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## Management of hypoglycemia in diabetic patients

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### Abstract

The risk of hypoglycemia increase among patient with diabetes mellitus and/or on insulin as compare to general population. Hypoglycemia is defined as blood glucose  $<70\text{mg/dl}$  or  $<4\text{ mmol/L}$ . Iatrogenic or medicine induce is most common cause of hypoglycemia.

Hypoglycemia is associated with various fatal complications. Among type 1 diabetes, it is relate with 4-10% of deaths. The mortality rate correlates with severe hypoglycemia in both type 1 and type 2 diabetes is 3.4 folds higher versus those with milder event.

It is necessary to give education regarding hypoglycemia prevention, drug dose adjustment, avoid skipping meal and treat immediately as "15-15 rule". Use injection glucagon or IV glucose in case of severe hypoglycemia.

**Keywords:** Management, hypoglycemia

### Introduction

Hypoglycemia is not common among the individuals without diabetes. The main causes of non-diabetic hypoglycemia are certain medications, alcohol, critical illnesses including major organs, malnutrition, malignancy etc. According to a retrospective review of 37,898 non-diabetic patients who admitted to the hospital due to non-critical illness, the frequency of hypoglycemia found to be 36 per 10,000<sup>[1-3]</sup>.

Risk of hypoglycemia increases 3 folds among the intensively treated diabetes patients, as compare to conventionally treated patients while Type1 diabetes intensively treated patients, and this risk increase in patients treated with insulin (70-80%)<sup>[4]</sup>.

### Definition

Hypoglycemia is defined as low blood glucose level  $<70\text{mg/dl}$  or  $<4\text{mmol/L}$ , causing both neurological and autonomic symptoms.

Whipple Triad is use for assessment of hypoglycemia, Includes;<sup>[5]</sup>

- Low blood glucose levels
- Symptoms of hypoglycemia
- Symptoms relief with treatment of hypoglycemia.

According to American diabetic association (ADA), the only sure way to know whether you are experiencing low blood glucose is to check your blood glucose, if possible. If you are experiencing symptoms and you are unable to check your blood glucose for any reason, treat the hypoglycemia<sup>[6]</sup>.

### Hypoglycemia Severity

**Mild:** blood glucose  $<4\text{mmol/L}$  ( $<70\text{mg/dl}$ ) with autonomic symptoms but individual is able to self-treat.

**Moderate:** blood glucose  $<3\text{mmol/L}$  ( $<54\text{ mg/dl}$ ) with autonomic and neuroglycogenic symptoms but individual is able to self-treat.

**Severe:** blood glucose  $<3\text{mmol/L}$  ( $<54\text{ mg/dl}$ ) with autonomic and neuroglycogenic symptoms and individual require assistance of another person.

### Causes

1. **Iatrogenic:** Among diabetes patients, the hypoglycemia is usually iatrogenic or medication side effect (insulin and insulin secretagogues plus other antidiabetic drugs).
2. **Insufficient exogenous carbohydrates:** Small amount of meal than usual, delayed or

