**The impact of a pharmacist on conversion of intravenous to subcutaneous insulin in cardiac surgery patients**

Megan Farrell, PharmD

St. Rose Dominican Hospital - Siena Campus

Henderson, Nevada

**Travis Merkle, PharmD, BCCCP**

St. Rose Dominican Hospital - Siena Campus, Henderson, Nevada

**Kathryn Mrzljak, PharmD, MBA, BCPS**

St. Rose Dominican Hospital - Siena Campus, Henderson, Nevada

Abstract:

**Background**

In 2009 the Society of Thoracic Surgeons (STS) published guidelines for perioperative glucose management in cardiac surgery.1 Per STS, continuous insulin infusion is recommended for perioperative glucose control; it is additionally recommended that infusion be initiated intra-operatively and continued for ≥ 24 hours postoperatively in diabetic patients. Perioperative hyperglycemia is an independent predictor of mortality in adults undergoing cardiac surgery, regardless of diabetic status.2,3,4 Maintaining blood glucose levels ≤ 180 mg/dL perioperatively decreases overall mortality and reduces length of hospital stay in both diabetic and non-diabetic patients. Once past the initial 24-48 hours postoperatively patients may be transitioned to subcutaneous insulin. In order to standardize the transition from intravenous to subcutaneous insulin and increase the amount of time in goal glucose range in cardiac surgery patients at Dignity Health - St. Rose Dominican Hospital, a pharmacy-driven protocol was created. This protocol allowed pharmacists to transition adult cardiac surgery patients from intravenous insulin to subcutaneous insulin once blood glucose has stabilized in the post-operative period.

**Methods**

This is a retrospective, quality improvement project conducted at Dignity Health - St. Rose Dominican Hospital. A pharmacy-driven protocol was introduced to allow pharmacists to automatically transition cardiac surgery patients from intravenous to subcutaneous insulin. Included patients were ≥ 18 years old, underwent an open-heart procedure (coronary artery bypass graft, surgical aortic valve replacement, mitral valve repair, or surgical mitral valve replacement), and received post-operative care in the ICU. The intervention group consisted of patients meeting inclusion criteria that were transitioned after protocol approval and the control group consisted of patients that were transitioned before protocol approval. The primary outcome was achievement of target glycemic goals (70-180 mg/dL) in the 48-hours following conversion of insulin regimen. Secondary analyses included total hypoglycemic events (glucose <70 mg/dL), incidence of acute kidney injury during admission, and incidence of post-surgical atrial fibrillation.

**Results**

There was no statistically significant difference observed in the primary outcome between the pre-protocol and post-protocol groups (85.9% versus 82.7%, p = 0.85). Compared to the pre-protocol group, the post-protocol group had larger doses of insulin glargine (8.8 versus 14.1 units, p = 0.001) and a shorter duration of insulin infusion (38.1 versus 31.5 hours, p = 0.018). There was no difference in incidence of hypoglycemia (4 versus 2, p = 1).

**Conclusion**

Use of a pharmacy driven insulin conversion protocol achieved similar glycemic control in a cardiac surgery population compared to standard care. There was also increased initial doses of insulin glargine and decreased duration of time on insulin infusion with no associated increase in hypoglycemic events observed in the intervention group. The findings of this project were limited due to sample size, inability to control for patient severity, and issues with protocol adherence.

Keywords: insulin, glucose control, cardiac surgery, pharmacist

1. Background

Stress hyperglycemia is generally defined as a transient increase in blood glucose levels occurring in patients without previously diagnosed diabetes due to medical or surgical stress.6,7,8 This transient state of hyperglycemia is commonly induced following major cardiac surgery and typically is most prevalent in the first 72 hours postoperatively.6,7,8 Hyperglycemia in the perioperative period is an independent predictor of mortality in adults undergoing cardiac surgery, regardless of diabetic status.1 Maintenance of blood glucose <180 mg/dL during the perioperative period has been associated with decreased overall mortality, decreased incidence of wound infections, decreased incidence of atrial fibrillation, etc. Guidelines for the perioperative management of glucose in adult cardiac surgery patients were published in 2009 by the Society of Thoracic Surgeons (STS).1 According to these guidelines, management of perioperative glucose involves several stages of management. During the preoperative stage, patients should be managed with subcutaneous insulin and home medications as appropriate. Intraoperative management involves initiation of an intravenous insulin infusion. Intravenous insulin is then continued for ≥ 24 hours postoperatively in diabetic patients and as appropriate in non-diabetic patients. As patients move past the initial 24-48 hours postoperatively they may be transitioned to a subcutaneous insulin regimen. The STS and American Diabetes Association (ADA) recommend that the transition from intravenous to subcutaneous insulin should be guided by institutional protocol.1,5

