GUIDELINES FOR MANAGEMENT OF HYPOGLYCEMIA

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PURPOSE

This guideline will provide direction for management of adult male and female diabetic, non-diabetic patients, pregnant females with hypoglycemia, critical ill patients and patients having terminal diseases with hypoglycemia.

SCOPE

These guidelines are for medical practitioners to help them in understanding pathophysiology of hypoglycemia, clinical management and complications of hypoglycemia

Contents of guidelines

- Definition of hypoglycemia
- Types of hypoglycemia
- Causes of hypoglycemia
- Diagnosis of hypoglycemia

RECOMMENDATIONS

Following steps should be considered in management of hypoglycemia.

- Clinical assessment of patients for assessment of hypoglycemia must be done after securing airway breathing and circulation.
- Determine the blood glucose level as soon as possible.
- Use quick acting carbohydrates Oral or IV as per required.
- Continued monitoring of blood glucose level must be done.
- Documentation of all activities must be done with time and date for medico legal reasons.

These guidelines are for adult male and female diabetic, non-diabetic patients, pregnant females with hypoglycemia, critical ill patients and patients having terminal diseases with hypoglycemia.

Definition.

Clinical hypoglycemia is defined as a plasma or serum glucose concentration low enough to symptoms or and signs, including impairment of brain functions.

No single plasma or serum glucose concentration categorically define Hypoglycemia in diabetic and non diabetic persons.

Patient with diabetes one should become alert, if blood sugar is <70mg/dl (3.9mmole/L). Remember floor of 4 (mmole/L). This is the value at which normally counter-regulatory measures are about to start. Patients with diabetes at this value whether symptomatic or asymptomatic should take any form of carbohydrate containing sugar and adjust the dose of insulin or oral hypoglycemic drugs. Re-check plasma glucose again to determine whether blood glucose levels falling.

Some authority say that alarming level

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of blood glucose should be <63mg/dl (3.5mmole/L) to avoid overly diagnose hypoglycemia in diabetics.

If diabetic patients becomes symptomatic but blood glucose is > 70mg/dl, it Relative hypoglycemia, only give some snack or 1-2 bannana or bisuit. Only treat for symptoms. It should be remembered that there is no rise of threshold for hypoglycemia in diabetes.

For non-diabetic persons, any low blood sugar level with clinical features consistent with hypoglycemia and resolution of symptoms and signs after correcting hypoglycemia (whipple triad) should be further evaluated.

Non diabetic should be treated for any low blood sugar if symptomatic, or otherwise treat at blood sugar level of 50-54mg/dl if asymptomatic.

Normal lower limit of blood sugar level in non-diabetic is 3.5mmole/L and symptomatic hypoglycemia not occurred in normal persons on fasting due to gluconeogenesis and glycogenolysis in liver.

Clinical significant hypoglycemia is defined as plasma glucose level <54 mg/dl.

Severe hypoglycemia, associated with severe cognitive impairment, for this no specific glucose threshold is defined. Some < 50mg/dl or <45mg/dl.

Hypoglycemia is the critical limiting factor in long term and short term glycemic management in diabetes.

Counter-regulatory physiological responses.
Glucagon and epinephrine secretion rises when plasma glucose concentration fall below 65-70mg/dl (3.6-3.9mmole/L).

Growth hormone secretion increases when plasma glucose concentration Fall below 60-65mg/dl (3.3-3.6mmole/L).

Cortisol secretion increases when plasma glucose fall below 60mg/dl (3.3mmole/L).

Clinical features.

Adrenergic symptoms. Usually seen early with a rapid decline in blood Glucose, these include tremors, sweating, palpitation, vomiting.
Neuroglycopenic symptoms. Usually associated with slower or prolonged Hypoglycema including altered mental state, altered behavior (agitation, aggression).

Types of hypoglycemia.

Fasting hypoglycemia.

It occur hours after fasting (post absorbtive State.

Reactive hypoglycemia.

Hypoglycemia occur post-prandially usually within 4 hours of meal. It may be idiopathic or due to dumping syndrome in patient with GI surgery. Idiopathic reactive hypoglycemia is debatable because 25% normal persons have hypoglycemia after OGTT. Occasionally insulinoma cause reactive hypoglycemia.

