RESEARCH ARTICLE

Diabetes Management

Evaluating a nurse-led insulin tele-titration program on diabetes control in primary care

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Abstract

Objectives: Primary care nurses have been titrating insulin doses through weekly telephone calls based on patients' home glucose monitoring records. This study aims to evaluate the benefits of a nurse-led insulin titration program on diabetes control, specifically assessing improvements in glycaemic control over time. As a secondary aim, this study will also determine if clinical indicators, patient demographics, insulin dose and quantity of calls are predictors of HbA1c improvement in this nurse-led tele-titration program.

Methods: A purposive sampling of 193 patients were enrolled into the program from May to December 2021. Repeated-measures ANOVA test was conducted to determine if mean HbA1c differed significantly across four time points (baseline, 3, 6, 9 months). Multiple linear regressions and correlations were used to compute which predictor (gender, ethnicity, insulin type, insulin dose, Type 2 Diabetes (T2DM) duration, age and those with optimal and suboptimal clinical indicators) has the highest bivariate correlation with the dependent variable (HbA1c improvement).

Results: Repeated-measures ANOVA test found that mean HbA1c differed significantly across the four time points ($p<0.001$). Linear regression models revealed 14.8% to 22.2% variation of HbA1c improvement, and is useful in explaining HbA1c improvement for all time points ($p<0.002$) except for the 6 to 9-month time point. There was no independent variable which was able to consistently significantly predict HbA1c improvement at 9 months. This study also found significantly more HbA1c reduction for patients on lower total daily doses of insulin ($p<0.01$).

Conclusion: Significant improvements in HbA1c over time reaffirmed effectiveness of nurse-led telephone consultations for optimising glycaemic control for patients on insulin. Since there are no consistently significant predictors for HbA1c improvement in this program, all eligible patients can potentially benefit from enrolment. Additionally, study findings also suggest that enrolment should be considered for patients at lower total daily doses of insulin. Further studies should explore the use of a control group to more accurately isolate the benefits of the nurse-led insulin tele-titration program for evaluation.

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KEYWORDS

- type 2 diabetes
- nurse-led insulin titration
- insulin
- teleconsult

Introduction

Background and literature review

In 2014, there were 440,000 diabetics in Singapore and this number is set to rise to 1 million by 2050 [1]. It is estimated that about 1 in 3 Singaporeans who have diabetes have suboptimal glucose control and are at a higher risk of diabetes-related complications [2]. Poor control of diabetes can lead to serious complications such as stroke, heart attack and kidney failure and should be mitigated where possible.

The Joint Asia Diabetes Registry has estimated that around 18.4% of those diagnosed with diabetes are treated with insulin [3]. Research has shown that it can take up to a few years to intensify insulin therapy to reach therapeutic dose and many continue to remain on insulin doses that are inadequate to achieve optimal diabetes control [4]. In view of such a gap, there is a need to improve insulin management such that diabetes can be more effectively managed.

A study done by Blackberry found that nurses who have been trained in insulin management and titration were effective in helping patients to titrate insulin to improve diabetes control [5]. In more recent studies, healthcare providers have been able to make use of technological advances such as using virtual consultations including phone and video calls as well as phone applications to improve the care of patients on insulin. A review conducted by Tchero, of 42 randomised controlled trials, demonstrated that patients in the telemedicine group have significantly higher reduction in mean HbA1c (Hedges'g=-0.37, $p<0.001$) [6]. Similar findings were noted in studies conducted by Levy where the intervention group with access to telephone calls for insulin titrations conducted by nurses saw a greater percentage of patients reaching their optimal insulin dose as compared to the control group [7,8]. More recently, Lemelin, found that when telemedicine was used by nurses to make adjustments in insulin therapy, patients experienced a significant decrease in HbA1c levels as seen in the intervention group compared to that of the control group (-0.61% and -0.06%, $p=0.048$) [9]. Moreover, this difference was sustained at both 3 and 6 months into the study. In addition, other studies have found that aside from improving diabetes control, the use of such mobile health technology can also improve patient satisfaction with diabetes treatment and have benefits that extend beyond clinical markers alone [10].

