

Factors Leading To Poor Adherence To Titration Of Once-Daily Basal Insulin Among Patients With Type 2 Diabetes Mellitus

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Abstract

Introduction: Given the increasing burden of diabetes worldwide as well as in the Philippines, understanding factors affecting diabetes management is crucial. We investigated the factors leading to poor adherence to titration of long-acting, once a day, basal insulin among patients with type 2 diabetes mellitus (DM) seen at the outpatient department (OPD) clinics of St. Luke's Medical Center, Quezon City.

Methods: This qualitative study included semi-structured individual interviews and focus group discussions (FGD). A total of 43 type 2 DM patients using once a day, basal insulin participated. 22 patients had one-on-one interviews while 21 patients were divided into three separate FGDs. Data were analyzed using thematic analysis.

Results: More than half (53.5%) of the type 2 DM patients included in this study did not have any method of titration of their once-daily basal insulin despite being taught by their attending physicians. The categorized themes identified

were the following: patient-centered, treatment-related, healthcare system-related, and psychological/social factors.

Conclusion: Lack of income or financial support, fear of insulin injection and its side effects, high cost of insulin, inaccessibility of medical assistance from healthcare facilities, negative attitude/fear of titration, and difficulty complying to lifestyle changes were some of the identified factors leading to poor adherence to the titration of once-daily basal insulin in this study. Good, constant communication between the patient and the doctor appears to improve adherence to insulin dose titration. Future studies may adapt the themes and concepts identified to improve adherence to titration of once-daily basal insulin among patients with type 2 DM.

Keywords: diabetes mellitus, insulin, hypoglycemia, hyperglycemia, blood glucose, patient education, healthcare

Introduction

Diabetes is a chronic disease and patients have the ultimate responsibility for managing his or her own care to prevent complications. He or she must have adequate knowledge and other facilitating factors towards compliance to therapeutic regimen.¹ As non-adherence to diabetes medications is associated with higher rates of mortality.² It has been noted that the rate of non-compliance in patients with chronic diseases in developed countries, on long-term treatment, is ~50%. This could be even higher in developing countries.³ In a Spanish study of 294 patients with type 2 diabetes mellitus (DM), patients self-assessed their level of compliance using a questionnaire. The highest compliance was seen in patients taking only insulin (67%), whereas the lowest compliance was in patients taking insulin plus an orally administered antihyperglycemic agent (OHA)(39%). Surprisingly, for patients taking only OHAs,

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the compliance level was similar for monotherapy and combination therapies.⁴

There are many potential reasons for non-adherence to medication and frequently, more than one is present for any given patient. They include age, perception and duration of disease, polytherapy, psychological factors, safety, tolerability, and cost. Some of these factors are amenable to modification.⁵ Understanding and improving medication adherence is crucial in diabetes management to improve glucose control and limit the development of complications.^{6,7}

Self-adjustment of insulin dose has been an established regimen that achieve better blood glucose control in Western populations of patients with type 2 DM.⁷ The Asian Treat to Target Lantus Study (ATLAS) has also shown that patient-driven titration of basal insulin is non-inferior to physician-led titration.⁸ Factors to non-adherence to medications and insulin initiation have been established. However, studies with regards to factors affecting adherence to insulin titration are limited. Hence, this study aimed to determine the clinical profile of subjects practising titration of their long-acting,

once a day, basal insulin and the perceived factors leading to poor adherence.

Methods

This is a qualitative study using semi-structured individual interviews and focus group discussions (FGD) that identified and explored the views of patients with type 2 DM on their perceived factors affecting adherence to self-titration of long-acting, once daily, basal insulin.

Ethical approval was obtained from the Institutional Ethics Review Committee (IERC) of St. Luke's Medical Center, Quezon City. All subjects were informed of the details of the study and consents were given prior to participation in the interviews or FGD.