Nocturnal hypoglycemia.

This usually occurs in diabetic who are on insulin, because normally insulin requirement at mid night are low and high on early morning. These patient usually present with fasting hyperglycemia, when blood sugar is checked at mid night, it is low (somogi phenomena).

Causes of hypoglycemia.

Following are the causes of hypoglycemia.

1). Drugs. Insulin/sulfonylurea, maglitinides (dose, type, time, missed meal, Accidental or factitious), large doses of aspirin, quinine, quinolones, Beta blockers, pentamidine.
2). Alcohol.
3). Critical illness e.g; CKD, cirrhosis of liver/ hepatic failure, Septicemia.
4). Non islet cell tumors. e.g; epithelial amd mesenchymal Tumors (colorectal carcinoma, hepatoma, carcinoid tumor, mesothelioma, Retroperitoneal sarcoma, fibrosarcoma), hematological malignancies (Leukemia, lumphoma).
5). Islet cell tumor e.g; insulinoma.
6). Islet cell Hyperplasia.
7). Autoimmune hyperinsulinemic hypoglycemia e.g; insulin Antibodies, insulin Receptor antibodies.
8). Hormone deficiencies e.g; growth hormone, ACTH, cortisole, thyroid Hormones.

Diagnosis.

There is a wide range of differential diagnosis which share same clinical features as presented with hypoglycemia, it is prudent to check plasma glucose in any patient with adrenergic or neuropsychiatric symptoms and signs.

In non-diabetic patients whipple's triad (s/s consistent with hypoglycemia, low blood sugar and reversal of s/s after restoration of normoglycemia) should always be present before doing further diagnostic investigations.

Glucometer are not ideal to detect low blood sugar level, ideally blood sample of 20cc should be taken, if hypoglycemia detected, and no obvious cause is found then centrifuge remaining blood at -200c to do test to determine the cause of hypoglycemia. These test are serum insulin, pro insulin, c peptide , beta hydroxy butyrate levels, insulin antibodies, insulin receptor antibodies, serum IGF 1, IGF 2, IGF 2/ IGF 1 ratio, serum growth hormone, cortisole, ACTH, thyroid Hormones, blood and urine sufonyleurea levels as suggested by clinical conditions and lab results. It also include Investigations regarding search for insulinoma and non-islet cell tumors (MRI abdomen, Radiolabelled ocreotide scan, cutaneous transhepatic venous sampling, wide list of tests if non islet cell tumor is suspected as a cause of hypoglycemia) Liver function test and kidney function tests, complete blood examination, chest x ray, blood and urine culture for sepsis as advised by physician according to the clinical status of patients to find the cause of hypoglycemia. Usually blood alcohol level not measured because hypoglycemia occur after 6-24 hours after intake of alcohol. 72 hour fast test or mixed meal test is advised when spontaneous hypoglycemia episode is not observed.

If plasma glucose is normal then think about various other differential Diagnosis; ACS (acute coronary syndrome), arrhythmia, uremic encephalopathy, hepatic encephalopathy, meningitis, encephalitis, cerebral malaria, cerebral abscess, CVA, alcohol intoxication, drug over dose/ poisoning, drug withdrawal, temporal lobe epilepsy, septicemia, psychiatric illness (mania, schizophrenia) and do relevant investigations accordingly.

MANAGEMENT.

Aims of management.

Aims of management are A) Acute management to prevent or limit neurological damage. B) Maintenance treatment to

prevent recurrent hypoglycemia. C). Subsequent management to treat the cause.

In hospital.

1. Any acutely unwell patient should be stabilized by maintaining airway, Breathing, circulation, simultaneously taking brief history and checking Capillary blood glucose by glucometer, if hypoglycemia found, go to next Step.
2. if hypoglycemia found on glucometer, send 20cc blood sample for glucose measurement and save serum for subsequent further tests if needed, but treatment of hypoglycemia should not be delayed.
3. Before correcting hypoglycemia, if there is history of alcohol intake then give I/V thiamine before giving glucose to prevent wernicks encephalopathy.

4 A. Oral regimens. If patient is able to take orally, then give 15-20grams quick acting carbohydrates (20-30grams if blood glucose < 50mg/dl).