Literature searches show that there is a paucity of similar studies done within the Singapore context. Primary care nurses in Singapore have been using analogous interventions to optimise diabetes control for patients on insulin. Although the use of nurse-led insulin teletitration has been ongoing both in the primary and tertiary settings and has been anecdotally been known to be beneficial, there has not been any studies evaluating its effectiveness in improving diabetes control for patients.

Research questions and hypotheses

In view of this identified gap in the literature, this study aims to evaluate the use of a nurse-led Insulin Tele-Titration program for patients with Type 2 Diabetes (T2DM) on their improvement in glycaemic control over time. It is hypothesised that patients enrolled in this program will have a clinically and statistically significant HbA1c improvement overtime. The secondary aim of this study was to determine if clinical indicators, patient demographics, total daily dose of insulin and quantity of calls are predictors of HbA1c improvement in the nurse-led tele-titration program. It is hypothesised that clinical indicators, patient demographics and quantity of calls will be significant predictors of HbA1c improvement in this program. Additionally, it is hypothesised that there will also be a significant relationship between total insulin dose and HbA1c improvement.

Materials and Methods

Study design and participants

To meet the study aims, a retrospective pretest-posttest study using data from May 2021 to December 2021 was conducted. Data used in the study was obtained from the participant's existing clinical health records and no additional information was collected in addition to usual care. The study site included 7 different primary healthcare centers in Singapore (polyclinics), each with its own unique pool of patients. Relevant clinical data was collected at the time of enrolment into the program and at 3, 6 and 9 months after enrolment. It was mandatory for all nurses involved in the insulin tele-titration program to undergo a structured training course and be certified competent before conducting this program.

All participants enrolled in the nurse-led insulin tele-titration program between May to December 2021 were included into the study. Additionally, to ensure that the full benefit of the program is conferred on the participants enrolled in the study, only participants who has a minimum of

4 teleconsultations with the trained nurses during the study period were included in the study. This study excluded participants who were considered to be more medically vulnerable and whom may require a more individualised protocol for insulin management. This group of patients excluded those who were age less than 21 years old or more than 80 years old, have type 1 diabetes, and who are pregnant at the time of enrolment. Patients who were previously recruited into the insulin titration program were also excluded from the study as previous enrolment might confound the ability to assess the full benefits of this program.

Purposive sampling was used to identify participants for this study. A review of records from the database identified 326 patients who were enrolled into the insulin titration program during the study period. After considering the inclusion and exclusion criteria, only 193 records were included in the study.

■ Visits and procedures of insulin tele-titration program

During the recruitment period, doctors will assess patient's willingness and suitability to be included in the insulin tele-titration program. If the patient is to be recruited into the program, the trained nurse would then review the patient on the same day to provide education on insulin management, glucose monitoring and lifestyle modification. Contact details and timing of the teleconsultation appointment are confirmed with the patient or their caregiver by the nurse on the same day.

The first teleconsultation after recruitment is conducted between 1-2 weeks after the time of enrolment. During a teleconsultation, the nurse will engage either the patient or their caregiver to assess medication and insulin compliance, hypoglycaemia, home glucose readings and also the patient's lifestyle. When there is a need to optimise insulin therapy, the insulin dose will be adjusted according to the institution's insulin titration protocols or in consultation with the primary care physicians. **TABLE 1** provides a summary of the insulin titration protocol used in this study [11]. Subsequent teleconsultations were typically scheduled between 1-2 weeks later to review the home glucose monitoring readings and the patient's response to the insulin changes made during the previous phone call. If knowledge gaps are identified regarding lifestyle or diabetes management, the trained nurse will provide education to both patient and caregiver on the phone. These teleconsultations will be continued until the next scheduled review in the clinic.

TABLE 1: Insulin titration protocol.

Basal insulin protocol			
Pre breakfast	**Titration**		
>7 mmol/L	Increase 2 units ON		
<5 mmol/L	Decrease 2 units ON		
Pre mixed protocol			
Pre breakfast	**Titration**	**Pre-dinner**	**Titration**
>7 mmol/L	Increase 2 units ON	>7 mmol/L	Increase 2 units OM
<5 mmol/L	Decrease 2 units ON	<5 mmol/L	Decrease 2 units OM
Basal-bolus protocol			
Pre breakfast	**Titration**	**2 hours post meals**	**Titration**
>7 mmol/L	Increase basal by 2 units	>10 mmol/L	Increase pre-meal dose by 2 units
<5 mmol/L	Decrease basal by 2 units	<7 mmol/L	Decrease pre-meal dose by 2 units

On the day of the next clinic review, the primary care physician will review the patient and their latest HbA1c levels to determine if the patient should continue with the insulin tele-titration program. If it was decided by both the primary care physician and patient to continue with the program, regular teleconsultation by the trained nurses were continued.