A pharmacy-driven insulin conversion protocol (See Appendix A) was accepted by The Pharmacy and Therapeutics Committee on October 25, 2022 to allow pharmacists to automatically transition appropriate cardiac surgery patients from intravenous to subcutaneous insulin. This project compares glycemic outcomes of cardiac surgery patients before and after implementation of a pharmacy-driven institutional protocol to standardize conversion from intravenous to subcutaneous insulin.

**2. Methods**

This was a retrospective chart review of records from February 1st, 2022 - October 31st, 2022 and November 21st, 2022 - February 28th, 2023 at Dignity Health – St. Rose Siena and San Martin campuses.

***2.1 Data Collection***

A report was generated from the EHR integrated surgical scheduler and the medical record for each patient meeting inclusion criteria was comprehensively reviewed.

* Inclusion criteria: Patients that underwent open-heart procedures: coronary artery bypass graft (CABG), surgical aortic valve replacement (SAVR), mitral valve repair (MVR) and surgical mitral valve replacement (SMVR) at Dignity Health - St. Rose Siena Campus and San Martin Campus and received post-operative care in the Intensive Care Unit (ICU). Patients must have been discharged before initiation of data collection.
* Exclusion criteria: Patients that died before transition from insulin infusion to subcutaneous regimen.
* Age Range: ≥ 18 years of age with no maximum age

See Appendix A for further information.

***2.2 Data Analysis***

Outcomes were analysed by a statistician utilizing t-tests. Based on an approximate rate of 61% of glucose measurements in range for diabetics institutionally, 206 total patients were required to detect a 19% increase with 80% power. A p-value less than 0.05 denoted statistical significance.

**3. Results**

In total, 243 patients met inclusion criteria and were included in the analysis. Baseline characteristics were similar and are listed in Table 1. In the intervention group, we found similar percentage of glucose measurements within goal (85.9 versus 82.7, p = 0.85), increased doses of insulin glargine (8.8 versus 14.1, p = 0.001), and shorter duration of time on insulin infusion (38.1 versus 31.5, p = 0.018). All outcomes can be found in Tables 2 - 4.

Table 1: Baseline Characteristics

|  |  |  |
| --- | --- | --- |
|  | Pre-protocol (n=140) | Post-protocol (n=103) |
| Age, yr (SD) | 68.6 ± 9.5 | 68.2 ± 9.4 |
| Female, n (%) | 47 (33.3) | 29 (28.2) |
| BMI, kg/m2 (SD) | 29.1 ± 6.1 | 31.4 ± 5.7 |
| Pre-operative HbA1c, % (SD) | 6.6 ± 1.6 | 6.6 ± 1.4 |
| Diabetic History, n (%) | 63 (44.6) | 49 (47.6) |
| Home Antidiabetic Agents, n (%) | 55 (39.3) | 37 (35.9) |
| CABG, n (%) | 116 (82.3) | 85 (82.5) |
| Post-procedural Steroids, n (%) | 24 (17.1) | 24 (23.3) |

Table 2: Primary Outcome

|  |  |  |  |
| --- | --- | --- | --- |
|  | Pre-protocol (n=140) | Post-protocol (n=103) | P-value |
| Glucose Measurements in Goal, % | 85.9 | 82.7 | 0.85 |