Interviews were conducted from April 2017 to April 2018. The study population consisted of adult patients, between ages 18-80 years old, diagnosed with type 2 DM on a once a day, long acting basal insulin for at least three months but not more than six months, insulin-naïve prior to starting current basal insulin, being seen at the SLMC-QC OPD in both private and social services. Exclusion criteria included pregnant/nursing/lactating mothers, patients with history of serious medical condition at time of insulin initiation, life-limiting malignancy, and hospice care enrollment, those who could not communicate with either tagalog/filipino or english, patients with significant cognitive deficits or psychiatric illness, and patients with visual impairment limiting insulin self-administration.

There is no gold standard to calculate the number of people to interview in qualitative studies; however in practice, 12-26 persons is considered sufficient to most researchers.⁹ Purposive sampling was utilized and the appropriate sample size was determined upon reaching data saturation. Simple random sampling was done using table of random numbers. 22 patients had one-on-one interviews while 21 patients were divided into three separate FGDs. A total of 43 subjects participated, achieving saturation of data.

The medical histories of the patients were reviewed including but not limited to the following risk factors: age and gender, educational level and marital status, monthly family income, duration of diabetes or age at diagnosis, HbA1c record within the last 12 months, list of any prescribed glucose-lowering medications including the dose of basal insulin being used, duration of use of basal insulin, method of self-titration, family medical and personal/social history, and frequency of health check-up. Physical examination was also done including height, weight, blood pressure, and waist circumference.

Interviews were conducted using a semi-structured

interview protocol. Topics included initial feelings about diabetes in general, feelings when insulin was first suggested, and factors perceived by patients leading to poor adherence to self-titration of long-acting, once daily basal insulin. Responses to main questions were followed by probing, rephrasing, and clarifying to expand the patient's comments and explore the issues in-depth. The duration of interviews ranged from about 15 to 30 minutes. All interviews were conducted by the first author, audio-recorded, and transcribed verbatim.

Verbatim transcriptions were analyzed using a thematic analysis approach to identify main themes. Data was encoded and processed using NVIVO7/11 (QSR International Pty Ltd, Doncaster, Victoria, Australia) and thematic analysis was done identifying themes found in each transcript.

Results

A total of 43 patients with type 2 DM participated, composed of 17 males and 26 females, majority were aged 60-80 years old (60%), college graduates (41.9%), married (72.1%), mostly with monthly income ranging from >20,000 (39.5%), with 11-20 year duration of diabetes (32.5%), and having quarterly check-ups (62.8%). The dose of basal insulin of most of the subjects was 10-15 units/day (34.9%). Comorbidities of the participants were chronic kidney disease (CKD) (93%), hypertension (76.7%), and dyslipidemia (20.9%). Most had family history of type 2 DM (79.1%) and hypertension (53.5%). Majority were obese (51.1%) based on the WHO Asia-Pacific classification while 23-48% have mild to moderate CKD. Baseline HbA1c levels in 67.4% of subjects ranged from 7-9%. Table I summarizes the characteristics of the subjects.

Themes identified (Figures 1 and 2)

Theme 1: Patient-related Factors

In general, the participants in this study identified insufficient income and lack of support from family (72%) as a source of poor adherence.

Theme 2: Treatment-related Factors

Another commonly perceived problem was apprehension to the side effects of insulin dose titration such as fear of injection (35%) as well as hypoglycemia (23%) and weight gain (5%).

Theme 3: Healthcare system Factors

Most of the subjects (54%) have mentioned the lack of accessible assistance in case of emergency after insulin dose titration, the cost of insulin as well as inadequacy of resources to avail insulin are affecting their adherence.

Theme 4: Psychological/Social Factors

More than half of the subjects have expressed their lack of

Table I. Subject characteristics (n=43)

