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BMH Med. J. 2017;4(3):91-98 **Review Article**

Update On Management Of In-hospital Hyperglycemia

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Abstract

Hyperglycemia is regarded as one of the most important poor prognostic factors that adversely affects the treatment response in patients admitted with medical or surgical conditions. The most effective way to treat this serious co-morbidity is by insulin. There are various confusing protocols for the management of in-hospital hyperglycemia in both critical and non critical patients. This article highlights the importance of in-hospital hyperglycemia and simplifies the approach to the treatment of hyperglycemia in various situations.

Keywords: In-hospital hyperglycemia, insulin, basal bolus regimen

Introduction

The incidence of diabetes is increasing at a rapid rate worldwide and it is estimated that more than 640 million people are likely to suffer from diabetes by 2040 [1]. Hyperglycemia on admission is associated with increased in hospital mortality and morbidity in critically-ill patients. Hyperglycemia in patients admitted with acute myocardial infarction or acute stroke is proved to be a bad prognostic factor in terms of both mortality and residual disability [2]. Hyperglycemia is also associated with prolonged hospital stay and increased incidence of infections.

With this introduction, we are highlighting the importance of tight in-patient glycemic control, that improves the outcome of primary disease with which a patient gets admitted.

Pathogenesis of in hospital hyperglycemia

Increased incidence of infections or worsening of pre-existing infections in diabetic patients is explained by the pathogenic mechanism depicted in Figure 2 [4]. The relationship between hyperglycemia and poor hospital outcome is explained in Figure 3 [5].

Screening for in hospital hyperglycemia [6]

All the patients admitted should be asked for history of diabetes. Patients without a history of diabetes and with a blood glucose of >140 mg/dL on admission must be monitored with blood

glucose testing for at least 24 to 48 hours. Patients with blood glucose >140 mg/dL require 8th hourly blood glucose testing and suitable therapeutic intervention. Patients on treatment with corticosteroids, octreotide, enteral nutrition and parenteral nutrition must be monitored with blood glucose testing for at least 24 to 48 hours after the initiation of therapy. Patients with blood glucose more than 140 mg/dL need 8th hourly blood glucose testing and suitable therapeutic intervention. All patients with history of diabetes must be tested for HbA1C level if it was not done in the preceding 2 to 3 months.

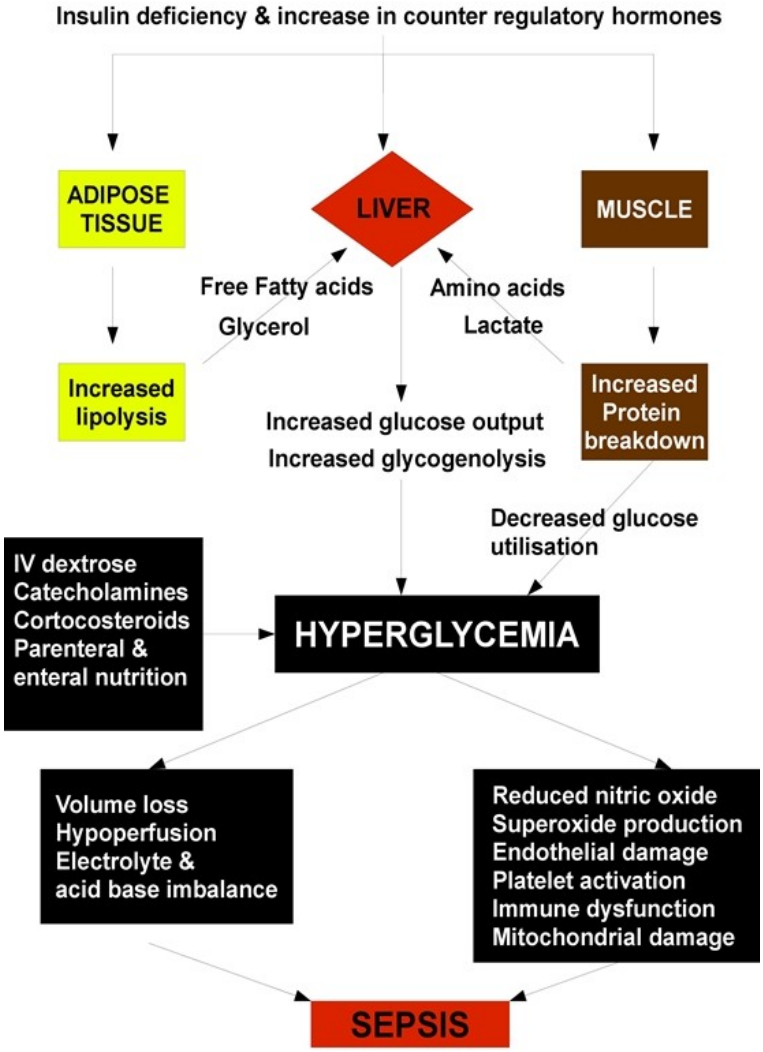

Figure1: Pathogenesis of hyperglycemia [3]