■ Data analysis

Hypothesis testing was conducted using the appropriate statistical tests. To test the primary hypothesis a repeated measures ANOVA analysis was conducted based on data from the 4 time points in this study. Pairwise analyses were used to compare the HbA1c means during different time points to determine if there was a significant improvement in mean HbA1c. To test the secondary hypothesis, multivariate models of regression were run to determine which of these independent variables including patient demographics, clinical indicators and total calls had the highest bivariate correlation with the dependent variable which was HbA1c improvement. 3 models were run for HbA1c improvement from baseline to the 3 subsequent timepoints in this study. Additionally, Spearman's rank correlation coefficient was calculated to assess the strength and direction of the association between total insulin dose and HbA1c

improvement. To ensure reliability and validity of the findings, appropriate assumptions and conditions for each of the statistical analysis tests was verified. All statistical analyses were performed using IBM SPSS, version 29. Significance in this study was defined as $p<0.05$.

■ Ethical considerations

Approval for this study was obtained from the National Healthcare Group Domain Specific Review Board. In addition, before commencing the review of clinical retrospective data, approval was sought from the institution data protection board. Since only retrospective clinical data was used, waiver of consent was approved for this study. Clinical data extracted from the existing records was de-identified and kept anonymous by the research team. Only clinical data relevant to the study were retrieved and this includes information such as participant demographic information, duration of diabetes, insulin types and dosage and laboratory results. As an added data protection measure, the data collected for this study was de-identified and stored in a password protected excel spreadsheet only accessible by researchers and no re-identification took place after data collection and analysis.

Results

A total of 193 patient records were included in this study. The baseline demographic and clinical characteristics of the participants are summarized in **TABLE 2** below. There was an almost equal number of males and female included in the study. Most of the study participants were Chinese and aged between 61 to 80 years old. More than 80% of the study participants had diabetes for more than 5 years and more than half the participants included in this study were on the basal insulin only regime.

TABLE 2: Participant demographics (N=193).

Demographics	Values
Gender, n (%)	
Male	97 (50.3)
Female	96 (49.7)
Ethinicity, n (%)	
Chinese	101 (52.3)
Malay	62 (32.1)
Indian	24 (12.4)
Others	6 (3.2)
Age n (%)	
21-40	12 (6.2)
41-60	81 (42.0)
61-80	100 (51.8)
Duration of T2DM (years), n (%)	
1 or less	16 (8.3)
2	12 (6.2)
3	4 (2.1)
4	5 (2.6)
5 or more	155 (80.3)
Insulin types, n (%)	
Basal	101 (52.3)
Basal-bolus	30 (15.5)
Pre-mixed	62(32.1)

To assess the primary aim of the study, a repeated-measures ANOVA test was conducted and it found that mean HbA1c differed significantly across four time points ($F(1.95, 173)=64.23$, $p<0.001$, multivariate partial eta squared=0.27). Pairwise analyses indicated that mean HbA1c (M) improved significantly ($p<0.001$) from baseline (M=9.94, SD=1.86), at 3 (M=8.83, SD=1.48), 6 (M=8.67, SD=1.51) and 9 months (M=8.67, SD=1.57) (**TABLE 3**). Mean HbA1c difference between 3 months and both 6 and 9 months was also significant ($p<0.05$). However, no significant difference was seen between mean HbA1c at 6 and 9 months ($p=0.927$). The percentage of patients with HbA1c 7.0% or less also improved continually across the 4 time points with 3.1% at baseline, 9.3% at 3 months, 15.0% at 6 months and 17.1% at 9 months.

To evaluate the secondary aim of the study, multiple linear regression models were run to evaluate HbA1c improvement from baseline and 3 months, 6 months and 9months (**TABLE 4**).