Table 3: Adjusted Primary Outcome

|  |  |  |
| --- | --- | --- |
|  | Post-protocol - Pre-protocol (SE)\* | P-value |
| Glucose Measurements in Goal, % | -3.2 (3.0) | 0.85 |
| Glucose Measurements in Goal -Controlled for Diabetic Status, % | -2.4 (2.6) | 0.36 |
| Glucose Measurements in Goal -Controlled for Steroid Use, % | -3.0 (2.9) | 0.31 |

\*Standard Error

Table 4: Secondary Outcomes

|  |  |  |  |
| --- | --- | --- | --- |
|  | Pre-protocol (n=140) | Post-protocol (n=103) | P-value |
| Hypoglycemic Events, n (%) | 4 (3.9) | 2 (1.9) | 1.0 |
| Time on Insulin Drip, h (SD) | 38.1 (24.8) | 31.5 (14.7) | 0.018 |
| Insulin Glargine Dose, Units (SD) | 8.8 (10.3) | 14.1 (13.9) | 0.001 |
| Acute Kidney Injury, n (%) | 73 (51.8) | 48 (46.6) | 0.437 |
| Atrial Fibrillation, n (%) | 56 (39.7) | 47 (45.6) | 0.431 |

**4. Discussion**

In the intervention group, percentage of glucose measurements within goal were numerically lower than in the control group. In terms of safety, there were numerically less hypoglycemic events in the intervention group. These differences were not statistically significant. Interventional patients also received higher doses of insulin glargine and had a shorter duration of time on intravenous insulin infusion. These differences were statistically significant.

***4.1 Limitations***

The limitations of this project include the small sample size, the project being a retrospective chart review, inability to control for patient severity, and protocol adherence. Examples of increased patient severity in the intervention group include increased numbers of patients on postoperative steroids (17.1% versus 23.3%), higher BMI (29.1 ± 6.1 versus 31.4 ± 5.7), more diabetic patients (44.6% versus 47.6%), and increased length of hospital stay (11.7 versus 13.2). It is important to note that protocol adherence at each site was not assessed during the course of this study and may have contributed to final glycemic control results.

**5. Conclusion**

The benefit of pharmacist intervention was unclear from this project alone. The increased initial doses of insulin glargine and decreased duration of insulin infusion suggest possible benefit to pharmacist intervention with standadardized protocol; however, due to study limitations this result is not supported by statistical significance. As protocol adherence is a cruical aspect of assessing protocol efficacy it is recommeded that adherence is assessed at both practice sites to identify needs for further education and training.

Conflicts of Interest

The author declares no competing interests.

Acknowledgements

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**Appendix A**

# POLICY/PROCEDURE

 CATEGORY: Clinical/Pharmacy Page 1 of 6

SUBJECT: **Transition from IV to Subcutaneous Insulin in Adult Post-Cardiac Surgery Patients**

 ORIGINATED: 02/23 EFFECTIVE: 03/23 SUPERSEDES: N/A

**============================================================================**

# 1.0 PURPOSE

**1.1** Scope – To define the process for converting IV insulin infusion to a subcutaneous insulin regimen in adult post-cardiac surgery patients at Dignity Health St. Rose Dominican (SRD).

**1.2** Objective – To provide guidelines to standardize the transition of intravenous insulin infusion to a subcutaneous regimen in adult post-cardiac surgery patients.

# 2.0 RESPONSIBILITIES

**2.1** Licensed Clinical Staff (Clinical Staff) – are responsible for administering medications to patients within their scope of practice as ordered by the LP.

**2.2** Licensed Practitioner (LP) – who are credentialed and privileged to do so, are responsible for initiating and monitoring IV insulin infusion for patients as needed according to diagnosis and risk factors.

**2.3** Pharmacists – are responsible for assessing the glucose levels and intravenous insulin requirements of patients in their assigned unit daily and automatically transitioning to subcutaneous dosage regimen when/if patient meets criteria.

# 3.0 DEFINITIONS

**3.1** Basal Insulin– long-acting insulin typically dosed once per day subcutaneously to provide steady glucose control in patients with higher insulin requirements.

**3.2** Correctional Insulin – rapid-acting insulin administered subcutaneously multiple times per day, e.g., at meals & bedtime or every six hours, on the basis of a pre-determined sliding scale to bring a high blood glucose level down to a target range.

