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14. ABSTRACT
During this research period, we have continued to recruit patients over age 70 with diabetes and poor glycemic control as defied by A1c>8%, and randomized them to either geriatric diabetes intervention team (GDT) or attention control team (ACT). We have now recruited 20 subjects in the control group and 21subjects in the intervention group. All subjects has completed initial cerebral blood flow study. We have analyzed baseline data and presented them at the annual scientific meeting of the American Diabetes Association. We have following important observations. 1) Higher exercise capacity in older adults with diabetes is associated with better self-care ability and less diabetes-related stress. 2) Unrecognized errors in insulin injection techniques are frequent in older adults even with longer duration of insulin use. 3) Inadequate social resources are associated with increased clinical, functional and economic burden in older adults and 4) The risk of hypoglycemia is a treatment-limiting factor in older adults even with poor glycemic control. In addition, we received permission from the Human Research Protections Office to perform continuous glucose monitoring in study subjects at baseline, 6 months and 12 months to assess glycemic pattern and glucose excursions, both during day and night time, and assess effect of intervention on these parameters. We expect to perform interim analysis on this data soon.

15. SUBJECT TERMS
Diabetes, Elderly, glycemic control, Cerebral Perfusion, care management

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INTRODUCTION:

Subject: Research regarding older adults and, in particular, those with diabetes, lags far behind research on other population segments. Considering the projected increase in elderly patients with diabetes, it is important to study novel but practical strategies to achieve better glycemic control and to improve quality of life in this population.

Purpose: To test whether short-term focused intervention by a geriatric multidisciplinary team with the addition of a geriatric life specialist is superior to usual care (with attention control) in improving glycemic, functional, economic and quality of life parameters in elderly patients with diabetes, and whether these interventions will have persistent effects on outcome measures. In addition, the study will also evaluate improvement in cerebral perfusion in elderly with type 2 diabetes following six months intervention and assess whether changes in cerebral perfusion persist at a one-year follow up.

Scope of the research: In this study, patients over age 70 with diabetes are randomized to care by either geriatric diabetes intervention team (GDT) or attention control group. Subjects in GDT group undergo comprehensive geriatric assessment and have individualized intervention performed with help of a geriatric life specialist. Intervention by GDT includes focused strategies to overcome barriers in the areas of clinical care, education, social environment, and finances. At the end of 6 months of intervention, the goal is to develop a support network that will empower patients to sustain improvements seen during the intervention. After 6 months of independence period (no contact from GDT), outcome parameters are measured again to see if improvement at 6 months is sustained after 12 months. The subjects in the control group have similar contact time as the GDT group, but with a research team without geriatric expertise. Improvement in clinical, functional, quality of life and economical outcome measures in both groups are compared at 6 and 12 months intervals. At these time points (0, 6 and 12 months) patients are also be evaluated for effect of improved glycemic control on cerebral perfusion and glycemic excursions.

PROJECT TASKS:

Task 1: Program Set-up & training and recruitment of study subjects (Mos. 0-21): at Joslin Clinic

During the first year of the study, we received approval from Human Research Protection office (HRPO) at the USAMRMC, for our protocol for compliance with applicable federal, DOD, and Army human subjects protection regulations. Final approval of the whole study protocol including the portion of the study to be performed at the BIDMC was received on 2/8/2008.

During the second year, we have received permission to recruit patients from the Beth Israel Deaconess Medical Center (BIDMC) to increase our recruitment pool. We also received permission to perform continuous glucose monitoring in study subjects to gain insight in to 24 hours glucose patterns and glucose excursions in elderly subjects. We have increased our recruitment efforts and have been able to increase the rate of recruitment.

- Program development, recruitment of geriatric life specialist and training of the geriatric life specialist (Mos. 0-3)

Our program setup was completed in year 1. The study personnel are well trained and are able to follow study protocol effortlessly.

- Identification of study subjects from electronic medical records and recruitment (Mos. 3-21)

We have an excellent system to identify eligible subject from medical records at the Joslin diabetes center. We have called/screened over 200 eligible patients. However, recruitment during winter season in Massachusetts has been difficult. Frequent inclement weather has caused many study visit cancellations in the elderly patients with diabetes, also affecting accrual to the study.

To modify this situation, we submitted our study protocol for approval at the Beth Israel Deaconess Medical Center. We received approval from the human subject protection committee at BIDMC, and submitted the protocol changes to the HPRO at the USAMRMC. Besides adding this center to improve enrollment, we have also encouraged different ways to facilitate transportation in elderly patients. These measures have improved enrollment.

Task 2: Baseline assessment (Mos. 4-21): at Joslin Clinic

- Baseline clinical & survey information collected
- Baseline functional assessment by geriatric diabetes team (GDT) members at the Joslin clinic including nurse practitioner, dietitian and nurse educator.

We have enrolled 41 patients; 21 patients are randomized to the intervention arm and 20 to the attention control arm. We have completed extensive assessments as per protocol and have analyzed data from baseline visits to understand characteristics of older patients with poor control of their diabetes. The results are discussed below in detail.

Task 3: Team assessment and active intervention by Geriatric care ambassador (geriatric life specialist (GLS) (mos. 4-27) at Joslin Clinic

- Multidisciplinary team meetings to discuss barriers and care plans
- Interventions by GLS and nurse practitioner, including home visits
- GLS performs monthly telephone visits with patients
- Monthly evaluation of care plan by GDT based on GLS tele-visits
- Monthly team meeting to discuss ongoing plan and improvement

Our geriatric lifestyle specialist (GLS) has been well trained and is implementing interventions effortlessly. She continues to work with the GDT and provides the team with a home assessment, performs interventions as directed, and follows up with phone calls to assist in implementing the interventions and strategies uncovered at the assessment and home visit. She provides invaluable feedback to the GDT team members. At the end of the intervention period, she sends plan of care to the study patients to help sustain benefits gained during the intervention period.

