

# Insulin Refusal in Iranian Patients with Poorly Controlled Type 2 Diabetes Mellitus

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Received: 13 Oct. 2012; Received in revised form: 28 Jan. 2013; Accepted: 20 Feb. 2013

**Abstract-** To achieve tight glycemic control in diabetic patients, it may be necessary to introduce insulin therapy much earlier in the disease course. Poor glycemic control is a risk factor for the development of diabetic complications. Many patients require insulin therapy after several years of disease in order to maintain good glycemic control and prevent complications. But many patients do not receive insulin therapy in a timely manner because of a negative appraisal of this treatment. Understanding the cause of this negative attitudes is necessary for better evaluation to overcome for this problem. The purpose of this study was to evaluate the reasons for insulin refusal among patients with type 2 diabetes. This is a descriptive cross-sectional study from Yazd Diabetes Research Center. 400 patients with type 2 diabetes who had an HbA1c  $\geq 8.0\%$  despite optimal oral therapy were identified that participated in this study. Data were obtained by patient interview using validated questionnaires. This study showed that Insulin refusal was common. 77% of participant reported being unwilling to take insulin if prescribed. Fear of injection is an important cause for insulin refusal among patients. Insulin refusal is an important problem among our patients with type 2 diabetes mellitus. Findings of this study suggest that interventions aimed at increasing insulin use should focus on injection-related concerns, education and correction of misconceptions.

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*Acta Medica Iranica*, 2013; 51(8): 567-571.

**Keywords:** Diabetes mellitus; Insulin therapy; Questionnaire

## Introduction

Management of diabetes is complicated by the progressive nature of the disease; as  $\beta$  cell function diminishes, oral hypoglycemic agents alone are frequently insufficient for maintaining glycemic control and insulin therapy is required. This was shown in the UK Prospective Diabetes Study, where more than half of newly diagnosed diabetic patients required insulin therapy within 6 years (1).

When managing type 2 diabetes, general focus is on achieving and maintaining good glycemic control while minimizing the potential for adverse events such as hypoglycemia. The value of this approach has been shown from evidence gained in landmark clinical and epidemiological studies where the reduced incidence of micro and macrovascular complications was apparent with intensive glycemic control (2-4) and has further been confirmed in a published meta-analysis of observational studies (5).

Although most providers agree that insulin is an

efficacious approach to the management of type 2 diabetes, many still consider insulin therapy as the last resort and indicate that their patients are hesitant to take insulin (6). A study conducted in the USA showed that 33% of type 2 diabetic patients were unwilling to use insulin therapy (7), while another study conducted among Bangladeshi patients found 42.5% of patients with type 2 diabetes unwilling to start insulin therapy initially, with 20.3% refusing insulin use even after repeated counseling (8). Reasons for insulin refusal in this patients was perceptions that requirement for insulin was an indicator of disease severity, needle anxiety, premature death from insulin injection, fear of hypoglycemia, weight gain, loss of independence and reliance on others to give insulin (8).

In another study in Singaporean patients with type 2 diabetes mellitus 7 of every 10 patients (70.6%) expressed unwillingness to use insulin therapy. The greatest differences in perceptions between patients willing to use insulin therapy and those who were not, included fear of not being able to inject insulin correctly,

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fear of pain, belief that insulin therapy would make it difficult to fulfill responsibilities at work and home (9).

The aim of this study was to determine the prevalence and reasons for insulin refusal among patients with poorly controlled type 2 diabetes in the province of Yazd. Yazd is a city in the center of Iran with high prevalence of diabetes (10).

**Materials and Methods**

This was a descriptive cross-sectional study

conducted among 400 type 2 diabetic patients who came to Yazd diabetes research center in Yazd. Subjects had the following inclusion criteria: age  $\geq 18$  years, diagnosis of type 2 diabetes for  $\geq 1$  year, poor glycemic control HbA1c  $\geq 8.0\%$  (normal range 4-6%), on maximum tolerated oral glucose-lowering therapy (metformin plus sulfonylurea), in whom insulin therapy was deemed necessary by clinician. Patients with type 1 diabetes mellitus, severe psychiatric illness, dementia and those on current insulin treatment were excluded.