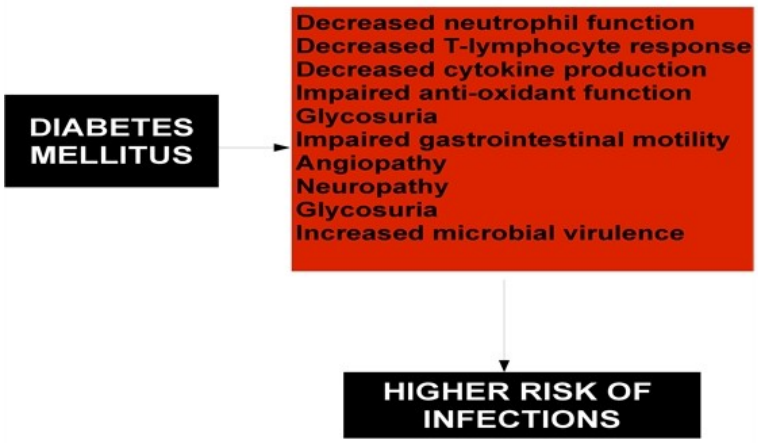

Figure 2: Pathogenesis of infections in diabetes

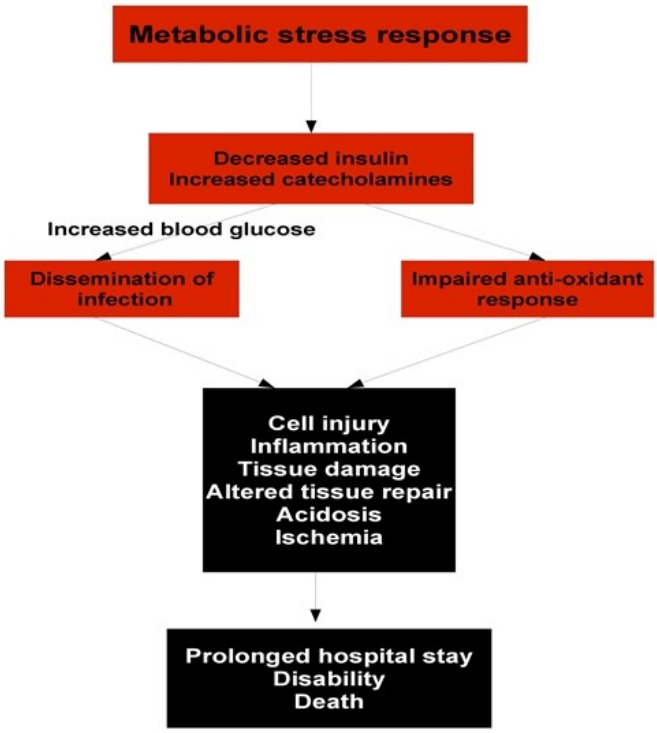

Figure 3: Hyperglycemia and its impact on treatment outcome

Glycemic Targets

Table 1: Glycemic Targets in the management of Hyperglycemia

Blood sugar	Non-critically ill	Critically ill
Pre-meal	<140 mg/dL	140-180 mg/dL
Random	<180 mg/dL	140-180 mg/dL

Blood sugar less than 100mg/dL should be avoided in critically-ill, as such stringent targets can cause severe hypoglycemia (<40mg/dL), which is a cause of increased mortality in critically-ill.

Insulin and in hospital hyperglycemia

Insulin is the best choice for management of in-hospital hyperglycemia, due to its anti-inflammatory, vasodilatory and anti-oxidant properties. Insulin exerts Nitric Oxide mediated vasodilatory effect on blood vessels that reduces the leucocyte adhesion to the endothelium and thereby, the leucocyte recruitment at the site of inflammation [7, 8].

These properties of insulin help in the improvement of outcome in patients admitted with conditions like myocardial infarction, stroke, sepsis etc., making insulin the prime choice of inpatient diabetes management.

Role of oral anti-diabetic drugs in the management of in hospital hyperglycemia (Table 2)

To summarize, all oral anti-diabetics have significant limitations for inpatient use and they hardly provide an opportunity to titrate the dosage according to blood sugar.