	Number of participants	Percentage (%)
Age (years)		
18-39	0	0
40-59	17	39.5
60-80	26	60.5
Educational attainment		
Elementary undergraduate	2	4.6
Elementary graduate	4	9.3
Highschool undergraduate	5	11.6
Highschool graduate	8	18.6
Vocational	3	7
College undergraduate	3	7
College graduate	18	41.9
Marital status		
Single	4	9.3
Married	31	72.1
Separated	1	2.3
Widow	7	16.3
Monthly income (range in Philippine pesos)		
5,000-10,000	10	23.3
10,000-20,000	16	37.2
>20,000	17	39.5
Duration of Diabetes (years)		
1-5	7	16.3
6-10	12	27.9
11-20	14	32.5
>20	10	23.3
Frequency of check-ups (in a year)		
Every 3 months	27	62.8
Every 4-5 months	6	13.9
Every 6 months	10	23.3
Dose of basal insulin (units)		
<10	0	0
10-15	15	34.9
16-20	7	16.3
21-30	11	25.6
31-50	8	18.6
>50	2	4.6
Duration of insulin use (months)		
3 months	20	46.5
4 months	5	11.6
5 months	1	2.3
6 months	17	39.5
Method of titration (adjusted daily)		
None/not known to patient	23	53.5
+/- 2 units	4	9.3
+2 units if CBG >130	1	2.3
-5 units	1	2.3
MD-guided (as texted per SMS)	10	23.3
+/-4 units	4	9.3
Other comorbidities		
CKD	40	93.0
Hypertension	33	76.7
Dyslipidemia	9	20.9
CAD/IHD/Previous MI	3	7
CVD/Stroke	3	7
PTB	2	4.6
Cardiac dysrhythmia (eg. AF, WPW)	2	4.6
Primary hypothyroidism	1	2.3
Bronchial asthma	1	2.3
Cataract	1	2.3

Table I. Subject characteristics (n=43)

	Number of participants	Percentage (%)
Fatty liver	1	2.3
Acid reflux disease	1	2.3
DVT	1	2.3
BMI (WHO Asia-Pacific Classification)		
<18.5	0	0
18.5-22.9	8	18.6
23-24.9	13	30.2
25-29.9	17	39.5
≥ 30	5	11.6
Waist circumference (in cm)		
70-80	5	11.6
81-90	18	41.9
91-100	13	30.2
101-110	7	16.3
Systolic Blood pressure (mmHg)		
90-110	12	27.9
111-120	9	20.9
121-130	8	18.6
131-140	7	16.3
141-150	3	7
151-160	1	2.3
>160	3	7
Diastolic Blood pressure (mmHg)		
60-70	17	39.5
71-80	19	44.2
81-90	5	11.6
91-100	2	4.6
101-110	0	0
>110	0	0
EGFR (based on CKD-EPI)		
>90	3	7
60-89	18	41.8
45-59	10	23.3
30-44	10	23.3
15-29	2	4.6
<15	0	0
HbA1c levels (prior to insulin use)		
<7%	0	0
7-9%	29	67.4
>9%	14	32.6
HbA1c levels (on follow-up)		
<7%	13	30.2
7-9	22	51.2
>9%	8	18.6

knowledge as to proper titration of insulin (53.5%) and others have negative attitude/fear of self-titration (21%) while 9.3% had difficulty in complying with lifestyle modification as recommended by their physician. Almost a quarter (23%) rely to their attending physician as to how they would adjust their basal insulin through text messaging/SMS.

Discussion

The American Diabetes Association categorizes barriers to adherence as either patient barriers, medication factors, or system factors. In this study we categorized the factors leading to poor adherence to titration of the subjects' once-daily, basal insulin, into: patient-related, treatment-related,