Task 4: Outcome parameters assessment and start of independence period (Mos. 10-33):

- Repeat baseline measures on control & intervention groups and assess outcome parameters (mos. 10-27)
- Patients undergo 6 months of independence trial without contact form GDT (mos. 28-33)

12 of our patients have completed intervention period and 2 have also completed independence period.

Task 5: Cerebral vascular studies at baseline, after 6 months of active intervention and 6 months of independence period. (Mos. 3-33) SAFE laboratory at Beth Israel Medical Deaconess Medical Center

- Cerebral perfusion tests including transcarnial Doppler studies, and cerebral vasoreactivity measurement evaluation. SAFE laboratory by Dr. Vera Novak

The subjects, who are randomized to the intervention arm of the study, are scheduled to have a cerebral blood flow study performed at the SAFE lab at BIDMC as per part B of the protocol. All intervention arm subjects have completed this portion of the study at baseline, 6 patients have completed 6 months and 5 have completed 12 months flow studies. One study subject could not complete all the components of the study due to uncomfortable feeling and the study procedure was stopped per protocol. All the other subjects have tolerated the study procedure well.

Task 6: Analysis of data and information distribution. (Mos. 34-36): Joslin Clinic

- Data analysis, conference presentations, preparations for publication

We have now performed interim data analysis mainly looking at the baseline data collected on the study subjects. We had one oral presentation and two poster presentations based on this analysis at the annual national conference of the American Diabetes Association. For the purpose of the analysis we have included data from a parallel study assessing older patients with poor glycemic control.

One important distinction between older vs. younger adults with diabetes is the high prevalence among elderly of co-existing medical conditions and functional disabilities that interfere with self-care[1]. Identifying possible barriers to diabetes self-care is an essential component of developing an effective, individualized diabetes management plans for older adults[2]. Because of the high prevalence of depression, physical disabilities, and cognitive dysfunction among older adults with diabetes, it is imperative that these barriers be identified by specific screenings before formulating a diabetes management strategy. In previous studies, we have shown that subtle, undiagnosed executive dysfunction is an unrecognized co-morbidity among older adults with diabetes and is associated with poor glycemic control[3].

1) Hypoglycemia in older adults

Hypoglycemia is the most important factor limiting efforts to improve glycemic control. However, in the older patient population it is especially dangerous and has poor clinical and functional outcomes [4]. The frequency of hypoglycemia among elderly with inadequate glycemic control remains unknown. We analyze frequency of hypoglycemia from baseline questionnaire in our study patients. All patients were using insulin. Despite poor glycemic control, 42 of 45 (93%) reported episodes of hypoglycemia during the previous 3 months Eighteen of forty-two (43%) reported a hypoglycemia frequency of “more than few episodes a month”, while 57% reported “rare episodes”. Although typical hypoglycemic symptoms, such as shakiness (56%) and sweating (51%), were frequently reported, atypical symptoms such as weakness (31%), change in behavior (16%), dizziness (16%), and vision changes (18%) were also common, and could

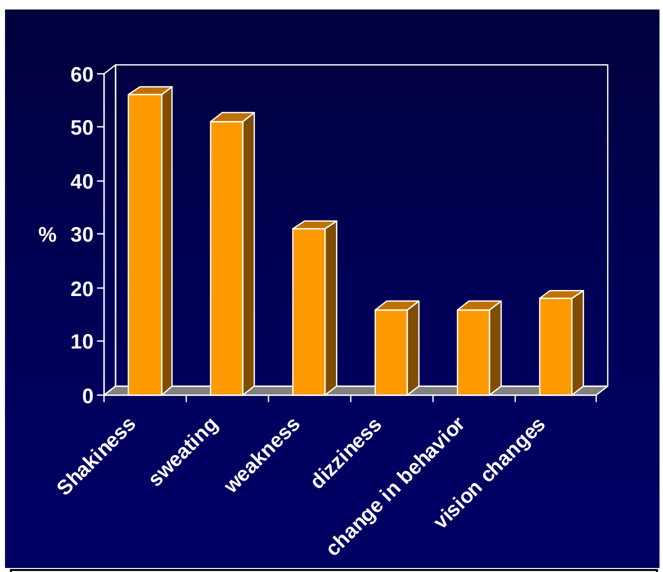

Figure 1: Significant numbers of older adults with diabetes present with atypical hypoglycemia symptoms that can be mistaken for other presentations, e.g. orthostasis, vasovagal episode or worsening of dementia.

easily have been missed if not asked for specifically (**Figure 1**). Twenty-four of 60 patients (53%) continued to drive but only 11 (24%) checked their blood glucose before driving. Only 36% with hypoglycemia reported "fear of hypoglycemia". We concluded that hypoglycemia should be carefully looked for among elders, even among those with poor glycemic control.

