Empowerment and Motivation in Subjects with Reduced Medication Adherence and Poor Diabetes Control — A Pilot Study

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Abstract

Aims: Reduced medication adherence contributes to suboptimal control and poor clinical outcomes. Appropriate interventions improving medication adherence are inadequately established. This pilot-study aimed to increase self-management capabilities in patients with type 2 diabetes with poor glycemic control and reduced medication adherence.

Methods: In patients with HbA1c ≥64 mmol/mol (8.0%), we assessed medication adherence for oral hypoglycemic agents, GLP1 analogues, aspirin, and lipid lowering drugs using proportion of days covered using a prescription register. Medication adherence below 80% (for at least one drug) was found in 61% of patients; these were either offered the intervention or served as controls. Change in HbA1c at the end of the intervention and after six months, in addition to medication adherence during these 6 months was evaluated. The intervention consisted of 3 individual consultations with focus on medication adherence and self-selected goals using a participatory approach with dialogue tools.

Results: A total of 22 patients accepted to participate and 19 completed the intervention, 22 served as controls. Baseline HbA1c in participants was 70.3 ±8 mmol/mol (8.6%) compared to 71.5 ±13 mmol/mol (8.7%) in controls (p=0.71). For participants the median decline in HbA1c was 2 (IQR -1 to 3) mmol/mol (0.2%) during the study compared to an increase of 2.5 (-2 to 4.5) mmol/mol (0.2%) (p=0.047) in controls. Improvement in HbA1c was achieved in 68% of participants and 35% of controls (p=0.04). No significant difference in medication adherence (p=0.60) was found.

Conclusion: In our pilot study HbA1c improved, but not medication adherence. Concordant with the patients’ own goals primarily focused on improving glycaemia.

ABBREVIATIONS

T2DM: Type 2 diabetes; PDC: Proportion of days covered; WHO: World Health Organization

INTRODUCTION

The Steno 2 study proved the importance of multifactorial intervention for patients with type 2 diabetes (T2DM) by lifestyle intervention targeting diet, smoking and exercise and pharmaceutical intervention affecting glucose, blood pressure, lipids and coagulation [1]. Consequently, the majority of patients with T2DM are prescribed multiple medications, and some of these, are used for non-symptomatic conditions. These treatments are perpetual and due to disease progression, the regimen is frequently intensified over time.

Medication adherence is the extent to which patients take medications as prescribed by their health care providers [2].

A recent meta-analysis found only 60% of patients to have good (≥80%) adherence to cardiovascular medications [3]. In agreement, data from our center revealed that only 59% of patients prescribed metformin had good adherence [4]. Generally, around half of medication prescribed for long-term treatment of chronic disease is used as prescribed [5,6].

Medication non-adherence for oral hypoglycemics, antihypertensives, and statin in patients with diabetes is linked to higher hospitalization rates and mortality [7,8]. In contrast, good medication adherence, even to placebo (the healthy adherer effect) may improve outcome [9].

Instead of the overall healthy behavior suggested in adherent patients, we hypothesized that reduced medication adherence reflects poor self-management capabilities, and that it can be used as an indicator hereof. Thus, decreased medication adherence may not only identify patients who have problems in regard to taking their medication, but also help to identify patients in need of a more general support.

The World Health Organization (WHO) states that increased adherence to already prescribed treatment, could have a higher impact on health than developing new treatment options [10]. Many factors linked to reduced medication adherence are already identified [2] and although attempts to increase medication adherence have been numerous and of different design, the results are inconsistent [5,11]. Thus, knowledge about the most appropriate intervention form and content is lacking, leaving an unmet need to further explore methods towards improving medication adherence.

Our pilot-project “Empowerment, Motivation and Medication Adherence” (EMMA) aims to improve HbA1c and medication adherence in patients with T2DM who have poor glycemic control and reduced medication adherence. The intervention is designed as an individual consultation process, which provides systematic person-centered support by a participatory, dialogue-based and goal-oriented approach addressing self-management capabilities with focus on the challenges of using medication.