Overall models were able to explain 14.8%-22.2% variation of HbA1c improvement, and it is significantly useful in explaining HbA1c improvement at all-time points ($p<0.002$) except for between 6 to 9 months. The R-square value indicates that 21% of the variance in HbA1c is explained by the predictor variables. At 3 months (Model 1) and 6 months (Model 2), multiple R shows a moderate correlation between the predictor variables and HbA1c ($R>.45$). At 9 months (Model 3), multiple R ($R=0.39$) showed a weak correlation between the predictor variable and HbA1c.

TABLE 3: Pairwise comparisons of HbA1c at different timepoints.

					95% Confidence for difference	
(I) Time	**(J) Time**	**Mean difference (I-J)**	**Std error.**	**Sig.**	**Lower bound**	**Upper bound**
1	2	1.11	0.115	0.001**	0.879	1.33
	3	1.34	0.142	0.001**	1.06	1.62
	4	1.34	0.146	0.001**	1.06	1.63
2	3	0.23	0.08	0.005*	0.072	0.388
	4	0.237	0.098	0.017*	0.043	0.43
3	4	0.007	0.075	0.927	-0.142	0.155

Note: ** p-value<0. 001; * p-value<0.05

TABLE 4: Linear regressions to determine predictors of HbA1c improvement.

Model	F (x, y)	F	p value	R	R2	R2 adjusted
3 months	12,155	3.38	0.001**	0.456	0.208	0.146
6 months	12,143	3.39	0.001**	0.471	0.222	0.156
9 months	12,149	2.16	0.016*	0.385	0.148	0.08

Note: ** p-value< 0. 001; * p-value<0.05

TABLE 5 shows the results of the multiple linear regression conducted to determine if clinical indicators, patient characteristics and total quantity of calls made by the nurses are predictors of HbA1c improvement in the nurse-led teletitration program. At 3 months, normal DBP had the greatest influence on HbA1c (ß=0.19, p<0.05) followed by Normal BMI (ß=0.18, p<0.05) and LDL (ß=0.17, p<0.05). At 6 months, age (ß=0.20, p<0.05) and ethnicity (ß=0.18, p<0.05) was found to be predictive of HbA1c improvement. However, none of the independent variables were found to be predictive of HbA1c improvement at 9 months.

TABLE 5: Multiple linear regression model results.

Characteristics	p value		
	Model 1 (3 months)	**Model 2 (6 months)**	**Model 3 (9 months)**
Gender	0.288	0 .547	0.708
Age	0.077	0.019*	0.166
Ethnicity	0.177	0.020*	0.128
T2DM Duration	0.213	0.055	0.082
Normal Body Mass Index (BMI)	0.019*	0.084	0.215
Normal Systolic Blood Pressure (SBP)	0.579	0.733	0.659
Normal Diastolic Blood Pressure (DBP)	0.012*	0.229	0.794
Normal High Density Lipoprotein (HDL)	0.385	0.561	0.640
Normal Low Density Lipoprotein (LDL)	0.023*	0.116	0.419
Normal triglyceride	0.489	0.533	0.259
Insulin type	0.568	0.673	0.800

Note: * p-value<0.05

Spearman's rank correlation was used to find out the direction and significance of the relationship between total insulin dose and HbA1c improvement after 3, 6 and 9 months. As seen in TABLE 6, there was a small positive correlation between HbA1c improvement and total insulin dose at all-time points (r=0.19, n=193, p=0.007; r=0.25, n=193, p=0.002; r=0.23, n=193, p=0.001). Since a larger negative value represented increased HbA1c reduction, significantly more HbA1c reduction was observed in patients with lower total daily doses of insulin.

TABLE 6: Spearman's rank correlations between total insulin dose and HbA1c improvement.

Spearman's rank correlations	3 Months	6 Months	9 Months
rs	0.196	0.25	0.231
p-value	0.007*	0.002*	0.001*

Note: * p-value<0.05

Discussion

Findings from this study support the anecdotal evidence that patient enrollment into the nurse-led insulin titration program improves HbA1c overtime. Other similar studies evaluating the use of nurse-led telemonitoring interventions aimed at improving diabetic control has also found that HbA1c improves overtime with the use of such interventions and programs [12-14]. This finding could be expected due to increased opportunities for nurses to provide education and support for patients enrolled in the program as compared to usual care. Furthermore, insulin doses are also titrated more frequently with weekly or fortnightly phone calls in comparison to usual care where insulin doses are only titrated during clinic visits which are usually spaced much further apart.

