

INTRODUCTION

Brittle diabetes is defined as severe instability of blood glucose levels with frequent and unpredictable episodes of hypoglycaemia or ketoacidosis that disrupts day to day life. Almost all diabetics experience swings of blood sugar which are less predictable and greater than in non diabetics. Brittle diabetes is uncommon (less than 1% of insulin taking population) and it causes a huge burden on the patient due to multiple hospital admissions. It is episodic and almost always related to stressful life situations. It affects 3/1000 insulin dependent diabetic patients mainly young women. Its prognosis is poor with lower quality of life scores, more microvascular and pregnancy complications and shortened life expectancy.

CAUSES OF BRITTLE DIABETES**Main causes includes**

- Non physiologic matching of meals/exercise and insulin administration.
- Malabsorption
- Certain Drugs (alcohol, antipsychotics)
- Defective insulin absorption or degradation
- Defect of hyperglycaemic hormones especially glucocorticoid and glucagon.
- Delayed gastric emptying as a result of autonomic neuropathy.
- Psychosocial factors are very important and factitious brittleness may lead to a self perpetuating condition. This is because of patient centred behavioral issues. Some of these problems may be short lived and related to a stressful situation (unhappiness at school or home).

CLINICAL MANIFESTATIONS

Patients have wide swings of blood sugar levels and report differing blood sugar responses to the same dose and type of insulin. Most patients are in their twenties or thirties. Their glycated haemoglobin (HbA1c) are typically elevated (10-14%) and acute complications (DK and hypo) and chronic microvascular complications are commoner (67% versus 25%). Brittle diabetics also had a lower quality of life score. The age of death ranges from 27-45 years with a predominance in young women. Those who survived had resolution of brittleness, but suffered a significant complication burden. Frequent hypoglycaemia even if asymptomatic causes both defective glucose counter regulation and hypoglycaemia unawareness and thus a vicious cycle of recurrent hypoglycaemia.

CLINICAL ALGORITHM TO DETERMINE THE ETIOLOGY

The diagnostic algorithm was the glucose response to 0.1 unit / kg insulin administered subcutaneously and intravenously. If this response was "normal" then psychosocial evaluations were completed, including psycholinguistic and health psychological testing. Then other parameters affecting blood glucose concentration eg. gastric motility, counter regulatory hormones, coeliac disease, hypothyroidism, adrenal insufficiency, insulin autoantibodies and most importantly patients compliance with prescribed regimens were assessed. If the response were "abnormal" the location of the insulin resistance was identified as being subcutaneous, intravascular or at the peripheral tissue.

EVALUATION AND DIAGNOSIS

A careful evaluation should be performed in patients with brittle diabetes. A detailed history as to the duration of diabetes, description of episodes of DK, severe hypos, presence of diabetic complications (particularly autonomic neuropathy) and prescribed insulin regimens should be taken. It should also be determined if there was a period of stable diabetes preceding the brittleness and what happened in the patient's life circumstances coincident with the onset of brittleness. Psychosocial factors need to be assessed. For patients with recurrent episodes of DK, a possible chronic cryptic infection (sinusitis, osteomyelitis, renal or perirenal abscess and lung abscess) should be excluded. For all patients a diabetic educational assessment is useful to evaluate whether the patients knows how to manage diabetes and rule out diabetes mismanagement (factitious brittle diabetes). In this case a "in hospital" assessment and management of blood sugar is necessary.

Iatrogenic hypoglycaemia is the result of the interplay of absolute or relative therapeutic insulin excess and compromised physiological and behavioural defences against falling plasma glucose concentrations in type 1 diabetes in type 1 diabetes mellitus (T1DM) and advanced type 2 diabetes mellitus (T2DM). Courtesy of Dr. Philip Cryer.

MANAGEMENT**Brittle diabetes is difficult to treat****General principle**

- Patients to be instructed how to match the insulin dose to the amount of carbohydrates ingested.
- Insulin regimens must be individually tailored to reduce the risk of hypoglycaemia while matching

Table 1: Counterregulatory response to hypoglycaemia

Condition	Glucose	Insulin	Glucagon	Epinephrine
Nondiabetic	↘	Decreases	Increases	Increases
T1DM	↘	No Decrease*	No Increase	Attenuated Increase*
T2DM				
Early	↘	Decreases	Increases	Increases
Late(Absolute endogenous insulin deficient)	↙	No Decrease*	No Increase	Attenuated Increase*

glycaemic control. The use of insulin analogues with ultrafast or ultraslow action and use of subcutaneous insulin pumps are effective in brittle diabetes.

- SMBG is an excellent tool for the patients and a motivated patient can use this tool to manage his blood sugars.
- CGM (Continuous glucose monitoring) may further facilitate the understanding of glycaemic variability.
- Sensor augmented insulin pumps (an insulin pump with a CGM device) improves glycemic control without hypoglycaemia.
- Fully automated closed loop systems of insulin delivery based on CGM sensing (bionic pancreases) are available. This device also integrates glucagon delivery.
- Islet cell transplantation –an effective therapeutic option entailing good expected outcomes. The limiting factor is the effect of immunosuppressive therapy and recurrence of autoimmunity.

SPECIAL SITUATIONS

- Hypoglycaemia unawareness A 2-3 Week period of scrupulous avoidance of hypoglycaemia is advisable since that often restores awareness (Table 1).
- Gastroparesis – promotility agents improved gastric emptying and relieved the symptoms of gastroparesis but did not help with metabolic control.
- Psychosocial – Psychotherapy may help in selected patients.

SUMMARY AND RECOMMENDATIONS

- Brittle diabetes is defined as severe instability of blood glucose levels with frequent and unpredictable episodes of hypoglycaemia or ketoacidosis.
- The diagnosis is established when a patient with absolute insulin deficiency (type 1 or type 2) has frequent episodes of hyper or hypoglycaemia.
- The major cause of brittle diabetes is patient

or clinician error in management, other causes being psychosocial, malabsorption, delayed gastric emptying, systemic insulin resistance.

- The treatment includes diabetes education, intensive insulin therapy with frequent or continuous glucose monitoring and constant interaction between patient and the clinician. Psychotherapy is advocated in selected patients.

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