MATERIALS AND METHODS

This pilot study was undertaken in order to develop and test a feasible program in daily clinical practice. The primary endpoints were changes in HbA1c during the study period and after 6 months of follow-up. Secondly, changes in medication adherence during follow up compared to the year before inclusion. Furthermore, medication regimen discrepancies between patients and medical record were assessed, as well as barriers of medication adherence. In addition, the patient’s own treatment goals, and means to attain these were addressed.

Medication adherence

Using Medicine Profile, a database which contains information on all medications dispensed from Danish pharmacies, the actual quantity and dosage of medicine bought was compared to the concurrent doses prescribed in the electronic patient records. Medication adherence was assessed as proportion of days covered with sufficient medication (PDC). Thus, if patients were in possession of adequate medication during 80 days in a 100 day period, the PDC was 80%. A PDC < 80% was classified as reduced medication adherence as recommended and most commonly used cut-off [3,12].

PDC for oral anti-diabetic agents, aspirin, cholesterol lowering drugs and GLP1 analogue were assessed for the year 2010, prior to inclusion. The mean of these represented baseline medication adherence. Follow-up PDC was calculated for a 6 month period after the last study visit. For controls, PDC was assessed for a 6 month period starting the 1st day of the third month after baseline. For all PDC calculations, we considered the last medicine purchase prior to the start date of the study. As individual adjustments and dosage changes in insulin and antihypertensive medication often are more frequent than this method can capture, we chose not to evaluate medication adherence for these drugs.

Study population

From a total of 617 patients with T2DM affiliated to one of three patient care teams in the outpatient clinic at Steno Diabetes Center, we identified 227 patients with an HbA1c ≥ 64 mmol/mol (8.0%) in January 2011. Only 172 native and self-sufficient patients were retained. Medication adherence for these drugs. As individual adjustments and dosage changes in insulin and antihypertensive medication often are more frequent than this method can capture, we chose not to evaluate medication adherence for these drugs.

The intervention

The intervention consisted of three interconnected one-to-one consultations and a phone call with the same health care professional, either nurse or doctor. Figure 1 demonstrates the agenda and timing of the sessions. To enhance reflection, dialogue and participation, and to promote informed patient decisions regarding self-management, different tools and exercises were used. These included visual and tangible materials such as pictures, peer quotes, questions, illustrations and worksheets. The flow of the consultation process was inspired by a ‘five-step empowerment model of goal-setting’ [13], health education principles [14], and ‘safe and effective use of medicine’ model. The use of tools was inspired by ‘the balancing person’ model and cultural probes methodology [15]. The exercises and dialogue tools, their developmental background and the implementation process has previously been described [16]. Below selected exercises are described briefly.

The patients were encouraged to bring their medication to the consultation (some only brought a list). The name, dose and timing were then compared to prescribed medication in the electronic patient record. All discrepancies were noted and
resolved. Occasionally, follow-up phone calls were needed post-session to clarify details.

Specific challenges with regard to T2DM and the medication regimen were explored by selection from 36 cards. The cards had pictures and quotations illustrating different challenges that were categorized attributing to WHO’s five dimensions of adherence (Figure 2) [10]. If more than five cards were chosen to be relevant, a reselection of the three most important cards was performed. These formed the basis for subsequent dialogue, exercises and goal-setting process.

The patients were guided to reflect upon and identify a SMART goal (Specific, Measurable, Attainable, Realistic and “Time-limited”) based upon their challenges, resources and wishes discussed during the sessions. Specific actions, deadlines, possible barriers and support options were deliberated.

Data collection and analysis

In addition to written exercises, the sessions were audio recorded and an observer was present.

For controls, baseline was defined as the first visit to the outpatient clinic after the study was initiated. Follow-up started 81 days after baseline (participants’ mean study duration) and lasted six months. As our study was a quality improvement study, we relied on routine measurements to compare the groups.