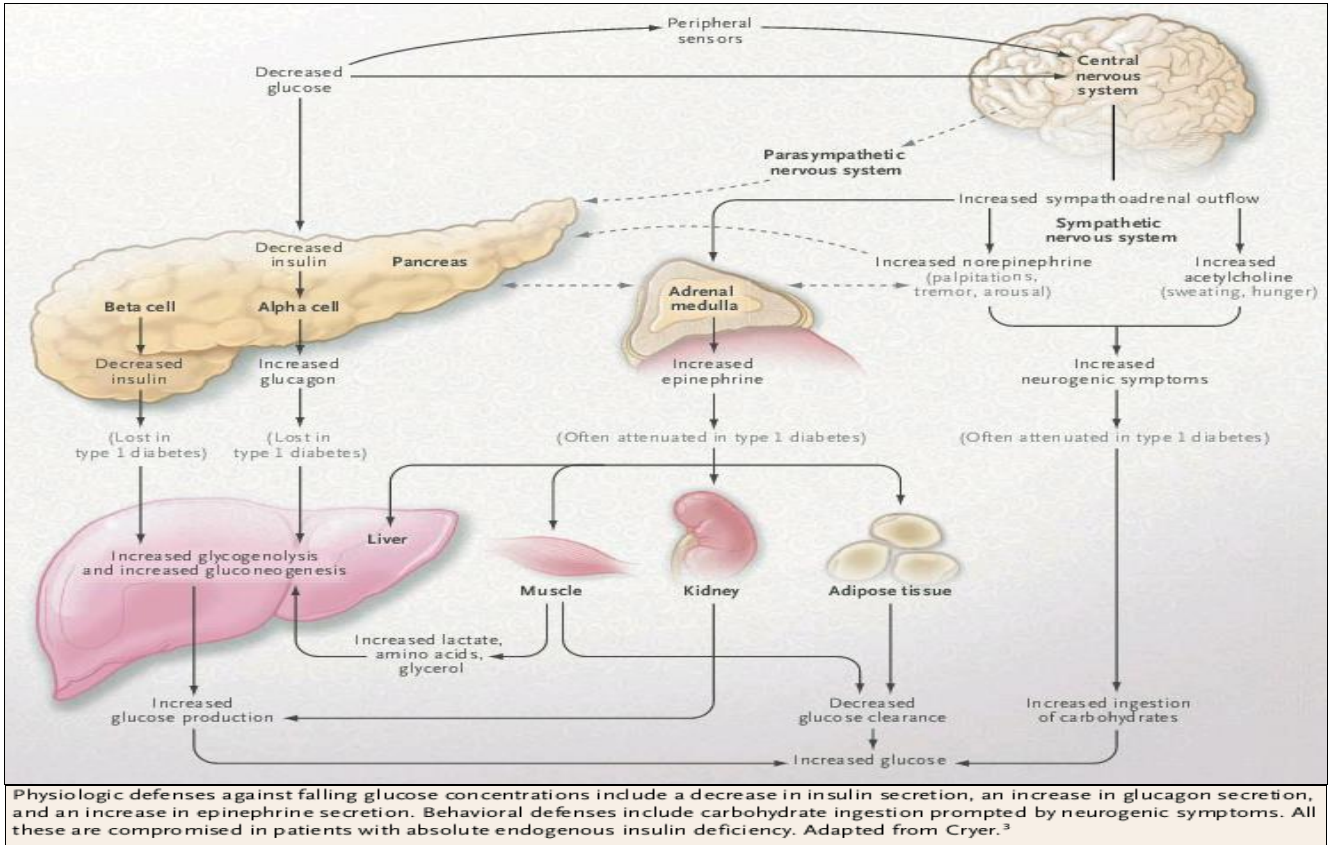
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3. skipping of meal or overnight fast.
4. **Increased physical activity** causes increase glucose utilization
5. **Increase sensitivity to insulin** as late after exercise, middle of night and after weight loss, increased fitness, or improved glycemic control
6. **Alcohol:** cause decrease endogenous glucose production
7. **Others:** old age, poly pharmacy, intensive glycemic control, infections, digestive problem, liver disease, post bariatric surgery, renal disease, thyroid and other endocrine disorders, gastro paresis, pregnancy.