**Table 1.** Barriers to insulin treatment questionnaire.

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**Expectations and concerns that people with diabetes might have about their condition and treatment with Insulin. Marking most cause of insulin refusal on a scale from 1 to 10.**

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1. I am afraid of the pain when injecting insulin.	totally disagree	totally agree
1 2 3 4 5 6 7 8 9 10		
<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
2. I am afraid of hypoglycemia	totally disagree	totally agree
1 2 3 4 5 6 7 8 9 10		
<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
3. I am afraid of weight gain	totally disagree	totally agree
1 2 3 4 5 6 7 8 9 10		
<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
4. Regular insulin treatment causes feelings of dependence.	totally disagree	totally agree
1 2 3 4 5 6 7 8 9 10		
<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
5. Fear of social stigma. Injections in public are embarrassing to me.	totally disagree	totally agree
1 2 3 4 5 6 7 8 9 10		
<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
6. I can't pay as close attention to my diets and works as insulin treatment requires.	totally disagree	totally agree
1 2 3 4 5 6 7 8 9 10		
<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
7. Insulin is expensive.	totally disagree	totally agree
1 2 3 4 5 6 7 8 9 10		
<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
8. Insulin can cause long-term complications due to diabetes.	totally disagree	totally agree
1 2 3 4 5 6 7 8 9 10		
<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
9. Erroneous beliefs regarding insulin therapy means Diabetes has worsened.	totally disagree	totally agree
1 2 3 4 5 6 7 8 9 10		
<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
10. Hardship from insulin injection.	totally disagree	totally agree
1 2 3 4 5 6 7 8 9 10		
<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		

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All patients were carefully counseled about the reasons why insulin was deemed necessary, the potential benefits and adverse effects of insulin therapy. Counseling was undertaken by one clinician. All participants gave written informed consent. Demographic and clinical data, such as age, sex, education level, duration of diabetes and HbA1c levels were obtained from the patients. First patients asked about willingness or unwillingness for insulin therapy. Next persons who disagreed to insulin when advised to commence it despite several consult must to report the most important cause of it and degree of unwillingness for this cause (slightly, moderately, or very disagree) from zero to ten with using questionnaire (Table 1). Questionnaire was developed by a group of endocrinologists in Yazd Diabetes Research Center involved with diabetes care, incorporating common themes associated with insulin refusal and the unique perceptions that were described in Iranian populations. The questionnaire was developed in Persian language. The questions are about their thoughts towards injecting insulin. The questionnaire consisted of 10 items. We examined unwillingness as a discrete variable for each 10 items, comparing degree of unwillingness (slightly, moderately, or very disagree) from zero to ten. The patient was either willing or not, and the gradations of unwillingness were scored. Differences in demographics, clinical characteristics and disagreement were analyzed using the Chi-square test or independent samples t-test when appropriate. Data were analyzed with SPSS version 16.0. Statistical significance was set at  $P \leq 0.05$ .

## Results

This was a descriptive cross-sectional study conducted

among 400 patients who came to Yazd diabetes research center in Yazd.

The mean age was  $57.9 \pm 10.6$  years, and the average diabetes duration was  $10.07 \pm 7.4$  years. The majority were female (69.3%) and 30.7 % was male. In this study 8.3%, 11.5%, 7.8% and 27% had retinopathy, nephropathy, diabetic foot and IHD respectively.

Insulin therapy unwillingness was common: 310 patients (77%) reported unwillingness to take insulin. 80.0% of females and 66.1% of males were unwilling ( $P=0.19$ ). Patients most frequently endorsed about pain of insulin injection (43.7%), hardship from insulin injection (14.2%), high cost of insulin therapy (7.4%), problematic hypoglycemia (5.4%), fear of weight gain (3.8%), continuous dependency to insulin therapy (6.4%), fear of social stigma (3.8%), limitation of daily works as carefully as insulin treatment requires (5.4%) and others as reasons to avoid insulin therapy (Table 2). Also score of each item from zero to ten is showed in table 2.

Statistical analysis showed no difference between educational level and cause of unwillingness to use insulin; 20% of patients with tertiary education were unwilling to use insulin due to fear of injection and 39.9% of patients with primary school or less report this problem.

There was no difference between groups with retinopathy, nephropathy, diabetic foot and ischemic heart disease (IHD) with other groups that had no these complication with respect to the most cause of unwillingness. Pain of injection was the most cause of unwillingness in patients with diabetic complications.

Also there was no difference between age groups and duration of diabetes for refusal to insulin. Pain of injection was the most problem in all of age groups.