A. Measure blood after 10-15 minutes , if hypoglycemia not corrected, repeat the dose, then again measure blood glucose after 10-15 minutes, if still not corrected give third dose and occasionally if still hypoglycemia not corrected then consider other intervention.

B. Type of quick acting carbohydrates used. 1. Glucose tablets. 2. Orange juice 150-200ml orange juice (which contain fructose) is popular treatment but not give in renal impairment. 3. Sugar or sucrose less commonly used. 3-4 heaped teaspoonful dissolved in glass of water.

Note. Chocolate are not recommended because of fat content which delays the quick acting carbohydrate absorption

5. If hypoglycemia corrected, oral carbohydrate will keep patients euglycemic for upto 2 hours, therefore give 20grams (40gms if prior glucagon inj given or liver glycogen stores depleted) thereafter. 20gms complex carbohydrates equal to 2 biscuit, I piece of bread or toast 200-300ml glass of milk(not soya) or regular meal if due(must contain carbohydrates).

6. If patient is not able to take orally due to confusion or unconsciousness, then give intravenous glucose. Following are the possible regimens;

- 25-50ml(12.5-25g) 50%dextrose or
- 5-10 ampules of 25%dextrose (12.5-25g) or
- 250ml 10%dextrose (25g).
- Maintenance treatment. Continue 100-200 ml 10% dextrose.

7. Regarding maintenance treatment, patient with hypoglycemia be monitored for 24-48 hours
8. If IV access not found or delay, give single injection glucagon 1mg S/C or I/M. Do not repeat it.
9. If patient become not well or still having impaired conscious level, then think of other differential diagnosis mentioned above. There may be a possibility, that due to prolong hypoglycemia, cerebral edema may occur, therefore give I/V mannitol and dexamethasone.
10. Treatment goal for optimum blood sugar level is to keep blood sugar above 70mg/dl in diabetic, and in non diabetic to keep blood sugar above 63mg/dl atleast?
11. Subsequent management is to treat the cause of hypoglycemia to prevent recurrent hypoglycemia.

In diabetic most common cause of

hypoglycemia is drug induced, for example insulin, sulfonylurea, maglitinites or missing a meal. Adjust the dose of insulin, counsel the patient about meal, remember in diabetics as soon as hypoglycemia corrected, adjust dose of insulin if patient already taking, not omit it to avoid hyperglycemia. Avoid drugs causing hypoglycemia. Injection octreotide can be given in patients with hypoglycemia due to sufonylurea.

In patient with critical illnesses like CKD, CCF, hepatic failure, septicemia, causing hypoglycemia, manage these conditions appropriately along with treatment of hypoglycemia.

Patient with autoimmune hypoglycemia should receive steroid and immunosuppressant.

If the cause is insulinoma, then treatment is surgical removal.

Non islet cell tumors. Treat appropriately with surgery, chemotherapy, radiotherapy. Give injection octreotide also.

If islet cell hyperplasia, treatment may be partial pancreatectomy.

If cause is alcohol, advise patient to avoid it.

Correct hormone deficiency, if causing hypoglycemia.

Nocturnal hypoglycemia in diabetic patients on insulin is management by adjusting the dose and time of insulin with some snacks before sleep.

Reactive hypoglycemia is managed by frequent small meals instead of large meals.

12. Management of hypoglycemia in pregnancy. In diabetic females same plan followed as adopted for diabetic patient generally as mentioned above. In non-diabetic pregnant female, rule out critical illness like severe hepatitis, pancreatitis, insulinoma, hormone deficiencies, alcohol intake, reactive hypoglycemia, autoimmune causes should be ruled out and manage accordingly as mentioned above.
13. Management of hypoglycemia in patients with terminal diseases.

Note.

Some diabetic are unaware of hypoglycemia due to impaired adrenergic response caused by autonomic neuropathy, hypoglycemia induced autonomic failure or reduced counter regulatory mechanism due to recurrent hypoglycemia.

These guidelines cover the evaluation and management of hypoglycemia in adult age 16 years or above, diabetic, non diabetic, patients with critical illness, patient with terminal illness and pregnant female. These guideline do not cove pediatric or infants patients.

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