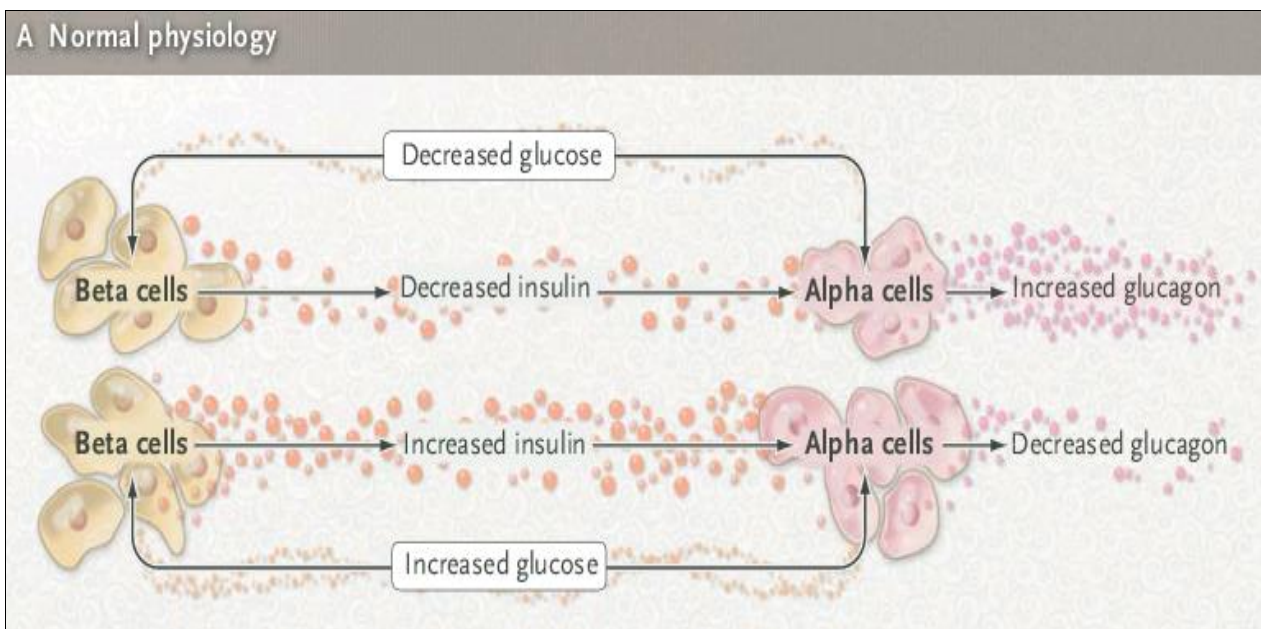
**Pathophysiological mechanism**

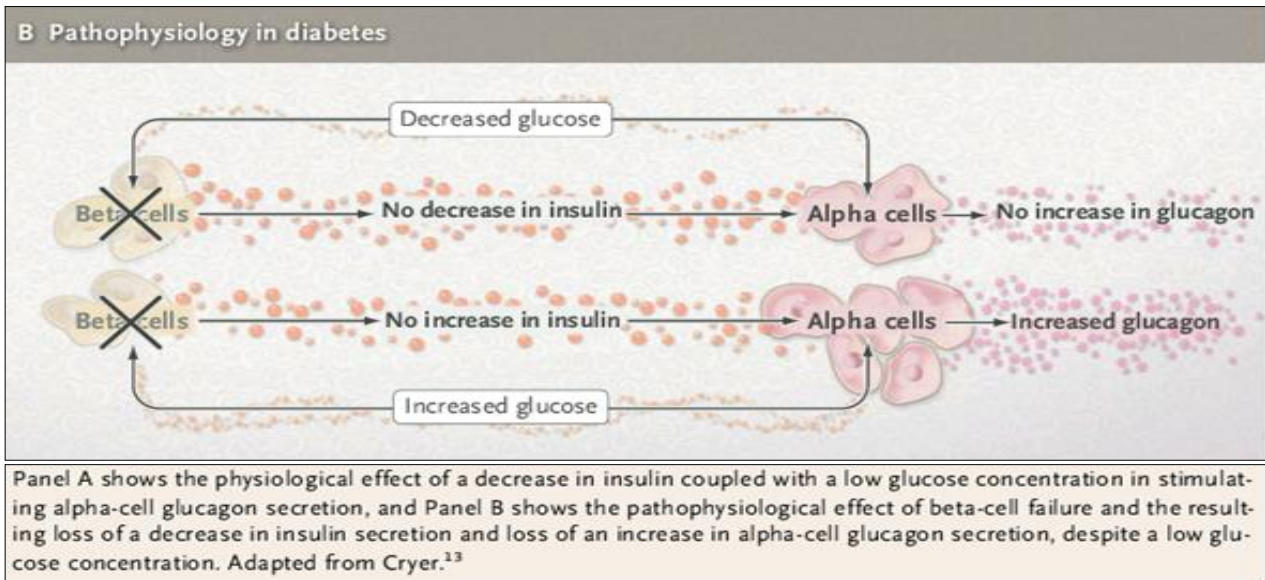
Normally hypoglycemia cause activation of autonomic nervous system and release of hormones such as Epinephrine, Norepinephrine, cortisol, growth hormone, and glucagon and inhibit release of insulin leads to glycogenolysis and gluconeogenesis result in increased blood glucose level.

Type1 patients and advanced type 2 patients having beta cell failure or absolute insulin deficiency, this defense is compromised, resulting in failure of insulin level to fall, failure of glucagon release and diminish epinephrine secretion [7-9]. This can result in increased risk of recurrent severe hypoglycemia as shown in figure 1 and 2.