2) Hypoglycemic and its complications in elderly

Hypoglycemia in older adults is associated with multiple adverse clinical outcomes [5 6 7]. Most feared of these is falls, and fear of falls, leading to decreased functionality and overall quality of life. In certain situations, traumatic falls can lead to institutional placement in older adults. We evaluated the effect of hypoglycemia among our study subjects at baseline. Ninety-three percent of patients reported having hypoglycemia during initial survey. Forty-three percent of patients reported having frequent hypoglycemia ("few times a week" or "few times a month"); 50% of patients had infrequent hypoglycemia ("rare" or "once in a while"), and 7% reported no hypoglycemia. Patients were followed for 3 months after the survey. The results are shown in **Table 1**. The risk of fall increased with increased frequency of hypoglycemia. Fear of falls remained high in all patients, irrespective of hypoglycemia frequency. The risk of emergency room visits and hospitalization increased with increased frequency of hypoglycemia. The A1c (reflecting glycemic control) decreased with increasing hypoglycemia, but remained in the poorly controlled range (A1c >8%). ***Conclusion*****:** Patients with hypoglycemia are fearful of falling, and have a higher incidence of falls and higher health resource utilization than patients without hypoglycemia.

	No hypoglycemia	**Infrequent hypoglycemia (rare, once in a while)**	**Frequent hypoglycemia (few times a week or month)**
Number	4	30	26
Falls	25%	41%	61%
Fear of falls	75%	52%	56%
ER visit	0%	16%	27%
Hospital admit	0%	3%	8%

Table 1: Higher frequency of hypoglycemia is associated with higher incidence of falls, emergency room visits, and hospitalizations

3) Use of continuous glucose monitoring in elderly patients

Continuous glucose monitoring systems (CGMs) are FDA-approved devices that measure interstitial glucose levels at intervals of 1-5 minutes for periods of 3-7 days [8 9]. A sensor with a small filament is inserted and stays under the patient's skin. The sensor is attached to a transmitter that receives glucose readings from the sensor and relays them to a receiver. The receiver is a monitor that receives, and may display, glucose readings from the transmitter (the receiver may also be "blinded" so that patients cannot see the glucose readings). We are using CGM in our patients to identify patterns of glucose excursions and episodes of hypoglycemia. **Figure 2** shows aggregated readings (each color line representing one day) in a representative study patient. As seen in the figure, the patient has significant glucose excursions and multiple hypoglycemic episodes over the 3-day monitoring period. We have performed continuous glucose monitoring in 13 insulin-treated study patients. On an average, the sensor recorded glucose values for 72 hours in all the patients. The range of glucose was 40- 400 mg/dl. Of all glucose values, 56.1 % were >180 mg/dl, and 1.2 % were <70 mg/dl. In this patient group with poorly controlled diabetes, hypoglycemia was not expected. Nevertheless, 7/10 (70%) patients had at least one episode of hypoglycemia (glucose <70 mg/dl) recorded in a 3-day period. The average number of hypoglycemic episodes, among patients with hypoglycemia, was 2.57/3-day monitoring period. By comparison, 4-times-a-day finger-stick glucose measurements, performed during the 3-day CGM monitoring period, detected hypoglycemia in only 2/10 (20%) of subjects. Out of a total of 18 hypoglycemia episodes (glucose <70 mg/dl), 6 episodes occurred during at night (10 pm - 6 am). Pronounced glucose increases and decreases (high and low excursions), as measured by continuous monitoring, occurred frequently in all study subjects and were observed on 36 of 38 CGM monitoring days. A total of 81 high excursions and 13 low excursions were observed. On average, patients experienced 2.1 high excursions and 0.34 low excursions per day. Only 2 patients did not experience any high/low excursions. We concluded that continuous glucose monitoring can be used successfully in older adults. Hypoglycemia can be measured objectively and successfully using CGM and has the added advantage of being able to measure the rate/dynamics of glucose fluctuations (i.e. excursions) as well as identifying nocturnal hypoglycemia episodes.

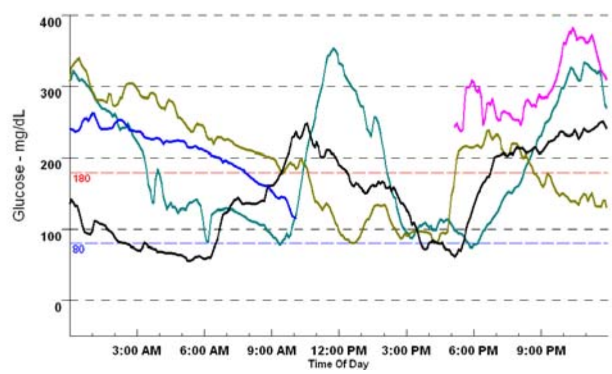

Figure 2: CGM reading in a representative patient showing multiple high and low blood glucose readings

4) Insulin errors in older patients

Co-existing medical conditions, such as cognitive dysfunction and vision/hearing problems, are common in older adults and may interfere with their ability to perform self-care. Insulin injections pose a particularly difficult problem. We evaluated insulin technique in 27 study patients. Twenty-two of 27 (81.4 %) were using insulin. Study participants on insulin were questioned about their insulin use and observed drawing or dialing up their insulin doses. When interviewed, none of the participants reported any trouble taking their insulin. However, when observed by a certified diabetes educator, 12/22 insulin users (54%) with long duration insulin use (average 13.1 years) were found to have difficulty with technique or dosing. Problems with technique included difficulty seeing the lines on the syringe, difficulty with mixing the insulin correctly, difficulty seeing air in the syringe, and inability to follow the insulin injection procedure correctly. Problems with dosing included taking too much or too little insulin, not understanding the insulin regimen, and reports of omitting insulin. The group having trouble with insulin technique and dosing were more likely to miss doses of other medications as well ($p=0.009$), suggesting problems with medication adherence in general, and were having trouble reading and interpreting food labels ($p=0.05$), suggesting possible problems with health literacy. Higher frequency of falls, fear of falls, and difficulty walking were more common in the group having problems taking insulin; however, these parameters did not reach statistical significance. There were no differences in glycemic control (A1c 9.5 vs 9.1%), vision problems, cognitive function, depression, or diabetes-related stress in the group having trouble with insulin, compared to the group without difficulty with insulin. We concluded that periodically observing insulin injection technique should be an important part of diabetes assessment in older adults, even among those with a long duration of insulin use. Co-existing medical conditions should be assessed and, where indicated, education regarding insulin injections should be modified to take co-morbidities into account.