The number of medication discrepancies and causes were reported based on written material from exercise and alterations in medication lists. Barriers of medication adherence were assessed based on the compiled list of quotations as the number of selected cards per patient (from primary selection) within each dimensions of adherence [10].

The goals were divided into three categories, whereas the planned action steps were covered by five categories (Figure 3). Some patients had multiple goals. The number of patients that improved HbA1c at end of study compared to baseline, within each goal and action, was reported (Figure 3).

Statistics

For comparison of changes in clinical variables we used Wilcoxon signed rank test to diminish the effect of outliers. Improvement in HbA1c (yes/no) was also examined as dichotomous variable applying Chi-Square test. The three patients that dropped out were excluded from analyses. Medication adherence was assessed as the mean of all PDC for prescribed medications of interest, individually for the hypoglycemic drugs, and finally as the number of non-adherent drugs (PDC<80%) before (during 2010) the intervention, and during the six month follow-up period. For these analyses and comparison of groups at baseline we applied student’s t-test. For database management and statistical analysis.
analysis, we used SAS software, version 9.2 or SAS Enterprise Guide 4.3 (SAS Institute, Cary, NC). Statistical significance was an α-level < 0.05 on two-sided tests.

RESULTS

There were three dropouts. These were due to cancer treatment, repeated hospital admittances and participation in a fulltime life-style intervention. Nineteen participants completed the study. Only two visits had to be rescheduled due to non-attendance. Baseline values are shown in Table 1 and results in Table 2.

At baseline HbA1c was 70 ±8 (8.6%) for the participants compared to 72 ±13 (8.7%) mmol/mol for controls (p=0.71). Mean medication adherence was 66 ±32 and 70 ±12 (p=0.63), respectively. Patients who declined to participate/or did not respond to our enquiry showed a tendency towards higher HbA1c (76 ±16 (9.0%); p=0.12) and lower medication adherence (64 ±25; p=0.81).

At baseline, participants were non-adherent for a mean ±SD of 1.2 ±0.7 prescriptions whereas the same number was 1.3 ±1.0 at follow up. The corresponding numbers for the controls were 1.6 ±0.7 and 1.5 ±1.0. Change in number of prescription in non-adherence did not differ between groups (p=0.65). Also, there were no significant changes in total medication adherence which increased by 1% from 66 ±32% for participants and decreased 3% from 70 ±12% for controls (p=0.60). For hypoglycemic drugs; the mean medication adherence improved 5% for participants compared to a decline of 4% for controls (p=0.46).

For the participants, HbA1c fell from 70 [64-78] mmol/mol (8.6%) to 68 [65-75] mmol/mol (8.4%) during the study (p=0.09). The median decline in HbA1c during the study was 2 (-1 to 3) mmol/mol (0.2%) for participants compared to an

![Figure 3 Goals and plans](image)

Table 1: Baseline status for participants and controls.

