

# Immunologic Desensitisation of Allergens and its Impact on Insulin Use in Type 1 Diabetes Mellitus: A Case Report

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## ABSTRACT

Type1 diabetes mellitus, also known as juvenile diabetes is an autoimmune disorder. It is a chronic condition in which there is a destruction of pancreatic beta cells by autoimmune response. Here, author's present a case of 13-year-old girl, weighing 32 kg and with a Body Mass index (BMI) of 13.9 kg/m<sup>2</sup> who reported to the family medicine clinic with complaints of weakness, increased appetite and thirst, and increased frequency of micturition for the past two months. Personal history revealed a consistent weight loss over the past six months with the problem of lice in the hair for past two months. A family history of diabetes, hypertension, and allergies was present. General physical examination revealed no abnormality and vitals were within normal limits. Blood investigations revealed increased levels of random blood sugar levels, glycated Haemoglobin (HbA1c) and Immunoglobulin (Ig)E. Hormonal assays were within normal limits, and skin prick test result revealed strong positive reactions to some allergens. The treatment included subcutaneous insulin, regular physical exercise and immunologic desensitisation of food allergens through Sublingual Immunotherapy (SLIT). The treatment resulted in controlled blood glucose levels with a reduction in insulin dose, a decrease in HbA1c levels, increased body weight and an improved BMI.

**Keywords:** Allergy, Autoimmune disorder, Random blood sugar levels, Sublingual immunotherapy

## CASE REPORT

A 13-year-old girl weighing 32 kg with a BMI of 13.9 kg/m<sup>2</sup> reported to the family medicine clinic with the complaints of weakness, increased appetite and thirst, and increased frequency of micturition for the past two months. Personal history revealed a consistent weight loss over the past six months and an increased problem of lice in the hair for the past two months. A family history of diabetes, hypertension, and allergies was present. General physical examination reveals no abnormality and vitals were within normal limits. Laboratory investigations like complete blood count, random blood sugar, HbA1c, IgE levels, anti-nuclear antibodies, Glutamic Acid Decarboxylase (GAD) 65 antibody for type-1 diabetes mellitus, hormonal assay, complete urine examination and skin prick test were performed, and the reports are given in [Table/Fig-1].

Based on the reports [Table/Fig-1], the patient was diagnosed with diabetes mellitus type-1. Premixed combined insulin was started

containing insulin degludec and insulin aspart in a ratio of 70:30, initially 30 units were given twice a day. From the skin prick test results, it was found that the patient developed food allergy that is a reproducible, immune-mediated and the adverse reaction that occurs after exposure to a particular food.

The immunologist prescribed the use of combination of food allergens extracts in low dose solutions which are given sublingually once a day in the morning in fasting state. They were given in doses titrated to prepare three levels of increasing concentrations starting from the lowest dose that is smaller than that required for inducing oral tolerance [1].

The methodology followed for SLIT included the testing of fasting blood glucose levels, administer 0.1 mL (2 drops) of low dose antigen solution (in a combination of 3 food allergens) sublingually for two minutes and then swallowing, re-check blood sugar levels after 15 minutes, give insulin dose and then food after 15 minutes.

The patient responded well to the insulin treatment with the blood sugar levels remaining within the initial target range of 140 to 160 mg/dL with average level of 141.06 mg/dL. Lifestyle modification included a combination of balanced diet recommended by the dietician from the list of food that are not allergic to the patient and a combination of aerobic exercises and resistant training for a duration of 60 minutes in a day in two divided sessions. It was noticed that with the use of the low-dose allergen solutions, the blood glucose levels fluctuated and rises to the levels of 200 mg/dL-250 mg/dL in the fasting state recorded within 15 minutes of administration of solution.

