

### DOES 'HONEYMOON PERIOD' EXIST IN TYPE 2 DIABETES MELLITUS?

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#### Abstract

Temporary remission of type 1 diabetes mellitus (T1DM) occurs following initiation of insulin therapy. This period of temporary remission without insulin therapy is called 'honeymoon period'. But no such temporary remission usually occurs in type 2 diabetes (T2DM). We report here two cases of type 2 diabetes mellitus where such honey moon period was observed.

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#### Introduction

In type 1 diabetes mellitus (T1DM), a period of temporary remission often occurs following initiation of insulin therapy. The period of remission is variable and it usually does not continue more than 6 months. Such temporary remission does not indicate cure. The residual beta cell mass is enough to maintain normoglycemia during this period.<sup>1</sup> This period of temporary remission is called 'honey moon period' in T1DM. Though, no such period of temporary remission is usually seen in type 2 diabetes mellitus (T2DM), we describe here such temporary period of remission in two cases which fulfill all the clinical criteria of T2DM.

#### Case I:

A 30 year old Bangladeshi got admitted in BIRDEM hospital in February 2007 with a history of diabetes and frequent hypoglycemic attacks. He was a Bangladeshi immigrant to USA. In USA, he was well till August 2006, when he noticed polyuria, polydypsia and general weakness, though not severe enough to hamper daily activities. He had no other systemic illness and occasionally used to take anxiolytic or sleeping pills. His body mass index (BMI) was 28.8 kg/m<sup>2</sup> and was normotensive. In USA, he was diagnosed as diabetic as his blood glucose level was 26.2mmol/l after 2 hours of glucose drink. Along with diet and exercise he was prescribed gliburide 5 mg in the morning and combination of metformin 500 mg +

rosiglitazone 2 mg twice daily. He was reasonably well till January 2007. Random blood glucose level was monitored occasionally during this period which remained within 4~6 mmol/l. However, he had complains of occasional weakness, lethargy, tiredness, but no other symptoms of hypoglycemia. He was asked to continue his medications. At the end of January 2007 in USA, while at home, he suddenly developed diarrhoea followed by sweating, palpitation, restlessness, tremulousness and feeling of impending doom. He had no chest pain or heaviness. He was admitted in hospital and treated for hypoglycemia. He was discharged from the hospital after a few days with counseling about hypoglycemia. Shortly after that he stopped taking oral anti-diabetic (OAD) drugs as he was planning to visit Dhaka. While in Dhaka he frequently felt symptoms mimicking hypoglycemia even though he was not taking any OAD. His symptoms abated with sweet/glucose drinks. But blood glucose level was never less than 5mmol/l by self monitoring with glucometer.

At the time of admission at BIRDEM, his BMI was 27.2 kg/m<sup>2</sup>, blood pressure 120/80 mm of Hg, pulse 88/min. Oral glucose tolerance test (OGTT) was done with 70 gm glucose drink. His fasting and 2 hours post glucose blood sugar levels were 4.3 mmol/l and 6.9 mmol/l respectively. Corresponding insulin and C-peptide level were also within normal reference range which excluded type 1 diabetes. Thyroid function and

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adrenal functions were normal. He was advised not to take any refined sugar on his own if he would experience hypoglycemia like symptoms because he was not taking any OAD drugs since January 2008. He had few episodes of hypoglycemia like attacks during his hospital stay. But his blood glucose level was always within 5-7 mmol/l without any sugar supplement during such symptomatic attacks. He was counseled for this panic attack and advised frequent small complex carbohydrate diet with high fiber. Psychotherapy and an anxiolytic (Clonazepam) was prescribed. He was discharged after 4 days with advice for regular follow up. Three months after discharge from the hospital he had normal blood glucose level and normal physical and mental health with no such attacks of hypoglycemia. The case was diagnosed as a T2DM having the so-called temporary remission.