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Participants</th>
<th>Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, (years)</td>
<td>68.3 (5.5)</td>
<td>64.6 (12.5)</td>
<td>0.22</td>
</tr>
<tr>
<td>Male sex, (%)</td>
<td>68</td>
<td>68</td>
<td>0.99</td>
</tr>
<tr>
<td>Adherence total, (%)</td>
<td>66.1 (31.7)</td>
<td>69.9 (11.6)</td>
<td>0.63</td>
</tr>
<tr>
<td>Adherence hypoglycemic drugs, (%)</td>
<td>73.1 (18.5)</td>
<td>73.6 (23.7)</td>
<td>0.95</td>
</tr>
<tr>
<td>Non-adherent prescriptions, (nr)</td>
<td>1.2 (0.7)</td>
<td>1.6 (0.7)</td>
<td>0.09</td>
</tr>
<tr>
<td>HbA1c (mmol/mol)</td>
<td>70.3 (8.0)</td>
<td>71.5 (13.4)</td>
<td>0.71</td>
</tr>
<tr>
<td>Hba1c, (%)</td>
<td>8.6 (0.7)</td>
<td>8.7 (1.2)</td>
<td>0.71</td>
</tr>
<tr>
<td>Weight, (kg)</td>
<td>93.3 (15.6)</td>
<td>95.2 (21.3)</td>
<td>0.74</td>
</tr>
<tr>
<td>Albumin/creatinine ratio, (mg/g)</td>
<td>48 [16-175]</td>
<td>11 [5-51]</td>
<td>0.05</td>
</tr>
<tr>
<td>Total cholesterol, (mmol/l)</td>
<td>4.8 (1.5)</td>
<td>4.5 (1.1)</td>
<td>0.50</td>
</tr>
<tr>
<td>HDL (mmol/l)</td>
<td>1.2 (0.3)</td>
<td>1.2 (0.3)</td>
<td>0.54</td>
</tr>
<tr>
<td>LDL (mmol/l)</td>
<td>2.0 [1.5-3.1]</td>
<td>2.0 [1.7-2.4]</td>
<td>0.89</td>
</tr>
</tbody>
</table>

Abbreviations: High density Lipoprotein; HDL; Light density Lipoprotein; LDL.
increase of 2.5 (-2.0 - 4.0) mmol/mol (0.2%) in the control group (p=0.32). From start to end of follow-up was 4.0 (-6.0 - 7.0) mmol/mol (0.4%) versus 0.0 (-8.0 - 7.0) mmol/mol (0%) for participants and controls, respectively (p=0.32). From start to end of the intervention 68% of the participants and 35% of the controls improved their HbA\textsubscript{1c} (p=0.04). In the period from start to end of the follow-up, HbA\textsubscript{1c} improved for 63% of participants compared to 48% of controls (p=0.04), whereas 58% of participants had lower HbA\textsubscript{1c} at both times (versus baseline) compared to 18% of controls (p=0.01).

For 11 (50%) participants, we found discrepancies between the electronic record and the patient-reported medication regimen. This inconsistency was often multi-causal: discontinuation of the medication (n=6), prescription from external sources (e.g. other hospitals or GP) (n=6), inconsistency in strengths or frequency of dosage (n=5), which were in three cases based on misunderstandings. In addition, 11 patients reported various levels of non-adherence with oral medication and seven with insulin. Furthermore, eight patients had resistance towards receiving or increasing their insulin dosage (all but one used insulin).

The distribution of barriers of medication adherence in accordance to WHO’s “five dimensions of adherence” [10] is shown in Figure 2. All dimensions were represented broadly, emphasizing the multifactorial character of non-adherence. Moreover, many patients chose several cards within the same category highlighting the significance of the individual patient’s challenges. The most prevalent card, chosen by 14 patients, stated, “I do not feel sick”. Furthermore, 14 different patients chose cards expressing either thoughts of medication being harmful, or doubts about the beneficial effect.

Sixteen patients chose goals directly regarding glycemic control, six wanted to lose weight and six had other goals, of which half considered quality, quantity, and timing of meals. Figure 3 shows number of patients that improved HbA\textsubscript{1c} within each goal-category, and by which means. Notably, all four participants that chose to address medication adherence, improved their HbA\textsubscript{1c}.

Details on the implementation and feasibility will be published (in preparation). It was feasible to conduct the program as planned, the tools were easy to use, and with practice the visits were performed within the allotted time. The patients gave the program a high rating and 95% felt that they profited from participating.

**DISCUSSION**

We succeeded in conducting the pilot study as planned, to identify barriers of medication adherence, develop self-defined goals and plans, with an intervention program of only three clinical visits and a phone call. Attendance was good, and dropouts were primarily due to serious disease. Although the aim was not to demonstrate significant outcome results, these were achieved for changes in HbA\textsubscript{1c} (at end of study) in comparison with controls.