**Table 2.** Distributions of cause of unwillingness to insulin therapy among Type 2 diabetic patients.

Variables	Number	Percent	Score
Fear of injection	134	43.7	3.46
Fear of hypoglycemia	17	5.4	6.03
Fear of weight gain	12	3.8	5.79
Continuous dependency to it	20	6.4	8.26
Fear of social stigma	12	3.8	2.01
Limitation of daily works	17	5.4	5.27
High cost of insulin therapy	23	7.4	6.06
Insulin cause DM complications	11	3.5	4.61
Insulin means worsening DM	20	6.4	3.84
Hardship from insulin injection	44	14.2	7.35
Total	310	100	

## Discussion

This study showed that unwillingness to insulin therapy was common (77%). This is the same as result in study conducted among Asian patients with diabetes in Singapore (9) but it was higher than those reported in studies conducted in the USA that report 28.2% and 33% respectively (7,11).

Fear of injection has often been thought to be one of the most important barriers to insulin use. In our study, injection-related concerns were found to be more common in patients who were unwilling to use insulin, which was likewise described in other studies (7,11-12). In our study fear of injection was the most important cause in all age, sex, educational level and patients with diabetic complication. Zambanini *et al.* study did not show any significant correlations between injection anxiety and age, sex, duration of diabetes mellitus (DM) (13). Although pain of injection is the most cause of insulin refusal in this study, severity or score of this item is 3.46 from 10 (Severity is mild to moderate). In this regard, physician should elicit the patient's true concerns regarding the use of injections. Studies have recommended counseling and education in overcoming injection-related barriers, which may include using insulin pens (14,15). Use of insulin pens has been associated with greater ease of use, lower pain perception (16,17).

Other causes of insulin refusal in this study was hardship from insulin injection, high cost of insulin therapy, hypoglycemia, fear of weight gain, continuous dependency to Insulin therapy, fear of social stigma, limitation of daily works as carefully as insulin treatment requires. In a qualitative study of Mexican-Americans with poorly controlled diabetes, similar negative attitudes to insulin therapy were elicited (18). These included increased disease severity, needle anxiety, fear of hypoglycemia and social stigma, concern about technical aspects of insulin therapy and cost. Cost was not deemed an issue in a study of Khan *et al.* in Bangladeshi patients with poorly controlled diabetes, because patients receiving free medication, and the technical concerns were not conveyed, perhaps as a result of them having an insulin pen (8).

Fear of hypoglycemia often stems from observing people with diabetes who take insulin. Point out that with the use of newer rapid-acting and long-acting insulins, hypoglycemia is less likely to occur and that very few patients with type 2 diabetes actually have severe hypoglycemia. Reassure patients and teaching

patients to correctly identify symptoms of hypoglycemia and strategies to facilitate insulin use is also often helpful (19).

Other lifestyle concerns are related to timing, difficulty in traveling, and loss of spontaneity and flexibility. If patients identify these concerns, provide information about insulin regimens that offer maximum flexibility for example insulin analogues, strategies for traveling with insulin, or other identified lifestyle barriers is necessary (19).

Patients' perceptions of social stigma for the self-injection of insulin in public can have a restrictive effect on disease-management efforts. The consequence of it may lead to a lack of motivation due to the inconvenience and embarrassment related to injections (20). Patients may select suboptimal locations to inject themselves while away from home, such as in public toilets, and may also cause some patients to delay injections and avoid social activities (21). Some patients worry that if they inject in public places they will be perceived as injecting illegal drugs. Insulin pens can be very helpful for overcoming this barrier by increasing patients' ability to inject discretely. Using only morning and or bedtime insulin regimens can also eliminate this barrier for some patients (19).

Many patients who begin insulin therapy gain weight with improved glycemic and greater meal plan flexibility. If this is a barrier, lifestyle change and consult with a dietitian before the initiation of insulin is necessary. New insulin analogues have been shown to be relatively beneficial in lessening weight gain during insulin therapy. Insulin detemir and insulin glargine (basal insulin) has demonstrated relative benefits with respect to weight (22).

Insulin refusal is an important and urgent problem that should be addressed. Most patients with type 2 diabetes will eventually require insulin therapy, and healthcare providers involved with care of these patients should be trained in counseling patients who refuse insulin therapy. Therefore, we recommend that education regarding insulin therapy be started early, even at diagnosis of type 2 diabetes.

## Acknowledgments

Great thanks to the Yazd Diabetes Research Center, Shahid Sadoughi University of Medical Science for the support and providing the facilities for this work. The authors declare that there is no conflict of interest.

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