ECRONICON OPEN ACCESS

EC GYNAECOLOGY
Research Article

Type II Diabetes Prevention in Adults with Impaired Glucose Tolerance

Aqela Hassan B Ismail[1]*, Zahra Ibrahim Alqarrash[2], Zahra Jaber Hussein[2], Maitham Jaafar Al Kuwaiti[2], Fadi Jandali Qara[3], Abdulaziz Khalid Maddah[8], Abrar Mubarak Taleb Al-Batati[4], Yousef Mohammed Y Alyousef[5], Fatmah Ibrahim Alabdullah[2], Fahimah Abdullah Al Rebh[6], Wijdan Abdulaziz A Almehman[3], Abdulrahman Hassan Khormi[7], Abdulaziz Hamid Albarakati[8], Rad Khaled Alhimi[8], Wail Adel Batarfi[8] and Khalid Ahmed Hussein Sherian[9]

[1]Maastricht University, Netherlands

[2]Imam Abdulrahman Bin Faisal University, Saudi Arabia

[3]King Abdulaziz University, Saudi Arabia

[4]Umm Alqura University, Saudi Arabia

[5]Almjmaah University, Saudi Arabia

[6]King Faisal University, Saudi Arabia

[7]King Fahad Central Hospital Jazan, Saudi Arabia

[8]Ibn Sina National College, Saudi Arabia

[9]Doctor Suliman Faqih Hospital, Saudi Arabia

***Corresponding Author**: Aqela Hassan B Ismail, Maastricht University, Netherlands.

Received: April 26, 2017; **Published:** May 06, 2017

Abstract

Background: Diabetes Mellitus is a life-long disease with an increasing trend. Some studies provided a body if evidence of a reduction in Type 2 Diabetes mellitus (T2DM) incidence in adults with impaired glucose tolerance (IGT) by lifestyle intervention with a focus on increased physical activity and dietary modification as well as weight reduction among overweight participants.

Methods: 84 Subjects participated (mean age 59 years, mean BMI 34 kgm-2). The intervention included individual motivational interviewing aimed at: weight reduction, increase in physical activity, fibre and carbohydrate intake and reduction of fat intake (secondary outcomes). The primary outcome was diagnosis of T2DM.

Results: The present study has a follow-up duration of mean of two years. T2DM was diagnosed in 15 participants (I = 4, C = 11). Absolute incidence of T2DM was 33.3 per 1000 person-years in the Intervention-group and 66.7 per 1000 person-years in the Control-group. The overall incidence of diabetes was reduced by 55% in the Intervention-group, compared with the Control-group: RR 0.45 (95%CI 0.2 to 1.2).

Explanatory survival analysis of secondary outcomes showed that those who sustained beneficial changes for two or more years reduced their risk of developing T2DM.

Conclusion: Results of this study is in line with other diabetes prevention programs trials. In explanatory analysis, small yet sustained beneficial changes in weight, physical activity or dietary factors were associated with reduction in T2DM incidence.

Keywords: *T2DM; Diabetes; Intervention; Diabetes Prevention*

Introduction

T2DM mellitus, non-insulin-dependent diabetes mellitus, is a serious, costly disease constitute a major and growing burden on health care systems globally [1]. Treatment prevents some of its devastating complications [2] but does not usually restore the normal glucose level or eliminate all the adverse consequences. The diagnosis is often delayed until complications are present [3]. Since current methods

of treating diabetes remain inadequate, prevention is preferable. The hypothesis that type 2 diabetes is preventable [4] is supported by observational studies and two clinical trials of diet, exercise, or both in persons at high risk for the disease [5] but not by studies of drugs used to treat diabetes [6].

People with chronic conditions are their own principal caregivers and health care professionals, regardless of degree of specialization, ought to act as consultants supporting patients in their self-management role [7].

The validity of generalizing the results of previous prevention studies is uncertain [8]. Interventions that work in some societies may not work in others, because social, economic, and cultural forces influence diet and exercise [8].

In this study, we describe the methods and report both pragmatic and explanatory analyses evidence for diabetes prevention by life-style modification in people with IGT.