Table 2: Limitations of oral anti diabetic drugs during hospitalisation

Group	Limitation
Sulfonylureas	Long duration of action & higher risk of hypoglycemia. Variation in duration of action between individuals
Metformin	Lactic acidosis in patients with high risk of hypoxia, hypoperfusion & renal insufficiency limit its usage for inpatient management
Thiazolidinediones	Slow onset of action & contraindication in heart failure make them unsuitable for inpatient management.

Latest Recommendations on in patient hyperglycemia managent

1) Critically ill patients:

Continuous insulin infusion (CII) is the best method. Regular or rapid acting insulin analogs should be for IV infusion. 50 units of regular insulin dissolved in 50 mL normal saline should be used as the infusion fluid with an electronic infusion pump or syringe pump and the dosage is titrated as per the following (**Table 3**).

Table 3: Dose of insulin infusion for continuous insulin infusion method

Blood glucose levels (mg/dL)	Dosage of insulin infusion (units/hour)
<100	No insulin
100-149	1-1.5
150-199	2
200-249	2.5
250-299	3
300-349	3.5
350-399	4

If the blood sugar increases further, it should be treated subjectively by the critical care physician. 50 mL of 25% dextrose should be given intavenous, if blood glucose is <50mg/dL and blood sugar should be checked after 15 min. If blood glucose increases to >100mg/dL start insulin infusion at 1 unit/hour. 50 mL of 25% dextrose should be given, if the blood sugar is between 50mg/dL and 75mg/dL with symptoms of hypoglycemia. If asymptomatic, 25mL of 25% dextrose should be given intravenous and blood sugar should be checked after 15 minutes and start infusion if it is >100mg/dL. Overlap with long-acting insulin should be done 1 to 2 hours prior to stopping the infusion, in case of transition to subcutaneous insulin. If rapid-acting analogs are being used, the overlap period can be reduced to 15-30 minutes.

2) Non-critically ill patients:

Hyperglycemia in this group is best managed with basal bolus regimen, that includes a basal long-acting insulin to cover the 24 hour insulin requirement and rapid-acting regular or insulin analog to

cover the post-prandial rise in blood sugar. Sliding scale insulin regimen is no longer a valid method. Total Daily Dose (TDD) calculation of subcutaneous insulin for various patient categories is given in **Table 4.**

Table 4: Dose of insulin in various situations

Patient category	TDD (units/kg body wt)
Old age Renal or hepatic dysfunction Hemodialysis	0.25
No co-morbid condition	0.5
Obesity Severe infection CABG Corticosteroid therapy Total parenteral nutrition	1

Example of a basal bolus insulin regimen for the management of non-critically ill patients with type 2 diabetes [6].

A. Basal insulin

Oral anti-diabetes drugs should be discontinued. For starting insulin, calculate the total daily dose as follows:

- 0.2 to 0.3 U/kg body weight in patients aged more than or equal to 70yr and/or glomerular filtration rate less than 60ml/min.
- 0.4 U/kg body weight per day for patients not meeting the criteria above and BG concentration is 140-200mg/dL
- 0.5 U/kg body weight per day for patients not meeting the criteria above and BG concentration is 201-400mg/dL

Total calculated dose should be divided approximately into 50% of basal insulin and 50% of prandial insulin.

- Basal insulin has to be given once daily (if glargine/detemir is used) or twice daily (if detemir/NPH is used), at the same time each day.
- Rapid-acting (prandial) insulin should be divided into 3 doses and should be given before each meal. If the patient is unable to eat, prandial insulin can be withheld.

Insulin dose can be adjusted as per the bedside capillary blood glucose levels daily.

B. Supplemental insulin

Supplemental (correction) should be with rapid-acting insulin analog or regular insulin. If a patient is able and expected to eat all or most of his/her meals, give insulin analog or regular insulin before each meal and at bedtime as per the "usual" column given below in the following **Table 5**.

Supplemental insulin adjustment:

If fasting and pre-meal plasma glucose are persistently above 140mg/dL in the absence of hypoglycemia, insulin dose should be increased from insulin-sensitive to "usual" level. If patient develops hypoglycemia (BG <70mg/dL), decrease the regular or rapid acting insulin to the "usual" level or from "usual" to insulin-sensitive level. For patients who are unable to eat, elderly and those

with renal dysfunction insulin should be started at insulin-sensitive level. If the patient is able or expected to eat all or most of his/her food start with "usual" level. If the patient is on corticosteroids and for those treated with more than 80U/day prior to admission, start with insulin-resistant level.