The insulin dose was adjusted according to the fluctuation of glucose levels by adding 2 units to the dose for every 50 mg/dL rise in blood glucose levels to the maximum level of 10% of total regular dose (6 units) after consulting endocrinologist. Insulin dose was adjusted to keep the blood glucose levels within the target range and to reduce the elevated levels of glycosylated haemoglobin. The dose of food allergen extract was further reduced with a dilution of 1:5 ratios. The blood glucose levels were well maintained within the normal range and the Insulin dose was fixed at 20 units in the

Investigations	Details	
Complete blood picture:	Haemoglobin=15.4 g/dL, RBC count=5.5 million/ µlitre White blood cells: 4700 cells/cm.	
Random blood sugar:	584 mg/dL	
HbA1c:	>12.5 estimated average glucose >367.7 mg/dL.	
Complete urine examination:	Negative for proteins, glucose and ketones.	
The total IgE levels:	218 IU/mL.	
The antinuclear antibodies:	0.41	
GAD 65 Antibody for type-1 diabetes:	9.12	
Hormonal assay	Prolactin	8.41 ng/mL
	Follicle stimulating hormone	4.49 mIU/mL
	LH	3.29 mIU/mL
	Fasting insulin	26.72 µIU/mL
	T3	148.25 ng/dL
	T4	9 µgm/dL
	TSH	2.57 mIU/mL

[Table/Fig-1]: Laboratory investigation reports.

morning and 20 units in the evening, 15 minutes before the meal. The immunologic desensitisation continued for a period of nine months with good control of blood glucose levels.

In the first three months, the HbA1c was 7.8 with estimated average glucose of 200.38 mg/dL. The fasting insulin was 20.26  $\mu$ IU/mL and the weight has been increased to 45 kg and her BMI improved to 19.5 kg/m<sup>2</sup>. The problem of lice in the hair has been also reduced and helped her to concentrate in her work and studies. The dose of insulin was adjusted to 10U in the morning and 10U in the evening, 15 minutes before the meal.

At end of nine months, the repeat skin prick test was negative for all the previous food items she was allergic to, except for the fungal, yeast and mite allergens, which were not included in SLIT [Table/Fig-2] [2,3].

Comparative investigations	Pre-treatment	Post-treatment (After 9 months)	
HbA1c:	>12.5 estimated average glucose >367.7 mg/dL.	7.5 estimated average glucose 190 mg/dL.	
Skin prick test:	<b>Allergen type</b>	<b>Pre-treatment</b>	<b>Post-treatment</b>
	<b>Food allergen:</b>		
	1. Curd,	4 mm	Negative
	2. Egg, Wheat, green peas, pigeon pea, guava	3 mm	Negative
	3. Mutton, Milk, Peanuts	2 mm	Negative
	<b>Fungal allergen:*</b>		
	Aspergillus fumigatus	4 mm	NA
	Mites: D pteronyssinus*	3 mm	NA
Yeast:*	3 mm	NA	
Oral food challenge test: post-treatment	<b>Food Item</b>	<b>Average blood glucose levels (mg/dl)</b>	
		Fasting	After 1 hour of
	Curd	127 mg/dL	387 mg/dL
	Egg	107.67 mg/dL	117.33 mg/dL
	Wheat	125.33 mg/dL	134.33 mg/dL
Green peas	128 mg/dL	146 mg/dL	
The total IgE levels:	<b>Pre-treatment</b>	<b>Post-treatment (After 9 months)</b>	
	218 IU/mL	152 IU/mL	
Fasting insulin	<b>Pre-treatment</b>	<b>After 3 months</b>	<b>After 9 months</b>
	26.72 $\mu$ IU/mL	20.26 $\mu$ IU/mL	9.28 $\mu$ IU/mL

[Table/Fig-2]: Comparative reports- Pre and Post-sublingual Immunotherapy (SLIT).

\*Not included in SLIT, NA: Not applicable

In the oral food challenge test, the blood glucose levels had not been risen more than 150 mg/dL, recorded one hour after the food was given and the difference in rise was not more than 10-20 mg/dL compared to pre-meal levels on three different occasions recorded by the glucometer after taking the allergen food for any of the previously listed food allergens.

The procedure of oral food challenge was to first select some of the food items which the patient was allergic to. The most commonly consumed food items with mild to moderate response on first skin prick test and negative in the second skin prick test were selected. Oral food challenge test was done with one food item at a time on three alternate days and the changes in blood glucose was monitored and the average of readings from three days was taken. Each test was done at fortnight.