5) Effect of exercise capacity in older adults

Exercise is an integral part of diabetes management for all patients but its effect on self-care ability and diabetes related stress in older adults is not well studied. We test exercise capacity in our study subjects using the 6-Minute Walk Test (6MWT). Self-care ability and diabetes-related stress are evaluated using Self-Care Inventory (SCI) and Problem Areas in Diabetes (PAID) questionnaires respectively. Forty-five subjects (age 76±5 years, diabetes duration 22±10 years) were divided into 2 groups based on distance walked during 6MWT at median value (313 meters). Subjects with higher exercise capacity tended to be male (77% vs. 48%, $p<0.05$), Caucasian (91% vs. 50%, $p<0.002$), and had lower BMI (31±6 vs. 35±9, $p<0.04$). This group scored higher on SCI (67±9 vs. 56±14, $p<0.003$) suggesting better self-care abilities and lower on PAID (18±10 vs. 30±16, $p<0.006$) reflecting less diabetes related stress, compared to subjects with lower exercise capacity. Depressive symptoms (measured by Geriatric Depression scale) were present in 18% of the subjects in the lower exercise capacity group as compared to none in high scoring group ($p<0.03$). Groups did not differ with respect to A1c and measures of cognitive function. However, the higher exercise group had better gait and balance (Tinnetti score 26±2 vs. 22±7, $p<0.004$) and was more likely to be independent in performing activities of daily living (IADL score 16± 0.8 vs. 14±3, $p<0.04$). We concluded that higher exercise capacity is associated with better self-care ability, less depression, less diabetes-related stress and better performance of daily tasks. Exercise education should be stressed in older adults with diabetes to maintain functional independence and optimize quality of life.

6) Effect of social resources in older adults

The effect of the availability of social resources on various aspects in older adults with diabetes in not well studied. We evaluated our study patients for the effect of available social resources on clinical, functional and economic burden. Social resources were assessed by OARS (Older American Resource and Services), a tool developed by the Duke OARS program to assess the availability of physical and emotional resources. A maximum score of 14 reflected excellent availability of social resources. The subjects were divided in to low vs. high resources groups at the mean OARS score of 12. Eighteen of 45 (40%) subjects had a low score on OARS compared to 27/45 (60%) with high score. Age was similar in both groups (76± 6 vs. 76±4 years). Compared to subjects in the high resource group, low social resource group tended to be female (83% vs. 48%, $p<0.01$), had longer duration of diabetes (25 vs. 18 years, $p<0.03$) and lived alone (56% vs. 19%, $p<.009$). In addition, the group with low social resources had higher A1c (9.4±1.2 vs. 8.9±0.5, $p<0.05$) indicating poor glycemic control, lower exercise capacity as measured by lower score on 6 minutes walk test (235 vs. 364 meters), and higher number of ER visits in past 3 months (44% vs. 15%, $p<0.04$) suggesting higher healthcare costs, compared to the higher social support group. There was no difference between the 2 groups in the areas of cognitive function, depression, stress related to diabetes management or self-care abilities. We concluded that in older adults with diabetes, inadequate social resources are associated with poor glycemic control, lower functionality and higher health care cost. It is important to assess individual older adults' resources while providing management plans.

KEY RESEARCH ACCOMPLISHMENTS:

1. Research data in older adults with diabetes is scarce. This study fills an important void in information regarding this fast growing population.
2. Research in frail elderly (like the study population – age over 70 years with poorly controlled diabetes) is difficult to conduct. We have recruited 42 patients in this category and have already gained important insight from baseline data.
3. Glucose excursions and pattern e.g. nocturnal glucose levels in older patients is unknown. We are performing CGM on study patients that will help us understand glucose variability in older adults.

REPORTABLE OUTCOMES:

Publications 2008-2009:

1. Angela Botts and **Medha N. Munshi**. Diabetes In the Elderly. In: Current Cardiovascular Risk Reports. Philadelphia: Current Medicine Group LLC;2008. p. 382-389
2. Alissa R. Segal, PharmD, CDE, **Medha N. Munshi**, MD. Insulin Therapy for Older Adults with Diabetes. In: Geriatrics and Aging. Toronto (Canada): Regional Geriatric Programs of Ontario;2008. p. 357-362.
3. Novak V, Haertle M, Zhao P, Hu K, **Munshi MN**, Novak P, Abduljalil A, Alsop D. White matter hyperintensities and dynamics of postural control. Magn Reson Imaging. 2009.
4. Elbert S Huang, Priya John, **Medha N Munshi**. Multidisciplinary approach for the treatment of diabetes in the elderly. Aging Health. 2009;5(2):207-216
5. Iwata I, **Munshi MN**. Cognitive and psychosocial aspects of caring for elderly patients with diabetes. Curr Diab Rep. 2009;9(2):140-6.
6. **Munshi MN**, Hayes M, Sternthal A, Ayres D. Use of serum c-peptide level to simplify diabetes treatment regimens in older adults. Am J Med. 2009;122(4):395-7

