducted

A web search of three relevant guidelines was also conducted
Methods: Research Design & Methods

**Critical appraisal and data extraction**

The standardised JBI Critical Appraisal Checklist for Randomised Controlled Trials (13 questions)

McMaster Quality Assessment Scale of Harms critical analysis tool (McHarm) (15 questions)

**Data synthesis**

Meta-analysis was as not conducted due to clinical and methodological heterogeneity
Identification

Records identified through database searching (n = 2974)

Additional records identified through other sources (n = 227)

Duplicates removed (n = 326)

Screening

Records screened (n = 2875)

Records excluded (n = 2664) based on title and abstract

Eligibility

Full-text studies assessed for eligibility (n = 211)

Studies assessed for methodological quality (n = 3)

Full-text studies excluded, with reasons (n = 208)

- Not original research (n = 88)
- Ineligible population (n = 10)
- Ineligible intervention (n = 84)
- Ineligible outcome (n = 19)
- Ineligible study design (n = 5)

Studies excluded following assessment of methodological quality (n = 0)

Included

Studies included in the systematic review (n = 3)
Results: Included Studies

Three RCTs met the inclusion criteria:

Atalan et al. 2013. **Morphine** is a reasonable alternative to **Haloperidol** in the treatment of postoperative hyperactive-type delirium after cardiac surgery.


Yapici et al 2011. **Dexmedetomidine** versus **Midazolam** in cardiac surgery patient who fail extubation and present with a delirium state.

In summary:

- Cohort representative of many cardiothoracic patients (40-80 years)
- Conducted in Turkey (n = 2) and Greece
- Delirium identified using RASS, CAM-ICU and 4 point (unvalidated) scale
Effectiveness:
- Low methodological quality across all 3 studies
- Due to information lacking related to true randomisation, allocation concealment, blinding and follow-up
Results: Included Studies

Harms

- Low quality across all 3 studies
- Harms reporting was found to be superficial and insufficient
- Blanket statements provided
Results: Included Studies

• Harms

“Atalan et al, 2013 “that no serious or adverse effects were observed in either the morphine or haloperidol group”

• Potential harms (not reported)
  • Morphine: Hypotension, increased risk of bleeding (vasodilation resulting from histamine release)
  • Haloperidol: arrhythmias and QT prolongation
Results: Included Studies

• Harms
  “Tagarakis et al, 2012 “that ondansetron was safer with milder side effects compared with haloperidol”

• Potential harms (not reported)
  • Ondansetron: confusion and agitation
  • Haloperidol: arrhythmias and QT prolongation
Results: Included Studies

• Harms
  Yapici et al, 2011 “observed hypotension and bradycardia in the dexmedetomidine group but with no haemodynamic compromise”

• Potential harms (not reported)
  • Dexmedetomidine: bradycardia and hypotension
  • Midazolam: confusion and increased risk of cognitive impairment
Results: Significance to clinical practice

• No practice recommendations can be made
  • lack of reporting on both **effectiveness** and **harms**
    to treat hyperactive delirium in reducing the severity
    or duration of delirium

• **Caution** needs to be exercised when using such
  evidence to develop guidelines and protocols
Conclusions

For the critical care nurse

• Awareness of the potential harms of medications used to treat delirium on an unstable and vulnerable heart

• Clinical trials are required to report both benefits and harms of all interventions

• Further RCTs investigating ALL interventions for the treatment of delirium in postoperative cardiac surgical patients is required

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Ely EW, Care Nurse. 2012;32(2):35


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