From the second food item, glucose monitoring sensor was used as the patient was not compliant with pricks on fingers for glucometer monitoring. The patient response for egg, green peas and wheat was similar with the average difference in rise of blood glucose levels of not more than 10-20 mg/dL compared to pre-meal levels. These foods were included in daily consumable food list individually but not combined at this stage. Though similar response was not seen with the curd, that gave maximum response in the primary skin

prick test and a negative response on repeat skin prick test after nine months of immunotherapy, with the average blood glucose levels rising to 387 mg/dL within 1 hour of oral food challenge test done with curd on three alternate days [Table/Fig-2]. The patient is under follow-up and further food items will be challenged to extend the list of consumables, firstly continuing with single food item and later with combinations. The patient continues to take 10U insulin daily and the oral food allergen extracts were stopped.

## DISCUSSION

Type 1 diabetes is an autoimmune disorder with the destruction of pancreatic  $\beta$  cells destroyed by the autoimmune response [4]. In this case, proper evaluation of history from the patient has played the key role to identify the possible role of type 1 hypersensitivity reaction as the triggering factor for the autoimmune reaction leads to the rise blood glucose levels [3]. The food allergens can trigger and show the symptoms of IgE mediated or non IgE mediated and sometimes mixed reactions [5]. According to studies done on effect of food allergies, most common foods to elicit reactions include milk, egg, peanut, tree nut, wheat, soy, fish and shellfish [6]. In the type 1 hypersensitivity reaction, antibodies are formed against the soluble antigens and is mediated through the IgE [7]. The decrease in the fasting insulin levels might be caused due to autoimmune response to pancreatic  $\beta$  cells in response to the food hypersensitivity [8,9].

The DAISY study by Norris JM et al., has shown that the timing of introduction of any type of cereal (gluten and non gluten containing) was associated with an increased risk of islet autoimmunity in a U-shaped relationship with nadir at introduction at 4-6 months of life [10]. In a similar study in Finland, Diabetes Prediction and Prevention (DIPP) reported that introduction of root vegetables by age four months doubled the risk of islet autoimmunity compared with later introduction and also that first exposure to egg before age eight months was associated with an increased risk of islet autoimmunity [11]. The development of new treatment modality as SLIT has brought a new scope in the treatment of allergic diseases [1].

In the present case, after desensitisation was done by the low dose food antigen extract (in a combination of 3 food allergens) 0.1 mL of low dose antigen solution was given sublingually for a period of nine months, the fasting insulin levels reaches near to the normal range and the range of fluctuations in the blood sugar levels on oral food challenge test has come close to the normal range (110 mg/dL to 150 mg/dL). For the substance like curd, that had negative response on second skin prick test but failed on oral food challenge test must be because of failure to develop tolerance as a result of desensitisation process and need to continue the SLIT for longer duration or as a single extract or it may require subcutaneous immunotherapy.

In the study done by De Boissieu D and Dupont C for SLIT in subjects allergic to milk, the dose was started at 0.1 mL and doubled every 15 days to the limit of 1 mL/day. The re-challenge after six months has shown that the milk challenge threshold significantly increased post-treatment and the Milk-specific IgE did not significantly change during this time period [12]. In the randomised, double-blind, placebo-controlled study done in children with IgE-mediated peanut allergy, some study subjects (n=11) received treatment for 12 months and the other group (n=7) received placebo. Post-study, the sensitivity to peanut titrated skin prick testing was significantly decreased in the active treatment group compared with placebo group [13].

The study of this case report reinforces the need to consider the allergens as the trigger factor and to consider the possibilities of type 1 hypersensitivity in the diagnosed cases of type 1 diabetes. This can be an adjunct to the insulin treatment and prevention of long term complications of type 1 diabetes. There might be many more such cases of type 1 hypersensitivity triggered autoimmune reaction that has escalated into frank diabetes because of improper

clinical history and investigations. In general, when a young individual is detected with raised blood glucose levels, it is considered as autoimmune type of Type 1 diabetes and the investigations, diagnosis and treatment work in this direction [4]. The systemic effects on different organs and systems have to be studied extensively. The diagnosed cases of type 1 diabetes has to be further evaluated and studies not just as an autoimmune disorder prescribed with Insulin to maintain the blood sugar levels within normal range, but this has to be considered multifactorial with subjective patterns.