Our study is unique in several ways. We targeted patients in poor glycemic control with medication adherence below 80% for at least one drug based on the prescription register. We hypothesized that a reverse “healthy adherer effect” existed, such that patients with reduced adherence also experience other self-management challenges and thus would benefit from an intervention with an open and broad approach targeting individual patients’ needs and resources. Finally, as the patients defined their own goals, the program is widely applicable also for other treatment targets and risk factors.

A third of all the patients with T2DM screened had HbA\textsubscript{1c} above 64 mmol/mol(8.0%) and of those 61% had medication adherence below 80%. This may have profound clinical implications and clearly demonstrates that multifactorial treatment of diabetes is often complicated; motivating patients to adhere to lifestyle advice and pharmaceutical therapy can be difficult, and treatment goals are not always reached. Furthermore, health care professionals often underestimate the extent of reduced medication adherence [17]. A recent study from our clinic showed that only 59% of patients with T2DM had medication adherence above 80% for metformin [4], similar to medication adherence for cardiovascular therapy which lies around 60% in other countries [3,18].

Another concern was that, even in a setting where patients are provided a written overview of prescriptions at each

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**Table 2:** Variable changes from baseline: The changes refer to end of follow up period, apart from those marked with *, these refer to end of study (visit 3).

<table>
<thead>
<tr>
<th>Changes during follow-up</th>
<th>Participants</th>
<th>Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total adherence, (%)</td>
<td>1.1 (23.7)</td>
<td>-2.5 (19.6)</td>
<td>0.60</td>
</tr>
<tr>
<td>Hypoglycemic adherence, (%)</td>
<td>4.5 (29.8)</td>
<td>-4.0 (33.5)</td>
<td>0.46</td>
</tr>
<tr>
<td>Non-adherent prescriptions, (nr)</td>
<td>0.1 (1.0)</td>
<td>-0.1 (1.0)</td>
<td>0.65</td>
</tr>
<tr>
<td>HbA\textsubscript{1c} (mmol/mol)*end of study</td>
<td>-2.0 [-3.0;1.0]</td>
<td>2.5 [-2.0;4.5]</td>
<td>0.05</td>
</tr>
<tr>
<td>HbA\textsubscript{1c} (%)*end of study</td>
<td>-0.2 [-0.3;0.1]</td>
<td>0.2 [-0.2;0.4]</td>
<td>0.04</td>
</tr>
<tr>
<td>HbA\textsubscript{1c} (mmol/mol)</td>
<td>-4.0 [-8.0;6.0]</td>
<td>0.0 [-7;8]</td>
<td>0.44</td>
</tr>
<tr>
<td>HbA\textsubscript{1c} (%)</td>
<td>-0.4 [-0.7;0.5]</td>
<td>0 [-0.6;0.7]</td>
<td>0.12</td>
</tr>
<tr>
<td>HbA\textsubscript{1c} improved (%)*end of study</td>
<td>64</td>
<td>35</td>
<td>0.12</td>
</tr>
<tr>
<td>HbA\textsubscript{1c} improved (%)</td>
<td>64</td>
<td>48</td>
<td>0.36</td>
</tr>
<tr>
<td>HbA\textsubscript{1c} improved (%)* at both times</td>
<td>58</td>
<td>18</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**Abbreviations:** High density Lipoprotein; HDL; Light density Lipoprotein; LDL.
visit and a systematic medication review every other year, discrepancies in the physician-prescribed and patient-reported medication regimens were present for 50% of the participants. The use of medicine substitution may play a role, as four patients reported confusion by new name and appearance of the drug. Using generic names in order and medication lists could conceivably diminish discrepancies. Equally, urging patients to evaluate the overview and bring an accurate medication list or pill boxes helps when conducting systematic medicine reviews, as patients may forget the dosage or frequency of a prescription.

