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The effect of insulin therapy algorithms on blood glucose levels in patients following cardiac surgery: a systematic review protocol

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The effect of insulin therapy algorithms on blood glucose levels in patients following cardiac surgery: a systematic review protocol

Abstract

Review question/objective The objective of this review is to determine the best available evidence related to the effect of insulin therapy algorithms on blood glucose levels in patients in critical care environments following cardiac surgery. More specifically, the review question to be answered is: Among adults within critical care environments who are in the acute postoperative phase (5 days) following cardiac surgery, what is the effect of insulin therapy algorithms for the control of blood glucose levels?

Disciplines

Medicine and Health Sciences | Social and Behavioral Sciences

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The effect of insulin therapy algorithms on blood glucose levels in patients following cardiac surgery: A systematic review protocol

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Review question/objective

The objective of this review is to determine the best available evidence related to the effect of insulin therapy algorithms on blood glucose levels in patients in critical care environments following cardiac surgery.

More specifically, the review question to be answered is:

Among adults within critical care environments who are in the acute postoperative phase (5 days) following cardiac surgery, what is the effect of insulin therapy algorithms for the control of blood glucose levels?

Background

Hyperglycemia, a condition characterized by elevated blood glucose levels (BGLs), is most commonly associated with diabetic illness.¹ However, hyperglycemia has also been found to have a high incidence after cardiac surgery. Current literature surrounding this topic suggests that hyperglycemia occurs almost universally after cardiac surgery; irrespective of whether a person has a pre-existing diagnosis of diabetes mellitus or not.¹⁻³ Conventionally, post-operative hyperglycemia following cardiac surgery was viewed purely as a natural adaptive physiological response of the body that was treated only when BGLs rose to what was considered excessively high levels;² generally greater than 12.2 mmol/L [220mg/dl].⁴ This view has since changed and hyperglycemia following cardiac surgery is now viewed as an adverse effect of surgery, occurring as a result of multiple factors that include: the intraoperative

hypothermic state, surgical stress, hypokalemia, adverse effects from pharmacological agents and the commonly occurring post-operative systemic inflammatory response.⁵⁻⁷

While generally only transient, an incidence of hyperglycemia during the initial post-operative period can have serious detrimental side effects following cardiac surgery such as deep sternal wound infection and an increased risk of mortality.⁸ Current evidence suggests that within critical care environments, the early recognition and treatment of post-operative hyperglycemia is imperative. This is achieved through the utilization of continuous intravenous insulin infusion algorithms, with the aim of maintaining BGLs within normal to near normal ranges, in order to prevent the adverse outcomes associated with hyperglycemia in post-operative patients.⁹

The practice of maintaining BGLs within strict pre-defined levels, via the administration and titration of a continuous insulin infusion, has become common practice within critical care environments over the past decade.¹⁰ Results from a study by Van Den Berghe et al., which included 970 cardiac surgery patients [63%] showed that the maintenance of BGLs below 110 mg/dl [6.1 mmol/L], using continuous insulin therapy lead to decreases in both mortality and morbidity rates among critically ill surgical patients.³ Since this time, multiple studies investigating the effects of continuous insulin infusion algorithms have concluded that the use of such algorithms for the management of BGLs in cardiac surgery patients has favorable effects, decreasing the incidence of post-operative complications and reducing the length of time patients are required to remain in hospital.¹¹

The use of continuous intravenous infusion algorithms for controlling BGLs in critically ill patients is further supported by the American Diabetes Association [ADA] who recommend the use of tried and tested insulin infusion protocols that demonstrate a low incidence of hypoglycemia.¹² The ADA go on to state that BGLs of critically ill patients, including postoperative patients who have undergone a cardiac procedure, should be maintained between 7.8 and 10 mmol/L [140 and 180mg/dl] with insulin therapy commenced at a threshold no higher than 10 mmol/L [180mg/dl].¹² While it is acknowledged that greater benefits may be achieved by the maintenance of BGLs at the lower ends of the range, the American Diabetes Association do not recommend targets less than 6.1mmol/l [110mg/l] due the high risk of causing significant hypoglycemia.¹²

A review of the literature shows that a number of insulin infusion algorithms, with varying methods and effects, have been developed for utilization by clinicians in critical care environments to guide the management of hyperglycemia. Due to the conflicting evidence that currently exists, the critical care clinician responsible for the provision of care to post-operative cardiac surgery patients needs to determine the best evidence in relation to the management of hyperglycemia, to maintain patient safety and ensure good surgical outcomes, free from complications. However, a review of the outcomes of these protocols for cardiac patients has not been published to inform the development of best evidence based practice guidelines. This systematic review therefore aims to review the various protocols to ascertain the best available evidence related to the effect of intensive insulin therapy algorithms on BGLs in post-operative patients in critical care environments following cardiac surgery.

Keywords

Hyperglycemia/hyperglycaemia; Blood glucose; Cardiac surgery; Heart surgery; Insulin; Insulin infusion; Intensive insulin infusion; Intravenous insulin infusion; Continuous insulin infusion; Postoperative; Critical care environment

Inclusion criteria

Types of participants

This review will consider studies that include adult patients aged 18 years and over admitted to a critical care unit following cardiac surgery and who received insulin therapy for glycemic control during the acute postoperative phase (five days) of admission.

In this review studies that include participants with a known diagnosis of Diabetic Ketoacidosis will be excluded.