Abstracts 2008-2009

1. Emmy Suhl, Laura Desrochers, Patricia Bonsignore, Adrianne Sternthal, Judy Giusti, **Medha N. Munshi**: Higher Exercise Capacity In Older Adults With Diabetes Is Associated With Better Self-Care Ability And Less Diabetes-Related Stress. . In: American Diabetes Association 69th Annual Meeting; New Orleans La; 2009. P. 367-OR
2. Bonsignore P DI, Suhl E, Sternthal A, Giusti J, **Munshi MN**: Unrecognized Errors In Insulin Injection Techniques Are Frequent In Older Adults Even With Longer Duration Of Insulin Use. In: American Diabetes Association 69th Annual Meeting; New Orleans La; 2009. P. 913-P.

3. **Munshi MN**, Iwata I, Suhl E, Giusti J, Bonsignore P, Sternthal A The Risk Of Hypoglycemia Is A Treatment-Limiting Factor In Older Adults Even With Poor Glycemic Control. . In: American Diabetes Association 69th Annual Meeting; New Orleans La; 2009. P. 2123-Po.
4. **Medha N. Munshi**, Emmy Suhl, Laura Desrochers, Adrianne Sternthal, Judy Giusti, Patricia Bonsignore: Inadequate Social Resources Is Associated With Increased Clinical, Functional And Economic Burden In Older Adults. In: American Diabetes Association 69th Annual Meeting; New Orleans La; 2009. P. 1870-P.
5. Alissa R. Segal, Elizabeth L. Staum, **Medha Munshi**: Polypharmacy Is Associated With Frequent Hypoglycemia, Cognitive Dysfunction, And Poor Nutritional Status In Older Adults With Diabetes. In: American Diabetes Association 69th Annual Meeting; New Orleans La; 2009. P. 562-P.
6. Vera Novak, Peng Zhao, Kun Hu, **Medha Munshi**, David C. Alsop, Jerry D. Cavallerano, Amir M. Abduljalil, Brad Manor, Laura Desrochers, Peter Novak: Relationship Between Inflammatory Markers And Regional Brain Atrophy In Older Diabetics. In: American Diabetes Association 69th Annual Meeting; New Orleans La; 2009. P. 721-P

CONCLUSION:

There is an urgent need to find innovative ways of managing diabetes in elderly patients. We are in a process of identifying variety of barriers faced by this population in performing self-management. We are now getting better at recruiting frail patient population. Our interim analysis of baseline data was well received and appreciated by a large audience at the annual national meeting of the American Diabetes Association. We look forward to finding new and helpful information from our study and plan to distribute the information by presentations at the various meetings and publications.

APPENDICES:

1) Higher Exercise Capacity in Older Adults with Diabetes is Associated with Better Self-Care Ability and Less Diabetes-Related Stress.

Diabetes in older adults is associated with multiple co-existing medical conditions that increase the overall burden of self-care and affect quality of life. Exercise is an integral part of diabetes management for all patients but its effect on self-care ability and diabetes related stress in older adults is not well studied.

Community-living adults ≥70 years, A1c>8%, were enrolled in a study to identify geriatric-specific barriers to diabetes management. Exercise capacity was tested using the 6-Minute Walk Test (6MWT). Self-care ability and diabetes-related stress were evaluated using Self-Care Inventory (SCI) and Problem Areas in Diabetes (PAID) questionnaires respectively. Subjects were also assessed for cognitive dysfunction, depression, and glycemic control (A1c).

Forty-five subjects (age 76±5 years, diabetes duration 22±10 years) were divided into 2 groups based on distance walked during 6MWT at median value (313 meters). Subjects with higher exercise capacity tended to be male (77% vs 48%, $p<0.05$), Caucasian (91% vs 50%, $p<0.002$), and had lower BMI (31±6 vs 35±9, $p<0.04$). This group scored higher on SCI (67±9 vs 56±14, $p<0.003$) suggesting better self-care abilities and lower on PAID (18±10 vs 30±16, $p<0.006$) reflecting less diabetes related stress, compared to subjects with lower exercise capacity. Depressive symptoms (measured by Geriatric Depression scalre) were present in 18% of the subjects in the lower exercise capacity group as compared to none in high scoring group ($p<0.03$). Groups did not differ with respect to A1c and measures of cognitive function. However, the higher exercise group had better gait and balance (Tinnetti score 26±2 vs 22±7, $p<0.004$) and was more likely to be independent in performing activities of daily living (IADL score 16± 0.8 vs 14±3, $p<0.04$).

Higher exercise capacity is associated with better self-care ability, less depression, less diabetes-related stress and better performance of daily tasks. Exercise education should be stressed in older adults with diabetes to maintain functional independence and optimize quality of life.

2) Unrecognized errors in insulin injection techniques are frequent in older adults even with longer duration of insulin use.

Co-existing medical coditions such as cognitive dysfunction and vision/hearing problems are common in older adults and may interfere with their ability to perform self-care. Insulin injections pose a particularly difficult problem.

As part of an ongoing study to assess barriers to diabetes management in older adults, an in-depth diabetes self-management assessment was conducted on 27 community living older adults (age 76.4±5.1 years, duration of diabetes 17.8±9.1 years). Twenty-two of 27 (81.4 %) subjects were on insulin. Study participants on insulin were questioned about their insulin use and observed drawing or dialing up their insulin doses.