Additionally, our study has identified that HbA1c improvement was most evident at the initial point of enrolment into the program i.e. between baseline to 3 months. One possible reason for the more pronounced improvement in HbA1c in the first 3 months could be due to insulin doses being optimised more quickly during the initial point of enrollment as there are more opportunities for the patient's significant care gaps to be addressed. As the patient's care and learning gaps are addressed, improvements in HbA1c are expected to be less pronounced as they continually move closer to the HbA1c targets. Furthermore, patients enrolled into this program are given constant feedback and education on diabetes self-management over the phone by the nurses. This could have resulted in increased self-care awareness and patient empowerment which was most evident at the initial stage of enrollment into the program and self-management skills plateau overtime as each patient's learning gaps are filled.

While the study data indicated HbA1c improvements from baseline, it was observed that HbA1c levels demonstrated a statistically significant improvement from baseline to 3 months as well as between 3 months and 6 months. However, data also revealed that there was no significant improvement in the mean HbA1c levels between 6 and 9 months after the intervention. This could be due to challenges in sustaining continual HbA1c improvements similarly observed in previous studies [13,15]. Although initial motivations could be high to optimise glycaemic control, this might become less sustainable in the long run [16].

While there were some significant associations between the variables and HbA1c improvement, the relationships were found to be weak and inconsistent in strength. Other studies have also tried to study the significance of these relationships and found similar inconsistencies in using these variables to predict HbA1c improvement [17-19]. Based on the current study as well as others studying the relationship between these variables and HbA1c improvement, we can see that these factors should not be used solely to predict the long-term impact on HbA1c for patients enrolled in these programs. Since there are no clearly predictive factors as to which groups of patients will clearly benefit, we should consider that all groups of patients have an equal opportunity to benefit from enrolment and should be offered this program where applicable.

The finding that larger HbA1c improvement was seen in patients with lower total daily doses of insulin is congruent with what we know from the pathophysiology of diabetes where is it likely that higher doses of insulin are needed by patients with higher body weight who might exhibit more insulin resistance [17]. One other possible reason for this study finding could be that higher insulin doses are often prescribed to patients with a longer duration of diabetes, associated with further decline in pancreatic beta cell function and poor glycaemic control. [17, 20,21].

Limitations

While the present study provides insight into the benefits of the nurse-led insulin tele-titration program on diabetes control, there are several limitations that should be considered when interpreting the results. Firstly, there was a lack of control group in this study. As this is a retrospective study, it was not possible for the study team to obtain a list of patients who were eligible for enrollment into this program but declined, hence it was challenging to identify a control group in this study. Future studies are recommended to factor in a control group to provide more evidence on the benefits of the nurse-led insulin tele-titration program in comparison to usual care.

Another limitation in this study was that this program was delivered by a pool of nurses across 7 polyclinics and hence it was not possible to account for the variations in care delivery. However, it was compulsory for all nurses involved in carrying out this intervention to undergo a telemedicine course

by the Ministry of Health and this could assist to mitigate practice variations between different nurses.

Although there were limitations in this study, this does not negate the significance of the findings on the impact of the nurse led insulin tele-titration on improving glycaemic control. Addressing these limitations can build upon the present study findings and contribute to a better understanding on interventions used to improve glycaemic control for patients on insulin.

Conclusion

The nurse-led Insulin Tele-Titration Program was effective in helping patients on insulin improve HbA1c up to 6 months later but its sustained effectiveness beyond that needs further scrutiny and strategic planning. Since there are no consistent and significant predictors for HbA1c improvement in this program, this would lead us to conclude that all eligible patients have similar opportunities to benefit from enrolment and should be enrolled in the nurse-led insulin tele-titration program where possible. Since this study also found that patients on lower total daily doses of insulin showed significantly more improvement in HbA1c, enrolment in the program should be considered even at lower total daily dose of insulin to optimise the benefit of the program. In conclusion, while acknowledging its limitations, the results of this study provide valuable insights on the benefits of the nurse-led insulin tele-titration program in improving glycaemic control for patients on insulin and offer opportunities for further investigation.

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