Materials and Methods

Study design, and end points

The study group have conducted a Randomised Controlled Trial (RCT) with one Control and one Intervention arm. Participants were randomly allocated either to a selected intensive behavioral interventions for a significant modification in dietary regimen coupled with a physical activity promotion plan or to a minimal intervention Control group.

Study Planned duration: The planned maximum follow-up for any individual was two years. Primary care physicians who identified eligible people likely to be at risk of impaired glucose regulation (using the criteria: aged over 40 and overweight (BMI > 25 kgm^{-2})) from their primary care databases and invited them to participate.

Inclusion Criteria

All of the below:

1. Aged over 40 years
2. BMI > 25 kgm^{-2}
3. Established IGT defined as a mean 2-hour plasma glucose value ≥ 7.8 mmol/l and < 11.1 mmol/l from two consecutive standard OGTTs (glucose load 75 g) conducted between one and 12 weeks apart (World Health Organisation 1999 classification).
4. If the 2-h OGTT value was just over the diabetes threshold (11.1 - 11.5 mmol/l) or under the IGT threshold (7.3-7.7 mmol/l), a second OGTT was performed within 1 - 12 weeks.
5. If the mean of the 2-h values from the two OGTTs was ≥ 7.8 and < 11.1 mmol/l the individual was eligible for inclusion.

Exclusion criteria

1. Subjects with previous diagnosis of diabetes, or with chronic illness that would make participation in moderate physical activity impossible.
2. Subjects on a special diet for medical reasons were excluded.
3. A diabetic value in the second OGTT was an exclusion criterion, even if the mean value was in the IGT range

Oral glucose tolerance tests (OGTT) were conducted in the Clinical Research Facility. Eligible participants (with IGT) were randomly allocated to the Intervention (I) or Control (C) group using randomisation lists, prepared independently by the EDIPS co-ordinating centre in Helsinki. Randomisation was stratified by sex and by two-hour plasma glucose value (derived from the mean of two standard oral glucose tolerance tests (OGTTs) - stratum 1: 7.8 to 9.4 mmol/l; stratum 2: 9.5 to 11.1 mmol/l). Blinding of participants and intervention staff was not possible. Data collection staff were blinded to the extent that this was possible given participants' knowledge of their allocation.

End Point and Outcomes

1. Primary end point is the Incidence of T2DM: two OGTTs conducted with 1 - 12 weeks of each other, assessed annually from baseline, was the primary study end point
2. Secondary outcomes were changes in BMI (kgm^{-2}), intakes of carbohydrate and fat (as percentages of total energy intake) and dietary fibre (g), and participation in physical activity (minutes of moderate aerobic physical activity per day).
3. Other end points were myocardial infarction or sudden cardiac death, intermittent claudication, stroke or death from other causes.

Measurement

Clinical Assessment prior to randomization

- Body weight was measured to the nearest 0.1 kg in light indoor clothing using SECA 770 electronic scales (Alpha Model 770, SECA Limited, Birmingham, UK).
- Height was measured to the nearest half centimetre using a SECA 225 stadiometer (SECA Limited, Birmingham, UK).
- Waist circumference was measured to the nearest centimetre at the midpoint between the iliac crest and the lower rib margin.
- Percentage body fat was measured by bioelectrical impedance, using a BODYSTAT 1500 (BODYSTAT Ltd, Douglas, Isle of Man, UK).
- Blood was collected from the antecubital vein with the participant in a sitting position using a needle to insert a cannula.
- Glucose was measured in venous plasma, using a Yellow Springs glucose analyser (Yellow Springs Instrument co Inc, Ohio, USA.).
- Food portion sizes were validated by the study dietician using a photographic food atlas9.
- nutrient composition was analysed using Microdiet software
- The activity diary covered the whole 24 hour period on all three days. Participants were asked to record activity for each 30 minute period throughout the day starting from midnight (midnight to 00.30, 00.30 to 1.00, 1.00 to 1.30 etc.) using an integer scoring system based on MET scores.
- OGTT, anthropometric and blood biochemistry measurements.

Health status questionnaire (RAND-36) [10], the WHO cardiovascular questionnaire [11] and annual three-day (two week days and one weekend day) diet and physical activity diaries.