When interviewed, none of the participants reported any trouble taking their insulin, however, when observed by a certified diabetes educator, 12/22 insulin users (54%), with long duration of insulin use (average 13.1 years) were found to have difficulty with technique or dosing. Problems with technique included difficulty seeing the lines on the syringe, mixing the insulin correctly, seeing air in the syringe and inability to follow the steps correctly. Problems with dosing included taking too much or too little, not understanding regimen, and reports of omitting insulin. The group having trouble with insulin technique and dosing were more likely to miss doses of other medications (p=0.009) suggesting overall problems with adherence, and were having trouble reading food labels (p=0.05) suggesting possible problems with health literacy. Higher frequency of falls, fear of falls, and difficulty walking were more common in the group having problems taking insulin, however, these parameters did not reach statistical significance. There were no differences between the two groups in areas of glycemic control (A1c 9.5 vs 9.1%), vision, cognitive function, depression, or diabetes related stress.

Observing insulin technique periodically should be an important part of the diabetes assessment in older adults even with a long duration of insulin use. Assessment of co-existing medical condition should be integrated in education regarding insulin injections.

3) Inadequate social resources is associated with increased clinical, functional and economic burden in older adults

Managing diabetes in older adults is complicated by co-existing medical, functional and psychosocial issues. The effect of the availability of social resources on these aspects in older adults with diabetes in not well studied

We evaluated patients >70 years age with poor glycemic control (A1c>8%) enrolled in a study to assess the barriers to diabetes management for the effect of available social resources on clinical, functional and economic burden. Social resources were assessed by OARS (Older American Resource and Services), a tool developed by the Duke OARS program to assess the availability of physical and emotional resources. A maximum score of 14 reflected excellent availability of social resources. The subjects were divided in to low vs high resources groups at the mean OARS score of 12. All of the subjects were tested for cognitive dysfunction, depression, and functionality. Data on overall health and health services utilization were collected by administering questionnaires.

Forty-five patients with diabetes were evaluated. Eighteen of 45 (40%) subjects had a low score on OARS compared to 27/45 (60%) with high score. Age was similar in both groups (76± 6 vs 76±4 years). Compared to subjects in the high resource group, low social resource group tended to be female (83% vs 48%, $p<0.01$), had longer duration of diabetes (25 vs 18 years, $p<0.03$) and lived alone (56% vs 19%, $p<.009$). In addition, the group with low social resources had higher A1c (9.4±1.2 vs 8.9±0.5, $p<0.05$) indicating poor glycemic control, lower exercise capacity as measured by lower socre on 6 minutes walk test (235 vs 364 meters), and higher number of ER visits in past 3 months (44% vs 15%, $p<0.04$) suggesting higher healthcare costs, compared to the higher social support group. There was no difference between the 2 groups in the areas of cognitive function, depression, stress related to diabetes management or self-care abilities In older adults with diabetes, inadequate social resources are associated with poor glycemic control, lower functionality and higher health care cost. It is important to assess individual older adults' resources while providing management plans.

4) The risk of hypoglycemia is a treatment-limiting factor in older adults even with poor glycemic control.

In older adults with diabetes, hypoglycemia is the most important factor limiting efforts to improve glycemic control. The efforts to avoid hypoglycemia may lead to poor glycemic control in these patients. Occurrence and frequency of episodes of hypoglycemia in this population with inadequate glycemic control, remains unknown.

Patients >70 years of age with poor glycemic control (A1c>8%), enrolled in a study to identify barriers to diabetes management were evaluated for hypoglycemic events. A detailed questionnaire was administered to characterize hypoglycemia. Demographic information and clinical data were collected by surveys. All of the subjects underwent testing for cognitive function, depression, and functionality.

We evaluated 45 patients with average age 75±5 years, duration of diabetes 22±10 years, and A1c 9.1±0.5%. Over 90% patents were receiving insulin in this group. Despite poor glycemic control, 42 of 45 patients reported episodes of hypoglycemia within past 3 months. Eighteen of forty-two (43%) subjects had frequency of more than few episodes a month, while 57% had rare episodes. Cognitive dysfunction was identified in 28% patients with high frequency and 33% patients with low frequency of hypoglycemia (p=NS) suggesting possibility of under-reporting of this condition. In patients with higher frequency of hypoglycemia A1c was lower (8.8±.5 vs 9.5± 1; p<0.01) suggesting wide glycemic excursions. Although typical hypoglycemic symptoms such as shakiness (56%) and sweating (51%) were frequently reported, atypical symptoms such as weakness (31%), hunger (31%), change in behavior (16%) dizziness (16%), and vision changes (18%) were also common, and can be missed if not asked for specifically. Twenty four (53%) patients continued to drive but only 11 (24%) patients checked blood glucose before driving. Only 36% patients with hypoglycemia reported fear of hypoglycemia.

Hypoglycemia should be carefully looked for even with poor glycemic control in the older population. Improvement of glycemic control may require improving wide glucose excursions in this population

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Use of Serum c-Peptide Level to Simplify Diabetes Treatment Regimens in Older Adults

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ABSTRACT

BACKGROUND: Diabetes management in older adults is challenging. Poor glycemic control and high risk of hypoglycemia are common in older patients on a complicated insulin regimen. Newer oral hypoglycemic agents have provided an opportunity to simplify regimens in patients with type-2 diabetes on insulin. Serum c-peptide is a test to assess endogenous production of insulin. We analyze the use of serum c-peptide level in simplifying diabetes regimen by decreasing or stopping insulin injection and adding oral hypoglycemic agents in older adults.