Table 5: Dose of supplemental rapid acting insulin in insulin sensitive and resistant patients

BG (mg/dL)	Insulin sensitive	Usual	Insulin resistant
141-180	2 units	4 units	6 units
181-220	4 units	6 units	8 units
221-260	6 units	8 units	10 units
261-300	8 units	10 units	12 units
301-350	10 units	12 units	14 units
350-400	12 units	14 units	16 units
>400	14 units	16 units	18 units

Sliding scale insulin vs basal bolus regimen

Sliding scale insulin (SSI) regimen with regular insulin was introduced by Elliot P. Joslin, which was based on the amount of glycosuria. Capillary blood glucose monitoring was introduced in 1970s, after which the insulin administration based on glycosuria was abandoned. The absence of an evidence based standard insulin regimen for the management of in-hospital hyperglycemia, lead to the evolution and popularity of sliding-scale regimen. It has some advantages like convenience and simplicity. But it has serious disadvantages like it is based on the assumption that insulin resistance is uniform in all patients which leads to common dosing formula for all, it chases the glucose value after the hyperglycemia has happened rather than preventing the hyperglycemia, it under-estimates the total daily insulin requirement and it does not differentiate basal and prandial requirement. All these disadvantages lead to ineffective glycemic control, increased risk of hypoglycemia and prolonged hospital stay. The RABBIT-2 trial proved that the basal bolus regimen is a clear winner over the SSI regimen in all these aspects [9].

3) Special conditions:

I. Peri-operative management:

- Glucose and insulin should be given through separate IV lines. Serum potassium should be checked before and after the infusion and should be maintained through supplementation, if the level is low.
- Minor surgeries like cataract surgery where patient need not remain nil per oral for a prolonged period can be continued on oral anti-diabetic drugs, provided, the blood sugar is well controlled.
- Strict glycemic control with insulin is required for the better outcome after a surgery, with targets of blood sugar between 110 and 140mg/dL. Blood glucose target remains the same for transplant patients also.

II. Acute Myocardial Infarction:

- Both hyperglycemia and hypoglycemia are dangerous
- Optimal glycemic control with insulin analogs is the best method

III. Glucocorticoid therapy:

- Regular blood glucose monitoring should be done
- Treatment of non-diabetic patients should be with insulin
- For patients already on insulin, 20% increment in total daily dosing should be done

IV. Enteral nutrition:

- Insulin analogs are preferred
- Basal plus multiple subcutaneous prandial boluses are to be preferred

V. Patients on parenteral nutrition:

- Intravenous insulin is the preferred treatment
- Glucose targets should be based on the severity of underlying illness

VI. Peri-partum:

- Insulin is the preferred choice in gestational and overt diabetes
- Aspart and lispro are the preferred rapid acting insulin analogs and detemir as basal insulin
- Patients in active labor should be on Dextrose, Potassium, Insulin (DKI) IV infusion to prevent hypoglycemia, hypokalemia and ketosis

VII. Transition to outdoor management

- Patients should be discharged on basal bolus or premix insulin regimen
- Education regarding insulin technique, self-monitoring of blood glucose (SMBG), hypoglycemia and self adjustment doses should be provided before discharge and during follow up.
- Initiation of insulin administration should be started at least one day prior to discharge to assess the efficacy and safety of this transition

Table 6: Showing various insulin preparations and their duration of action

Insulin preparation	Onset (hour)	Peak (hour)	Effective duration (hour)
Short-acting			
Lispro	<0.25	0.5-1.5	3-4
Aspart	<0.25	0.5-1.5	3-4
Glulisine	<0.25	0.5-1.5	3-4
Regular	0.5-1.0	2-3	4-6
Long-acting			
NPH	1-4	6-10	10-16
Detemir	1-4		24
Glargine	1-4		24

Supportive management with medical nutrition therapy, physical activity and behavioral therapy is always crucial.

Key aspects in hypoglycemia managemen [6]

- Standard definitions and protocols should be made to identify hypoglycemia and severe hypoglycemia in the hospital
- Sulfonylureas and other oral hypoglycemic drugs should be discontinued at the time of admission
- Proper training should be provided to the nursing staff in identification of the symptoms of hypoglycemia, its treatment and time interval at which blood sugar should be rechecked

- depending on the blood glucose levels of each patient
- Directions should be given to the nursing staff on adjustment of insulin dose and/or administration of dextrose-containing IV fluids for both planned and sudden changes in nutritional intake
- Documentation and reporting of hypoglycemic events including severity, potential causes, treatment provided, physician notification and treatment outcome should be recorded in a standard format by the nursing staff

Conclusion

Strict glycemic control with insulin therapy is the key for a successful treatment outcome in any patient admitted with medical or surgical condition. Individualized and patient centered approach is essential in the effective management of hyperglycemia. Apart from these, training of nurses, education of support staff and using simple protocols are important to achieve satisfactory results.

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