**3.3** Intravenous Insulin – short-acting insulin administered intravenously as a continuous infusion to maintain tight glycemic control.

**3.4** Nutritional Insulin – rapid-acting insulin provided to cover carbohydrate intake from food, tube feeds, parenteral nutrition or dextrose from other sources, e.g., IV fluids.

# 4.0 POLICY

**4.1** The Pharmacist will review daily post-cardiac surgery patients on an IV insulin continuous infusion for eligibility criteria to transition IV insulin therapy to a subcutaneous regimen. (See Attachment A)

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### SUBJECT: **Transition from IV to Subcutaneous Insulin in Adult Post-Cardiac Surgery Patients**

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**4.2** If the patient meets criteria the Pharmacist will automatically convert the IV insulin infusion to one of the following subcutaneous regimens using the delineated criteria: (See Attachment B)

4.2.1 Low SubCut Insulin Requirement

4.2.2 Usual/Moderate SubCut Requirement

4.2.3 High SubCut Insulin Requirement

**4.3** The pharmacist will order the insulin subcutaneous regimen using the *Insulin SubCut, Glycemic Control* powerplan.

4.3.1 The pharmacist will choose *No Cosignature Required* as the communication type. (See Reference 7.1)

**4.4** Upon initiating the conversion, the pharmacist will discontinue the IV insulin infusion order.

4.4.1 The pharmacist will choose *No Cosignature Required* as the communication type.

**4.5** If basal insulin is ordered, the pharmacist will schedule the basal insulin dose to be administered two (2) hours prior to the discontinuation of the IV insulin infusion.

# 5.0 PROCEDURES

**5.1** The Decentralized Pharmacist will review adult post-cardiac surgery patients receiving IV insulin infusion to determine if the patient meets criteria for conversion to a subcutaneous regimen. (See Attachment A)

**5.2** The pharmacist will monitor the subcutaneous regimen daily and modify insulin orders per protocol and/or contact the LP to facilitate maintenance of blood glucose levels in the target range of 70 – 180 mg/dL.

# 6.0 DOCUMENTATION

**6.1** The pharmacist will process order(s) in the patient’s electronic health record. (See Reference 7.1)

# 7.0 REFERENCES

**7.1** *Elements of Medication Orders*, SRDH Clinical/Pharmacy Policy #Pharm 07-33.

## DIGNITY HEALTH ST. ROSE DOMINICAN-POLICY/PROCEDURE

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# 8.0 ATTACHMENTS

**8.1** *Patient Criteria for the Automatic Conversion from Intravenous to Subcutaneous Insulin*, Attachment A

**8.2** *Selecting a Subcutaneous Regimen,* Attachment B

**Revision Reviewed/Approved:**

Pharmacy & Therapeutics Committee, November 2022

Medical Executive Committee, November 2022

Multidisciplinary Policy & Procedure Committee, January 2023 CNE Council, February 2023

**Author/Owner:** Pharmacy Department

## Attachment A

**Patient Criteria for Automatic Conversion of IV to a Subcutaneous Insulin Regimen**

|  |
| --- |
| **Inclusion Criteria**  |
| Patient located in the intensive care unit  |
| Patient has undergone one of the following cardiovascular surgical procedures: * Aortic valve replacement (AVR)
* Coronary artery bypass graft (CABG)
* Mitral valve repair or replacement (MVR)
* Tricuspid valve repair or replacement
 |
| Patient has received a minimum of twenty-four (24) hours of IV insulin therapy  |
| Blood glucose readings in the previous six (6) hours have been within the goal range of 70 – 180 mg/dL  |

|  |
| --- |
| **Exclusion Criteria**  |
| Continuous Renal Replacement Therapy  |
| High inotropic and/or vasopressor requirements defined as follows: * DOBUTamine rate greater than 5 mcg/kg/min
* EPINEPHrine rate greater than 5 mcg/min
* norepinephrine rate greater than 5 mcg/min
* vasopressin rate greater than 0.03 units/min
 |
| LP Request to Exclude Patient  |
| Mechanical Circulatory Support Including: * Extracorporeal Membrane Oxygenation
* Impella®
* Intra-Aortic Balloon Pump
* Left Ventricular Assist Device
 |
| Open Sternum or Sternal Wound Infection  |
| Unstable IV Insulin Infusion Rate Defined as:   Rate changes greater than 2 units/hour in the previous 6 hours  |