METHODS: One hundred patients aged over 65 years with either poor glycemic control or difficulty coping with insulin regimen seen at a geriatric diabetes clinic were analyzed for this study. The data on serum c-peptide levels and A1c, along with demographic information, were obtained from medical charts.

RESULTS: Sixty-five of 100 patients (aged 79 ± 14 years, duration of diabetes 21 ± 13 years) had detectable serum c-peptide levels. Forty-six of 65 patients were available for simplification of regimen. Eleven of 46 patients had other co-morbidities preventing use of oral hypoglycemic agents. In 35/65 patients, simplification was completed successfully. Nineteen of 35 patients were converted to all-oral regimens (off insulin), while 16/35 had simplification of regimen by addition of oral hypoglycemic agents and lowering the number of insulin injections from an average of 2.7 to 1.5 injections/day ($P = .001$). Glycemic control improved significantly in patients with a simplified regimen (8.0% ± 1.5% vs 7.4% ± 1.5%; $P < .002$), and patients reported fewer hypoglycemia episodes.

CONCLUSIONS: Serum c-peptide level can be used to simplify insulin regimen in older adults with diabetes.
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KEYWORDS: c-Peptide; Diabetes; Older adults; Simplification; Treatment

With aging, patients with diabetes face an increased incidence of multiple co-morbidities.[1,2] Some of the medical co-morbidities include cognitive dysfunction, depression, polypharmacy, and physical dysfunction. It is difficult for primary care providers to manage diabetes in patients who have a difficulty performing self-care and following a complicated treatment regimen. Even patients who are on an insulin regimen for a substantial period of time find it difficult to cope due to the added burden of co-morbidities.[3] Regimens with multiple insulin injections that require insight into the carbohydrate-insulin interaction as well as multiple finger-stick monitoring can lead to increased risk of complications such as hypoglycemia and associated falls.[4] Thus, older adults may benefit from a simplification of their regimen. The ability of patients who have longstanding diabetes and are on insulin treatment to respond to oral hypoglycemic agents remains unclear. In this study, we evaluate use of serum c-peptide levels to guide simplification of diabetes regimen.

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RESEARCH DESIGN AND METHODS

We retrospectively analyzed all of the patients over the age of 65 years seen at a geriatric diabetes clinic from 2001 through 2006 in whom serum c-peptide levels were measured to identify those with endogenous insulin production. Serum c-peptide levels were measured in patients with either poor glycemic control or difficulty coping with insulin regimen. In patients with detectable serum c-peptide levels (>1.1 ng/mL; normal range 1.1-3.2 ng/mL), one or more oral hypoglycemic agents were added to simplify the regimen. Thioglitazone and metformin were used as insulin sensitizers in patients requiring large amounts of insulin. These medications were avoided in patients with co-morbidities that prohibit their use (eg, coronary artery disease, congestive heart failure, leg edema, renal failure). Insulin secretagogues (sulfonylurea and nonsulfonylurea compounds) were used in patients with low risk of hypoglycemia and were avoided in patients with erratic eating habits and hypoglycemic unawareness. If patients were unable to tolerate any oral hypoglycemic agents, we attempted to decrease the number of insulin injections (eg, changing the regimen from basal-bolus to mixed or longer-acting insulin twice a day). Medical and demographic information was collected from the chart.

We collected data on A1c measurements, as well as data on reports of hypoglycemic episodes at baseline and as available up to 4 consecutive visits over a period of up to 1 year following regimen change from the chart notes. Any episodes of hypoglycemia in the past 6 months were considered positive for the purpose of history. The study was reviewed by the committee on human subjects and was found to be exempt.

CLINICAL SIGNIFICANCE

- Older adults with long duration of diabetes, on insulin therapy, may have preserved endogenous insulin production as seen by detectable serum c-peptide level.
- Serum c-peptide levels can be used to guide simplification of the diabetes regimen in older adults who have difficulty coping with a complicated insulin regimen.
- The simplification of the diabetes regimen may lead to reduced risk of hypoglycemia without compromising glycemic control.

STATISTICAL METHODS

We calculated descriptive statistics and frequency distributions for all variables. Data are presented as mean ± SD for continuous data and as n (%) for frequency data. The differences between clinical and demographic variables were compared between patient groups before and after simplification of regimen using the unpaired *t* test for discrete or continuous data and the chi-squared test for frequency distribution. Within-group changes from baseline in A1c were analyzed using the *t* test for paired data. A value of $P < .05$ was considered to indicate statistical significance.

RESULTS

Sixty-five of 100 older adults had detectable serum c-peptide levels. The average age of these patients was 80 ± 6 years (range 67-93 years), and 65% of the patients were women. Patients were taking 8.7 ± 4 medications/day (range 3-16) and the mean duration of diabetes was 20.8 ± 12.5 years (range 1-50 years). Thirty-seven of 65 patients reported hypoglycemic episodes during their office visit. The Table shows characteristics of patients with detectable serum c-peptide levels and patients who had successful simplification of regimen.