Medication adherence was not assessed for insulin as we were unable to determine PDC based on long term purchase of insulin due to individual adjustments and changes in requirements. However, insulin was a much discussed topic and 11 participants optimized their insulin regimen during the intervention, which probably contributed to the significant decline in HbA1c in patients in the intervention group as compared to the controls. We did not achieve an effect on medication adherence, although the direction of change from baseline was positive.

Ruling out any effect of medication adherence is premature, as we were unable to consider all medications and not dimensioned to show significant effect on the outcomes.

As medication adherence was assessed using PDC, we cannot evaluate whether the drugs were administered at the correct time. On the other hand, PDC is an objective measure and was considered over long time, minimizing faults, including the effect of stockpiling towards the end of the reimbursement-period [19]. High concordance between pill counts and prescription claims has been reported, suggesting that those who purchase their medicine also take it [20]. However, as discrepancies in medication regimen are common, PDC could classify patients erroneously.

Our program is based on established motivational principles, and well known health behavior theories tailored to clinical setting, focusing on making an implementable program useful in the clinic. The tools were developed to focus on the patient's perspective and to make the consultations less formal. The tools enabled us to dig deeper into barriers and adherence problems than in usual consultations, and to establish rapport and trust from the very beginning. The quotations may have legitimized and given awareness of certain thoughts or feelings, which facilitated discussion of relevant barriers. The majority (14 patients) expressed distrust in their medication at baseline. Patient's health beliefs are of importance [21] and patients’ lack of trust in their medication, may obstruct adherence [22]. Similarly, attempts to improve this have shown improved outcome [23].

We demonstrated that barriers of medication adherence and glycemic control are diverse and complex. Our open approach allowed for discovery of multiple barriers, and supported the patients in addressing what they considered the most important issues; these often regarded self-management other than medication. Only four patients choose to address medication adherence, although, the program aimed to improve medication adherence. This illustrates that patients and health care professionals may have different agendas, and that directly focusing on medication adherence may not clasp the patient's interest.

Generally, attempts to increase medication adherence have not provided clear methods for general application. A few simple measures, such as abridging drug regimens or lower dose frequencies, have shown positive effects [11,24-27]. Attempts with pill boxes, cues and reminders, can help patients to take their medication, but unlikely to help patients that believe that the prescribed medication is detrimental. Approximately half of behavioral interventions were successful [28]. A recent nurse led telephone coaching intervention with similar aim as our study was not effective in reducing HbA1c [29] whereas several interventions using motivational interviewing and self-management were effective [30]. Multimodal involvements with regular follow-ups have been most successful [5,30], however these are time and cost consuming and the positive effect is often short lasting, and may not affect clinical parameters [5,11].

WHO has called for alternative approaches to increase medication adherence [10]. In this study, patients were identified through a prescription database, and health education principles and methodologies were implemented, putting the patient in centrum, with focus on their needs and wishes which we see as a prerequisite for change.

Our pilot study must be interpreted within the context of its potential limitations. First, we did a quasi-randomization based on a factor that we considered not to influence outcome (birthday). Second, the controls were identified and followed with routine examinations; they could thus be less motivated than the participants who were asked to participate. However, asking the controls could increase their awareness of medication adherence and glycemic control, and thereby introduce risk of bias.

We demonstrated that reduced medication adherence is extensive among poorly regulated patients with T2DM. A simple program to increase self-management capabilities, focusing on medication use and self-selected goals improved HbA1c in these patients. These positive findings have to be substantiated in future well powered studies.

CONCLUSION

We demonstrated that reduced medication adherence is extensive among poorly regulated patients with T2DM. A simple program to increase self-management capabilities, focusing on medication use and self-selected goals improved HbA1c in these patients. These positive findings have to be substantiated in future well powered studies.

ACKNOWLEDGEMENTS

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CONFLICT OF INTEREST

Steno Diabetes Centre funded this research. All authors are or have been employed by Steno Diabetes Center. Other than that, none of the authors have a conflict of interest.

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