Patient-related Factors	Treatment-related Factors
<p>"Yung sa pera kapos din. Namamasada lang asawa ko. P400 lang kada araw ang kinikita. Depende lang din sa pasada. Eh ang ginagastos ko sa insulin mga P900 para sa 2 linggong insulin. May iba pa ring gastusin sa bahay."</p> <p>"Wala lang akong kita. Kaya minsan kinakapos ng pambili ng insulin. Binibigyan lang ako ng P2,000 kada buwan ng kaibigan ko."</p> <p>"Minsan wala rin pambili ng insulin...dati isang buwan. Yung anak ko flight stewardess, hindi naman lagi nakakapagpadala."</p> <p>"Walang pera eh."</p> <p>"Medyo mabigat sa panggastos yung pambili ng insulin."</p> <p>"Minsan walang pera pambili ng insulin...mahal kasi...pero kailangan."</p> <p>"Medyo hirap sa gastos...kasi mahal yung insulin."</p> <p>"Merong concern sa gastos para sa insulin kasi mahal."</p> <p>"Mahal ang insulin...ako lahat nagbubudget...may time na hindi nakaka-inject ng insulin...kulang sa budget."</p>	<p>"Hindi ako nag-aadjust ng insulin kasi natatakot akong mag-hypo (hypoglycemia)"</p> <p>"Natatakot din ako sa pagturok. Kaya hindi ko rin binabago o pinapalitan yung unit. Kung ano yung reseta, yun lang. Minsan kapit-bahay ko o sa Mercury Drug ako nagpapatok kasi nga takot ako."</p> <p>"Minsan, nakakapagod lang kakatusok – pagcheck ng sugar."</p> <p>"Dati natakot din akong mag-inject ng insulin...takot kasi ako sa karayom."</p> <p>"Natatakot din bumagsak sugar minsan."</p> <p>"Nung una, medyo natatakot ako sa pag-inject ng insulin. Pero ngayon, okay naman. Saka kadalasan ung anak ko naman na nurse yung nag-iinject."</p> <p>"Nung una, natakot din ako nung sasabihan na kailangan mag-insulin. Takot ako sa pag-inject. Pero ngayon nasanay na rin."</p> <p>"Natatakot ako mag-hypoglycemia."</p> <p>"Hindi ako nag-adjust kasi natakot ako sa side effects gaya ng hypo."</p> <p>"Nagkaroon dati, natakot ako. Nakatulog ako, hindi magising, 46 na lang sugar. Pag-gising ko nasa ospital na ako."</p> <p>"Takot din ako sa pag-inject...baka masakit."</p> <p>"Yung anak ko ang nag-iinject sa akin eh. Takot ako mag-inject. Sa braso nga lang ako nag-papainject. Ayoko sa tiyan."</p> <p>"Takot ako sa injection. Medyo natakot din nung sinabing kailangan maginjection."</p> <p>"Noong una, natakot ako sa pag-inject ng insulin."</p> <p>"Nung sa insulin, syempre noong una, natakot. Pero naexplain naman mabuti bakit kailangan."</p> <p>"Takot ako mag-prick o magtusok sa sarili...kaya dati sa Generika ako nagpapa-prick"</p> <p>"Noong una...natakot sa needle."</p> <p>"At first, takot sa needle."</p>