The treatment regimen was not simplified in 19 of 65 patients with detectable c-peptide levels; 9 patients preferred to remain on insulin (did not want to add oral medications) and 10 patients were lost to follow-up before changes could be instituted. Of 46 patients available for simplification of regimen, 11 patients were unable to use oral hypoglycemic agents due to presence of multiple co-morbidities. Regimen was successfully modified in 35 patients. Metformin was added in 14 patients, sufonylurea was added in 16 patients, and thioglitazones were added in 19 patients. Twenty-three patients had one oral agent added, while 8 patients needed 2 oral agents and 4 patients were on 3 oral agents (median: 1 oral agent/patient; range: 1-3). Of these, the insulin therapy in 19 patients was completely discontinued and patients were maintained only on oral hypoglycemic agents. In the other 16 patients, an oral hypoglycemic agent was added and the number of daily insulin injections was decreased from an average of 2.7 ± 1 to 1.5 ± 0.8 injection/day ($P = .001$). In 3 of the patients, glycemic control deteriorated on oral medications, and once-daily long-acting insulin was added.

Table Characteristics of Patients with Detectable Serum c-Peptide Levels and Patients Who had Successful Simplification of Regimen

	All Patients with Detectable c-Peptide	Patients with Successful Simplification of Regimen
Number	65	35
Age (years)	80.2 ± 6	80 ± 6
Sex (M/F)	23/42	13/22
Duration of diabetes	21 ± 13	19 ± 12
Average c-peptide	2.3 ± 1	2.43 ± 1.2
No. of medications/day	8.7 ± 4	8 ± 4
No. of insulin injections/day	2.5 ± 1	2.6 ± 1
No. of patients reporting hypoglycemia (%)	55	63

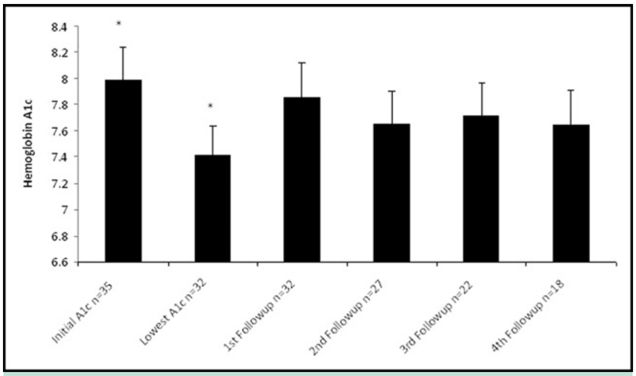

Figure A1c at the initial visit, at the lowest level, and at up to 4 consecutive visits in 1 year following simplification of regimen. *$P < .002$.

Among the 35 patients whose regimen was simplified, initial A1c, before change in the regimen, was 8.0% ± 1.5%, compared with 8.1% ± 1.4% in patients whose regimen could not be simplified. In patients with simplified regimen, we evaluated the excursion of A1c as available during 4 consecutive visits over a period of up to 1 year following addition of oral hypoglycemic agents (Figure). The number of subjects at the initial A1c measurement was 35, and the subsequent measurements were 32, 27, 22, and 18, respectively. A1c improved from a pre-intervention level of 8.0% ± 1.5 % to 7.4% ± 1.5% at the lowest level ($P < .002$). In 3 patients, follow-up A1c was not available after the changes were made. Although this was not a randomized study, the patients whose regimen was not simplified had their A1c change from 8.1% ± 1.4% initially to 7.8% ± 1.4% at the lowest level ($P =$ not significant).

Eleven of these patients had A1c >8%, while 22 patients had A1c ≤8% at the time of serum c-peptide measurement. Following modification of the regimen, improvement in A1c was observed in the group with high A1c (9.3% ± 1.5% to 8.2% ± 1.8%; $P < .0001$); while in the group with lower A1c, the favorable A1c was maintained (7.0% ± 0.8% to 6.9% ± 1%; $P =$ not significant).

Before simplification of the regimen, 22 of 35 patients reported episodes of hypoglycemia during their office visit. Following simplification of the therapy, report of hypoglycemic episodes significantly decreased, with only 2 patients reporting such episodes.

DISCUSSION

This study shows that a majority of older adults with long duration of diabetes have preserved endogenous production of insulin. In addition, we have shown successful utilization of detectable serum c-peptide levels to simplify treatment regimen. Such change in the study population decreased the reported episodes of hypoglycemia, and maintained or improved their glycemic control.

Many older adults have long duration of diabetes and were started on insulin regimen early on. Although most older patients have type-2 diabetes, primary care providers usually feel uncomfortable trying oral medications in patients with long duration of diabetes and face difficulties in patients who are unable to perform self-care. In recent years, with the introduction of new oral hypoglycemic agents, more options are available.[5-7] However, there is currently a lack of data about the type of patient that can be safely converted to a simpler regimen or an effect of the change on glycemic control. Serum c-peptide levels can be used as a simple tool in such situations. Due to the retrospective nature of the current study, it is not possible to attribute the improvement in A1c to regimen change; however, it was reassuring to see that glycemic control did not deteriorate after simplification. It is likely that improvement in A1c seen in patients with simplified regimen is due to their ability to better cope with the simplified treatment.

A major concern for older adults with diabetes is the risk of hypoglycemia. In a recent study, older patients on insulin had a higher risk of falls with tighter control.[8] Falls lead to fractures and decreased functionality, directly affecting quality of life in this age group.[9] If a simplification of regimen can lower the risk of hypoglycemia as shown in this study, it may lead to significant cost-saving and improvement in quality of life.

The limitation of this brief report is its retrospective nature. However, this is an important observation and provides rationale for future prospective randomized studies to develop specific protocols and guidelines to simplify diabetes regimen in older adults.

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