Interventions

Behavioral interventions through:

a. Regular individual advice from a dietician and physiotherapist trained in motivational interviewing [12].

b. group sessions, notably 'cook and eat' events.

c. regular quarterly newsletter. The newsletter contained: healthy eating recipes, nutritional information, suggestions for local walks, and exercise options

Dietary interventions

Provided advice and counselling to develop an individual plan for behaviour change, with the aim of achieving: > 50% total dietary energy intake from carbohydrate, reduced total and saturated fat intake with < 30% total dietary energy from fat, increased fibre intake, and weight loss to achieve BMI < 25 kgm^{-2} [13].

Physical Activity

Participants received an information pack detailing facilities and opportunities for physical activity with a personal trainer dedicated when possible at a local leisure center.

Activity description: Accumulating 30 minutes of moderate aerobic physical activity per day. Analysis of participants' three day activity diaries, collected quarterly, was used in motivational feedback and to tailor goals for increasing physical activity, which were negotiated at each visit.

Control condition

Both Intervention and Control groups were offered standard health promotion advice including widely available contemporary written leaflets on healthy eating and physical activity. Control group participants were otherwise offered 'usual care' by their primary care physician.

Analysis

The baseline characteristics, weight, height, BMI, waist circumference, hip circumference, body fat %, plasma glucose (fasting, 30 minute, 60 minute and 120 minute), plasma insulin (fasting, 30 minute and 120 minute), age, sex, socioeconomic status and working capacity of the 'sustained change' and 'no sustained change' groups for each secondary outcome were compared for equality with t-tests or Chi-squared tests as appropriate.

Independent t-tests to compare continuous variables and Chi-squared tests to compare categorical variables in the Intervention and Control groups at baseline. Pragmatic (intention-to-treat) analysis of the primary endpoint was conducted using Kaplan-Meier survival analysis to determine the difference in relative risk of cumulative incidence of diabetes between the Intervention and Control groups.

For secondary outcomes we used independent t-tests to compare the Intervention and Control group means of continuous variables at baseline and in each year of the study. We also used independent t-tests to compare the 'sustained change' and 'no sustained change' group means and the difference between the groups for each of the secondary outcomes at baseline and in each year of the study. Two years of sustained change was chosen as the criterion for explanatory analysis groups after consideration of other possibilities (e.g. one year or two years) and with reference to the findings of our qualitative study linked to this trial [14].

Results

Recruitment

We recruited 48 participants to the study and they were randomised in equal numbers to the Intervention and Control groups.

Comparison of Intervention and Control groups at baseline

There was little difference in any of the anthropometric, clinical, social or demographic characteristics of the two groups measured at baseline (Tables 1 and 2). Participants were taking a range of drugs, including statins, beta blockers, anti-inflammatory medication and ACE inhibitors. There were no significant differences in medication between Intervention and Control groups.

		Control (n = 42)	Intervention (n = 42)
	Age [mean (range)]	58.5 (40 - 77)	54.5 (38 - 71)
Gender	Female	25 (59.5)	26 (61.9)
	Male	17 (40.4)	16 (38.1)
Socio-economic status by type of work	Manual	22 (52.4)	19 (45.2)
	Non-manual	15 (35.7)	16 (38.1)
	Data unavailable	5 (11.9)	7 (16.7)
Current working capacity	Fulltime /Full Capacity	178 (42.9)	15 (36.1)
	Retired	21 (50)	20 (45)
	Unable to work	1 (2.4)	5 (11.8)
	Data unavailable	2 (4.8)	2 (5.9)

Table 1: *Study groups base characteristics: number (%) by trial group for demographic variables.*