**Fig 1:** physiologic and behavioral defenses against hypoglycemia in humans.





**Fig 2:** Mechanisms of loss of the Glucagon Response.

**Symptoms of hypoglycemia** <sup>[6]</sup>

A low blood glucose level triggers the release of epinephrine (adrenaline), the “fight-or-flight” hormone. Epinephrine is what can cause the symptoms of hypoglycemia such as thumping heart, sweating, tingling, and anxiety.

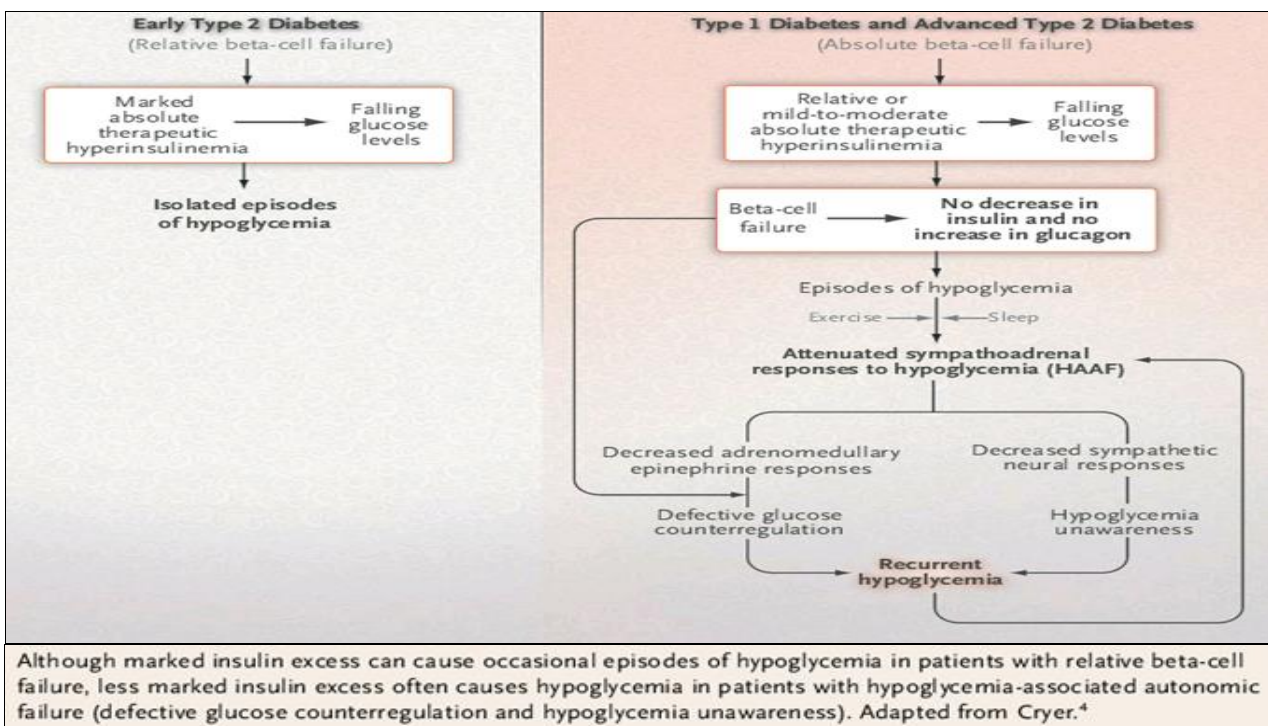
If the blood glucose level continues to drop, the brain does not get enough glucose and stops functioning as it should. This can lead to blurred vision, difficulty concentrating, confused thinking, slurred speech, numbness, and drowsiness. If blood glucose stays low for too long, starving the brain of glucose, it may lead to seizures, coma, and very rarely death <sup>[6]</sup>.

**Hypoglycemia unawareness**

Hypoglycemia symptoms occur when blood glucose levels

fall below 70 mg/dL but many people have blood glucose readings below this level and feel no symptoms called hypoglycemia unawareness. People with hypoglycemia unawareness are also less likely to be awoken from sleep when hypoglycemia occurs at night. People with hypoglycemia unawareness need to take extra care to check blood glucose frequently. Hypoglycemia unawareness occurs more frequently in those who:

- Frequently have low blood glucose episodes can result in Hypoglycemia associated autonomic failure (HAAF) as shown in figure # 3, which can cause you to stop sensing the early warning signs of hypoglycemia <sup>[9]</sup>.
- Have had diabetes for a long time
- Tightly control their diabetes, which increases chances of having low blood glucose reactions <sup>[6]</sup>.