Figure 1. Patient-related and treatment-related factors

Healthcare System Factors	Psychological/Social Factors
<p>"Malayo bahay namin sa ospital. Hindi agad makakatako kung mag-hypo."</p> <p>"Kaya every 6 months lang din follow-up namin kasi sa malayo kami nakatira tapos pinag-iipunan pa pamasaha."</p> <p>"Saka hindi ko rin kasi lagi namomonitor sugar ko. Walang pambili ng strips."</p> <p>"Dati, nakakahingi ng insulin sa PCSO. Pero medyo mahirap kasi kailangan pa ng medical abstract tapos medyo matagal din...kailangan i-followup."</p> <p>"Sa gastos para sa insulin, medyo mahal...pero kinakaya."</p> <p>"Inisip yung gastusin"</p> <p>"Minsan hindi nasusunod pagbago o pag-inject ng insulin kasi medyo mahal."</p> <p>"Medyo mahal siya noh...pero if you try to compare to orals, mas mura siya...pero syempre may combination of orals pa rin ako..."</p> <p>"Medyo malayo din kasi biyahe sa probinsya. Di agad minsan nakakabili ng insulin."</p>	<p>"Hindi ako naturuan tungkol sa pag-adjust ng insulin."</p> <p>"Kapag mataas ang sugar, magdadagdag ng 2 units. Pero hindi ko rin nagagawa kasi natatakot akong mag-adjust basta-basta."</p> <p>"Nahiya rin akong magtanong sa doctor sa pag-adjust ng insulin."</p> <p>"I actually have no fear or worries naman when I was told to start insulin"</p> <p>"I would just call Dr. _____ (AMD) for adjustment of insulin dose"</p> <p>"Sa pag-adjust ng insulin, wala naman gaano problema kasi tinetext ko lang si doktor ng sugar tapos sinasabihan nya ako ng kung ilang dapat ang iinject. Basta kailangan inaintain ng 100 ang sugar. Kapat medyo mataas, nagdadagdag ng 2 units ng insulin."</p> <p>"Hindi ko inaadjust ang insulin, kung ano lang yung reseta."</p> <p>"Hindi ko lang alam pag-adjust."</p> <p>"Natetext ko naman yung doctor ko kung pano ko iadjust insulin"</p> <p>"Yung pag-adjust ko ng insulin, kapag bumaba sugar, binabawasan ko ng 4 units."</p> <p>"Hindi naman ako natakot sa pag-inject ng insulin kasi tinuruan ng doktor kung pano."</p> <p>"Hindi rin ako natakot sa hypoglycemia dahil naexplain naman ng mabuti."</p> <p>"Wala namang po akong naiisip na magiging sagabal kasi natuturo naman."</p> <p>"Dinadagdag ko ng +2 units yung insulin kapag higit 130 ang sugar ko sa umaga. Tapos kung maging <80, babawasan din ng 2 units...Hindi pa naman nangyari yun."</p> <p>"Madali naman sundin yung pagbago ng dose...importante lang din ang komunikasyon sa doktor sakaling may problema."</p> <p>"Naturuan naman ako sa pag-adjust... binabawasan ng 5 units kapag nag-hahypo. Pero hindi ko kadalasan dinadagdagang kung mataas. Minamaintain ko lang kung ano ung nireseta."</p> <p>"Hindi ko naadjust insulin kasi tatlong beses sa isang buwan lang ako nagmomonitor ng sugar."</p> <p>"Tinigil ko yung insulin ko for 3 months. Wala lang. Ako lang. Kasi gusto ko subukan magbago ng lifestyle baka mag-improve sugar."</p> <p>"Lifestyle modification – nag-vegan diet, exercise. Pero wala eh."</p> <p>"Natakot. Nung sinabing kailangan ko na mag-insulin. Umiyak ako ng umiyak. Ang alam ko kasi noon, grabe na kapag mag-insulin."</p> <p>"Hindi ko alam pag-adjust ng insulin"</p> <p>"That I don't know? If ever I would be told, probably I could be doing also."</p> <p>"Minsan matigas din ang ulo. Hindi ako araw-araw nag-iinject ng insulin. Takot din ako if ako ang mag-adjust."</p> <p>"Mayroong time na hindi naiinject insulin...nakakalimutan...kasi minsan akala ko natinject na..."</p> <p>"Sa pagkain...minsang napapadami...mahilig kasi ako sa sweets...lalo na mga cake."</p> <p>"Pagkain. But then you know what I am doing now, I lessen the carbo. Pero sometimes, baka naman sobra sa ulam, kahit na konti ang carbo. Nagkrave ako minsan...like I like to eat chips...and then kapag may nagbigay ng chocolates, o sige I'll take 1 small piece, then o tawad another small piece. Natural ko na kumakain...hindi na mabago...natatakam ka."</p> <p>"Malakas kumain...problema ko di mapigilan sa pagkain...gusto lang, masarap kasi kumain."</p>

Figure 2. Healthcare system and psychological/social factors

healthcare-system related, and psychological/social factors. For patient-related factors, our subjects identified lack of sufficient income and support from their respective families as the major factor to poor adherence to insulin titration. This is a common problem in third world countries, like the Philippines, wherein most patients have meager salary just enough to get them by with their daily needs and acquisition of medications would be of lesser priority. This is similar to other studies that showed a significant proportion of patients having lack of financial resources to continue with insulin

therapy after several months of treatment.¹⁰ Apart from its cost, glucometers and glucose test strips are required for self-monitoring of blood glucose which are often out-of-pocket expenses and likely to be too expensive for patients in many parts of Asia.¹¹ Missed and mistimed insulin doses are often unintentional, however, dose reductions are often made on purpose.¹² Some patients may intentionally reduce their insulin dose due to fear of hypoglycemia,¹³ while others may do so due to the high cost of basal insulin therapy.¹¹