Types of intervention(s)/phenomena of interest

This review will consider studies that evaluate the use of intravenous insulin therapy algorithms to control blood glucose levels in acute postoperative phase patients in critical care environments following cardiac surgery.

In this review, studies will be included if they make one of the following comparisons:

1. Intravenous insulin therapy algorithm compared to another insulin therapy algorithm.
2. Intravenous insulin therapy algorithm compared to no treatment.
3. Intravenous insulin therapy algorithm compared to a placebo.

In this review, studies that include a Glucose-Insulin-Potassium (GIK) infusion as an intervention or a comparator will be excluded.

Types of outcomes

This review will consider studies that include the following outcome measures:

Primary outcome:

- Overall control of blood glucose levels as measured by time to target BGL range, time spent in BGL target range and time above or below target BGL range.

Secondary outcome:

- Incidence of adverse events, including:
 - Hypo/hyper glycemia, measured by standard point of care glucometers, arterial blood analysis, or venous blood analysis, with hypoglycemia defined as a BGL reading $<3.9\text{mmol/L}$ (70mg/dL)¹³ and hyperglycemia defined as a BGL reading $>7.8\text{mmol/L}$ (140mg/dL).¹³
 - Sternal wound infection, identified by a positive wound culture or a positive wound exudate culture.¹⁴
 - Mortality rate measured by in-hospital mortality (from day of operation to day of discharge) and/or 30 day mortality.¹⁵

Types of studies

This review will consider any experimental study design including randomized controlled trials, non-randomized controlled trials, quasi-experimental and before and after studies for inclusion.

Search strategy

The search strategy aims to find both published and unpublished studies. A three-step search strategy will be utilized in this review. An initial limited search of MEDLINE and CINAHL will be undertaken, followed by analysis of the text words contained in the title and abstract and of the index terms used to describe the article. A second search using all identified keywords and index terms will then be undertaken across all included databases. Thirdly, the reference lists of all identified reports and articles will be **hand** searched for additional studies.

Studies published in the English language will be considered for inclusion in this review. Databases will be searched with no limits placed on the date of publication, allowing authors to search as far back as possible.

The databases to be searched include:

MEDLINE, CINAHL, PubMed, Embase, SCOPUS, Cochrane Trials, Dare, Social Science Index.

The search for unpublished studies will include:

ProQuest Dissertations & Theses and MedNar

Initial keywords to be used will be:

Hyperglycemia/hyperglycaemia

Blood glucose

Cardiac surgery

Heart surgery

Insulin

Insulin infusion

Intensive insulin infusion

Intravenous insulin infusion

Continuous insulin infusion

Postoperative

Critical care environment

Assessment of methodological quality

Papers selected for retrieval will be assessed by two independent reviewers for methodological validity prior to inclusion in the review using standardized critical appraisal instruments from the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) (Appendix I).

Any disagreements that arise between the reviewers will be resolved through discussion, or with a third reviewer.

Data collection

Data will be extracted from papers included in the review using the standardized data extraction tool from JBI-MASARI (Appendix II). The data extracted will include specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives.

Data synthesis

Quantitative data will, where possible, be pooled in statistical meta-analysis using JBI-MASARI. All results will be subject to double data entry. Effect sizes expressed as odds ratios (for categorical data) and weighted mean differences (for continuous data) and their 95% confidence intervals will be calculated for analysis. Heterogeneity will be assessed statistically using the standard Chi-square and also explored using subgroup analyses based on the different study designs included in this review. Where statistical pooling is not possible, the findings will be presented in narrative form including tables and figures to aid in data presentation where appropriate.

Conflicts of interest

No conflicts of interest can be identified or foreseen in relation to this proposed systematic review.

Acknowledgements

Nil

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Appendix I: Appraisal instruments

MAStARI appraisal instrument

JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial

Reviewer Date

Author Year Record Number

	Yes	No	Unclear	Not Applicable
1. Was the assignment to treatment groups truly random?	☐	☐	☐	☐
2. Were participants blinded to treatment allocation?	☐	☐	☐	☐
3. Was allocation to treatment groups concealed from the allocator?	☐	☐	☐	☐
4. Were the outcomes of people who withdrew described and included in the analysis?	☐	☐	☐	☐
5. Were those assessing outcomes blind to the treatment allocation?	☐	☐	☐	☐
6. Were the control and treatment groups comparable at entry?	☐	☐	☐	☐
7. Were groups treated identically other than for the named interventions?	☐	☐	☐	☐
8. Were outcomes measured in the same way for all groups?	☐	☐	☐	☐
9. Were outcomes measured in a reliable way?	☐	☐	☐	☐
10. Was appropriate statistical analysis used?	☐	☐	☐	☐
	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info. ☐

Comments (Including reason for exclusion)

Appendix II: Data extraction instruments

MAStARI data extraction instrument

JBI Data Extraction Form for Experimental / Observational Studies

Reviewer Date

Author Year

Journal Record Number

Study Method

RCT ☐ Quasi-RCT ☐ Longitudinal ☐

Retrospective ☐ Observational ☐ Other ☐

Participants

Setting

Population

Sample size

Group A Group B

Interventions

Intervention A

Intervention B

Authors Conclusions:

.....
.....

Reviewers Conclusions:

.....
.....

Study results**Dichotomous data**

Outcome	Intervention () number / total number	Intervention () number / total number

Continuous data

Outcome	Intervention () number / total number	Intervention () number / total number