#### **Case II:**

A 24 year old male student of Dhaka University, who came from a lower middle class farmer family, having no family history of diabetes mellitus, was admitted to a local district hospital in an unconscious state. After admission, he was diagnosed as a case of diabetic ketoacidosis (DKA) with 38.0 mmol/l blood glucose. After initial treatment he was referred to BIRDEM hospital, Dhaka where he was admitted under Endocrinology unit. He had a history of viral hepatitis one year back. For this latter conditions he was treated with traditional medicines and took plenty of glucose drinks and sugarcane juice. Jaundice gradually improved but there was weight loss and general weakness. He also noticed polyurea and polydypsia. At BIRDEM hospital, he was found to have very high blood glucose and DKA. He was treated for DKA accordingly. There was mild renal impairment (serum creatinine 1.9 mg/dl), due to transient acute renal failure which subsequently became normal. On the second day he became conscious, oriented. Acidosis was corrected. Blood glucose was 6-10 mmol/l throughout the day. Insulin infusion was stopped and switched over to subcutaneous insulin as oral feeding was started. He was on Actrapid HM 10 IU pre-breakfast, and 8 IU pre-dinner and Insulin retard HM 14 IU pre-breakfast and 10 IU pre-dinner times. His blood glucose profile remained within normal limits. He was investigated to classify his diabetes. He was labeled as a case of type 2 diabetes based on clinical features, plain x-ray abdomen and normal c-peptide

level. Education for diabetes was given to the patient as well as his family members. During regular follow up, his insulin requirements were gradually lowered and ultimately stopped with advise for strict follow up. After few months of stopping insulin his blood glucose level remained within normal limit. At this time he was prescribed gliclazide 40 mg once daily. After another couple of months, oral OAD drug was stopped due to occasional hypoglycemic symptoms and low blood glucose level (3.5-5 mmol/l). In subsequent follow up, his blood glucose was found within normal physiological limits without any OAD drug. OGTT was done which showed fasting plasma glucose at 5.2 mmol/l, and 2 hours post glucose at 6.7mmol/l. His HbA<sub>1C</sub> was 5.2% and BMI was 23 kg/m.<sup>2</sup> He was diagnosed as a case of type 2 diabetes mellitus having the period of temporary remission.

#### **Discussion**

The 'honeymoon period' (temporary remission) is characterized by reduced or no insulin requirement in T1DM when good glycemic control is maintained.<sup>2</sup> The clinical significance is the potential possibility for pharmacological intervention during this period to either slow down or arrest the ongoing destruction of the remaining beta-cells. Less severe disease has more chance of temporary remission. Hypoglycemia and low blood glucose are also commonly seen in the course of treatment in this period. Beta cell function, c-peptide level and also the insulin level varies in these patients with or without temporary remission. The incidence and duration of honeymoon phase varies depending on residual beta-cell function and insulin resistance at the onset of type 1 diabetes. The duration usually varies from 6 months to 2 years.<sup>1</sup> It is never considered as a 'permanent cure'.

The two cases described above show that temporary remission of the disease might also occur in T2DM. This temporary remission in T2DM was observed after the initiation of anti-diabetic treatment for glycemic control. The remission was similar to the honey moon phase of T1DM. The patients did not require any anti-diabetic agents and maintained a normal glycemic status. However, the duration of such remission in T2DM needs to be determined. There are few reported cases of temporary remission in type 2 diabetes.<sup>3</sup> At this period, residual beta-cell mass might be enough to maintain normoglycemia. It is better to closely

monitor these cases regarding their progression to T1DM or T2DM.

Our second case presented with DKA. Recently, in an editorial of *Diabetes Care* journal, there is a discussion on “Ketosis prone type 2 diabetes”.<sup>4</sup> These patients were without autoimmunity but preserved  $\beta$ -cell function (A- $\beta$ +). Despite their presentation with DKA or severe metabolic decompensation, most patients showed clinical and biochemical characteristics of type 2 diabetes. Most A- $\beta$ + subjects have new onset diabetes and are usually obese, middle aged males with a strong family history of type 2 diabetes. Evidences showed that they do not require any insulin or ODA therapy after sometime. Our second case probably falls under this category of patients. Therefore, temporary remission or honey moon phase may also be encountered in T2DM.

## References

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