In terms of treatment-related factors, our study showed that contributing to the generally negative attitudes toward adherence to insulin titration included fear of injection and side effects (eg. hypoglycemia, weight gain). This is no different to a study published in 2014 where they have identified that the most common barriers to insulin adherence by patients with diabetes were injection site reactions (90.2%), fear of hypoglycemia (87.4%), injections being time-consuming (63.2%), interference with physical activity (61.6%), and lack of adequate injection instructions (59.6%). Type 2 DM patients conveyed more concern about insulin injections interfering with daily activities, meal planning, and physical activity with reported higher incidence of injection site reaction, weight gain, and forgetfulness.¹⁴

The lack of optimal systems of health care delivery is another barrier to effective diabetes management. Current health care systems are poorly structured and often fragmented to deliver optimum health care for chronic conditions.¹⁵ Rates of insulin usage are generally low across Asia which is likely a result of several resource constraints: 1) low number of endocrinologists compared with the growing number of people with diabetes; 2) consultations are usually too brief to educate patients on using insulin safely and effectively; 3) shortage of diabetes educators, nurses, and diabetes care teams to provide patient support; 4) unavailability of insulin or insulin analogs in rural regions; and 5) insufficient coverage of longer-acting insulin analogs, syringes, needles, glucometers, and glucose test strips by medical insurance or public subsidies.¹¹ Other identified healthcare system factors in our study were costs of insulin, inadequacy of resources as well as inaccessibility of medical assistance from healthcare facilities or hospitals should there be any problems from titration of insulin.

For psychological/social factors, glycemic goals may not be met when patients are not adherent to lifestyle changes and pharmacologic treatment regimen. A significant finding in this study was the lack of knowledge of the subjects on proper titration of insulin. More than half (53.5%) maintained their initially prescribed dose of insulin, and claimed to have no knowledge as to how they should have titrated or adjusted their insulin. However, upon review of charts, 21 out of the 23 patients who claim to have no knowledge of insulin titration were actually taught by their attending physicians. The others who were knowledgeable about titration but still opted not to comply, do so because of fear of side effects and lack of confidence. In a survey of primary care physicians, 29 out of 125 cited that patient nonadherence to nonpharmacologic and pharmacologic therapy as well as lack of patient motivation were considered as significant obstacles to achieving optimal diabetes care.¹⁶ A systematic review on adherence citing retrospective analyses showed that adherence to insulin therapy among patients with type 2 DM ranged from 62% to 64% which was even lower compared to adherence to prescribed oral antidiabetic

agents.¹⁷ It has also been reported that more patients with type 2 DM believe that insulin has an overall negative effect on their health and that they feel worse after taking insulin.¹⁴

Clinical practice guidelines for dose increments and frequency of titration for basal insulin vary between countries.^{18,19} The Philippine Practice Guidelines on the Diagnosis and Management of Diabetes Mellitus 2014 does not actually specify a standardized algorithm for titration as response depends on the individual patient's metabolism and the type of insulin taken.²⁰ Despite the lack of standardized algorithm, certified diabetes educators are available during outpatient visits and prior to hospital discharge to provide patient education on insulin administration and titration. However, most patients still depend on their doctors for subsequent titration of insulin doses.¹¹ Importance of constant communication and proper education of patients cannot be overemphasized. The limitation of our study is that there was no cohort evaluation done on the side of the healthcare provider about the specific details on how the physician educated the patient with regards to insulin titration and how long the instructions were done. Future studies may be done to address this issue.

Conclusion

Lack of income or financial support, fear of insulin injection and its side effects, high cost of insulin, inaccessibility of medical assistance from healthcare facilities, negative attitude/fear of titration, and difficulty complying to lifestyle changes were some of the identified factors leading to poor adherence to the titration of once-daily basal insulin in this study. Good, constant communication between the patient and the doctor appears to improve adherence to insulin dose titration. Future studies may adapt the themes and concepts identified to improve adherence to titration of once-daily basal insulin among patients with type 2 DM.

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