## Attachment B

**Selecting the Appropriate Subcutaneous Insulin Regimen**

1. Determine the need for **basal insulin**, i.e., insulin glargine.

- For **diabetic** patients, e.g., reported history of diabetes, hemoglobin A1c greater than or equal to 6.5%, or on treatment for diabetes:

 The *initial* **basal insulin** dose will be 50% of the *average 24-hour IV insulin requirement* which is calculated by averaging the hourly insulin requirement in the six (6) hours prior to transition and multiplying by twenty-four (24)*.*

*Average 24-hour IV insulin requirement* = 6 hour insulin rate average x 24 hours

 **Please Note**: For patients with home basal insulin therapy, if the calculated basal dose is less than 50% of the home dose, order 50% of **home basal dose** instead of the calculated dose.

##  **Order insulin glargine dose as a one time *now* order and QAM. Reassess dose based on morning glucose levels.**

 - For patients ***without*** diabetes:

 Calculate the *6-hour insulin rate average* by averaging the hourly insulin requirement in the six (6) hours prior to transition.

###  If the *6 hour insulin rate average* is less than 1 unit/hour:

* Do **not** order basal insulin  Discontinue insulin infusion and only order insulin correctional scale using the available subplans (see #2 below).

 If the *6 hour insulin rate average* is greater than or equal to 1 unit/hour:

* The *initial* **basal insulin** dose will be 50% of the *average 24-hour IV insulin requirement* which is calculated by averaging the hourly insulin requirement in the six (6) hours prior to transition and multiplying by twenty-four (24).

*Average 24-hour IV insulin requirement* = 6 hour insulin rate average x 24 hours

* **Order insulin glargine as a one time *now* order and reassess the need the following day.**

* **If basal insulin is ordered:**

 Communicate with the patient’s nurse to stop the IV insulin infusion 2 hours after the insulin glargine dose is administered.

 - Example of basal insulin calculation:

* Patient’s insulin doses in the last 6 hours: 1.6, 2, 1.6, 1.7, 1.6, 1.6
* The 6 hour insulin average is (1.6 + 2 + 1.6 + 1.7 + 1.6 + 1.6) / 6 = 1.7 units/hr

 The 24-hour IV insulin requirement is 1.7 units/hr x 24 hr = 40.8 units

 The insulin glargine dose = 40.8 x 0.5 = 20.4 units (rounded to 20 units)

### Attachment B cont’d

**Selecting the Appropriate Subcutaneous Insulin Regimen**

1. Order one of the following ***CORRECTIONAL* insulin scale subplans** based on the following patient criteria**,** use the *Insulin, SubCut Glycemic Control* powerplan:

* + Low Insulin Requirement:

 Actual body weight is less than 70 kg or BMI less than 30

* + Usual/Moderate Insulin Requirement:

 Actual body weight 71 – 90 kg or BMI 31 – 35

* + High Insulin Requirement:

 Actual body weight greater than 90 kg or BMI greater than 35 **Receiving steroid therapy**

1. Determine the need for ***nutritional* insulin**, i.e., insulin lispro with meals.

* + For **diabetic** patients **AND** insulin glargine doses greater than 20 units **AND** expected to eat greater than 50% of their meals  **order NUTRITIONAL insulin doses** with each meal.

* + Order **NUTRITIONAL** insulin based on correctional insulin in the power plan **with the following adjusted doses**:

 Low Requirement:

 Insulin lispro 2 units subcut TID with meals, i.e., 1 unit of insulin / 30 gm carbs

 Usual Requirement:

 Insulin lispro 4 units subcut TID with meals, i.e., 1 unit of insulin / 15 gm carbs

 High Requirement:

 Insulin lispro 6 units subcut TID with meals, i.e., 1 unit of insulin / 10 gm carbs

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