The possible underlying immune mechanism triggered by the allergic food on the blood glucose and insulin levels and the complete antibody response, B cell and T cell response to SLIT and its significance as an underlying mechanism in decreasing the blood glucose levels and fasting insulin levels was beyond the scope in this case presentation. An extensive study at the molecular level is required in a larger cohort to understand the immunological changes due to type 1 hypersensitivity, its relationship with the pathophysiology and pathogenesis of type 1 diabetes and effective use of immunologic desensitisation method to prevent blood glucose fluctuations and decrease the use of Insulin.

## CONCLUSION(S)

The present case report (of type 1 DM patient) has found that the use of the low dose antigen solutions as SLIT, does desensitisation of the allergic foods that were responsible for rise in blood glucose levels and decreasing the fasting Insulin levels. As a result of this, patient developed tolerance to the allergic foods which lead to decrease in average glucose levels, reduction in the HbA1c levels and the dose of the Insulin required. Further, there was increase in body weight and improvement in the BMI.

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## REFERENCES

- [1] Gotoh M, Kaminuma O. Sublingual immunotherapy: How sublingual allergen administration heals allergic diseases; current perspective about the mode of action. *Pathogens*. 2021;10(2):147.
- [2] Muthupalaniappan L, Jamil A. Prick, patch or blood test? A simple guide to allergy testing. *Malays Fam Physician*. 2021;16(2):19-26.
- [3] Bignardi D, Cornite P, Mori I, Ferrero F, Fontana V, Bruzzone M, et al. Allergen-specific IgE: Comparison between skin prick test and serum assay in real life. *Allergol Select*. 2019;3(1):09-14.
- [4] Kawasaki E. Type 1 diabetes and autoimmunity. *Clinical Pediatric Endocrinology*. 2014;23(4):99-105. Published online 2014 Nov 6.
- [5] Calvani M, Bianchi A, Reginelli C, Peresso M, Testa A. Oral Food Challenge. *Medicina (Kaunas)*. 2019;55(10):651.
- [6] Narisety SD, Keet CA. Sublingual vs oral immunotherapy for food allergy: Identifying the right approach. *Drugs*. 2012;72(15):1977-89.
- [7] Abbas M, Moussa M, Akel H. Type I hypersensitivity reaction. *StatPearls Publishing*; 2022 Jan. <https://www.ncbi.nlm.nih.gov/books/NBK560561/>.
- [8] Diagnosis and Classification of Diabetes Mellitus, American Diabetes Association, *Diabetes Care*. 2014;37(Supplement\_1):S81-S90.
- [9] Rewers M, Ludvigsson J. Environmental risk factors for type 1 diabetes. *Lancet*. 2016;387(10035):2340-48.
- [10] Norris JM, Barriga K, Klingensmith G, Hoffman M, Eisenbarth GS, Erlich HA, et al. Timing of initial cereal exposure in infancy and risk of islet autoimmunity. *JAMA*. 2003;290(13):1713-20.
- [11] Virtanen SM, Takkinen HM, Nevalainen J, Kronberg-Kippilä C, Salmenhaara M, Uusitalo L, et al. Early introduction of root vegetables in infancy associated with advanced  $\beta$ -cell autoimmunity in young children with human leukocyte antigen conferred susceptibility to Type 1 diabetes. *Diabet Med*. 2011;28(8):965-71.
- [12] De Boissieu D, Dupont C. Sublingual immunotherapy for cow's milk protein allergy: A preliminary report. *Allergy*. 2006;61(10):1238-39.
- [13] Kim EH, Bird JA, Kulis M, Laubach S, Pons L, Shreffler W, et al. Sublingual immunotherapy for peanut allergy: Clinical and immunological evidence of desensitization. *J Allergy Clinical Immunology*. 2011;127(3):640-46.

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