**Fig 3:** Schematic diagram of hypoglycemia-Autonomic failure (HAAF) in diabetes.

### Relative Hypoglycemia

Patients with high HbA1c levels may have symptoms of hypoglycemia at higher blood glucose levels above normal range. This phenomenon called Relative hypoglycemia. It usually occurs when patient intensively control their blood glucose. It is self-limiting and takes 2-4 weeks to adjust with new glucose levels [9].

### Complications of hypoglycemia

Hypoglycemia is associated with various fatal complications. Among type 1 diabetes, it is relate with 4-10% of deaths. The mortality rate correlates with severe hypoglycemia in both type 1 and type 2 diabetes is 3.4 folds higher vs those with milder event [10].

Acute hypoglycemia is a pro-inflammatory condition, with high platelet activation and reduced fibrinolysis, leading to pro-thrombotic conditions [11]. The increased heart rate related to hypoglycemia can lead to high systolic BP, raised contractility of myocardium, prolonged QT interval, and high stroke volume and increase the risk of arrhythmia.

The rate of cardiovascular events are higher in those having frequent hypoglycemic attacks. The ADVANCE trial found significant higher rates of macro and microvascular events related with hypoglycemia in those patients having strict glycemic control [12].

Severe hypoglycemia can result in permanent impairment of cognitive function. Patients with type2 diabetes have 1.5-2.5 folds higher risk of dementia vs normal population. Other neurological complications include seizures, cerebellar ataxia, and functional brain failure and brain injury [13].

Several studies demonstrate the psychological effects of hypoglycemia, which can lead to adverse quality of life and decline in general health [14, 15].

### Prevention of hypoglycemia

- **Patient education:** This can result in improvement of outcomes such as dose of medications, timing, exercise level and inquiry about any hypoglycemic episode. Enrollment to insulin training programs or glucose monitoring training programs can help [16].
- **Dietary Interventions:** Ensure adequate diet control, take inter-prandial and bed time snacks, avoid skipping meals, and timing of insulin injections.
- **Exercise:** Advice for glucose monitoring before, during and after exercise. Insulin dose and meal should be adjust for planned exercise.
- **Medication Adjustment:** Use rapid acting insulin to decrease risk of inter-prandial hypoglycemia (lispro, Aspart, Glulisine) and use basal insulin to nocturnal hypoglycemia [17].
- **Glucose Monitoring:** SMBG reduce the risk of hypoglycemia. Check before meal, bedtime and during symptoms.
- Limit Alcohol intake
- **Adjust Glycemic Targets:** HbA1c <7% in healthy adults and <8% in elderly.

### Treatment of hypoglycemia

The "15-15 Rule" have 15 grams of carbohydrate to raise your blood glucose and check it after 15 minutes. If it is still below 70 mg/dL, have another serving. Repeat these steps until your blood glucose is at least 70 mg/dL. Once your blood glucose is back to normal, eat a meal or snack to make sure it does not lower again. This may be:

- Glucose tablets, Gel tube
  - 4 ounces (1/2 cup) of juice or regular soda (not diet)
  - 1 tablespoon of sugar, honey, or corn syrup
  - Hard candies, jellybeans, or gumdrops.
- Infants may need 6 grams, toddlers 8 grams, small children 10 grams and young children <15 grams.

**Glucagon:** After putting the patient in recovery position, 1mg dose can be injected in arm, buttocks or thighs either I/M or S/C. It is used in insulin-induced hypoglycemia in adults and children over 8 years of age or body weight over 25kg. Family member or friends should be inform how to use Glucagon kits in case of emergency. After recovery patient might experience nausea and vomiting so avoid giving fluids or juices might cause choking.

Hypoglycemia due to oral antidiabetic drugs should be admit to hospital as the effect of these drugs may persist for 12-72 hours.

Do not hesitate to call 911. If someone is unconscious and glucagon is not available or someone does not know how to use it, call 911 immediately.

**Intravenous Glucose Administration:** Intravenous administration of 75-80 ml of 20% glucose or 150-160ml of 10% glucose should be administer if hypoglycemia persist. Blood glucose level should be check repeatedly and after recovery, patient should take snack or meal [6].

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