	Measurement	Intervention group (n = 42)	Control group (n =42)
	Weight (kg)	93.4 (16.0)	90.6 (12.5)
	Height (cm)	165.5 (8.9)	164.9 (10.2)
	BMI (kgm-2)	34.1 (5.5)	33.5 (4.6)
	Waist (cm)	104.6 (11.3)	104.3 (9.2)
	Hip (cm)	111.0 (11.7)	110.3 (9.0)
	Body fat %	40.2*(9.4)	40.1 (9.9)
Plasma glucose (mmol/l)	Fasting	5.7 (0.6)	5.8 (0.5)
	30 minute	9.9 (1.3)	9.8*(0.9)
	60 minute	11.5 (1.9)	11.5*(1.6)
	120 minute	8.7 (1.1)	8.9 (1.3)
Plasma insulin (mU/l)	Fasting	16.9 (12.4)	17.3 (7.4)
	30 minute	97.5 (47.1)	85.08 (40.4)
	120 minute	118.0 (58.0)	122.18 (55.3)

Table 2: *Study groups base characteristics: number (%) by trial group for demographic variables.*

Outcomes

Main outcomes

T2DM was diagnosed in a total of 15 participants (I = 4, C = 11). The absolute incidence of T2DM was 33.3. The relative risk of T2DM in the Intervention group, compared with the Control group was 0.45 (95% CI: 0.2 to 1.2). After year two of follow-up, there were no further incidences of T2DM in the Intervention group. Thus, overall the cumulative incidence of diabetes was 55% less in the Intervention group compared with the Control group. Kaplan-Maier Survival analysis for Intervention and Control groups.

Secondary outcomes

Results of the study revealed no significant differences in mean values for secondary outcome measures between the Intervention and Control groups weather at baseline or at the quarterly follow-up. Analysis of difference from baseline value in these secondary outcome measures showed a significant difference between Intervention and Control groups in weight loss at year 1 follow-up only (mean weight

change: Intervention group = -2.3 kg, Control group = 0.01 kg; mean difference -2.5 (95% CI: -4.2 to 0.7) kg, p = 0.007). Only three participants achieved BMI < 25 kgm^{-2}.

The results of the survival analyses are shown in the following tables 3 and table 4.

	Number in intervention group (%)	Number in control group (%)	Number in control group (%)	Total Number	Number of cases of T2DM over Two years follow-up
Body weight	Sustained beneficial change	18 (43)	20 (47)	38 (45)	2
	No sustained beneficial change	24 (57)	22 (53)	46	10
% energy by carbohydrate intake	Sustained beneficial change	12 (29)	13 (31)	25	2
	No sustained beneficial change	30 (71)	29 (69)	59	12
% energy by fat intake	Sustained beneficial change	18 (43)	17 (41)	35	2
	No sustained beneficial change	24 (57)	25 (59)	49	11
Dietary fibre intake	Sustained beneficial change	12 (29)	11 (26)	23	3
	No sustained beneficial change	30 (71)	31 (74)	61	12
Physical activity score	Sustained beneficial change	14 (33)	16 (38)	30	2
	No sustained beneficial change	28 (67)	26 (62)	52	13

Table 3: *Shows the correlation between the sustained beneficial change in secondary outcomes and T2DMprogression by trial group.*

Outcome	Year	Participants	Sustained beneficial change	Participants	No sustained beneficial change	Difference	p-value
		n	Mean (SD)	n	Mean (SD)	Mean (95% CI)	
Weight (Kg)	Year 0	38	89.4 (12.8)	46	91.1 (15.6)	-1.3 (-7.2, 4.5)	0.68
	Year 1	38	86.4 (14.7)	29	91.5 (13.8)	-4.5 (-10.8, 1.3)	0.15
	Year 2	38	85 (13.7)	15	92 (17.0)	-6.6 (-14.1, 0.9)	0.08
Carbohydrate (% energy)	Year 0	25	42(07)	59	47.5 (08)	-4.5(-8.1,1.0)	0.013
	Year 1	22	46 (11)	38	46.5 (10)	-0.3(-5.4,4.6)	0.89
	Year 2	20	48 (07)	33	44.5 (10)	3.3(-1.2, 7.9)	0.15
Fat (% energy)	Year 0	35	35 (07)	49	29.5 (09)	6.2 (2.6, 9.7)	0.001
	Year 1	39	29 (10)	27	32.5 (06)	-2.2 (6.5, 2.1)	0.306
	Year 2	37	29 (06)	22	33.5 (06)	-4.4 (7.8, -1.0)	0.011
Fibre (g/day)	Year 0	23	15.6 (6.1)	61	19 (6.5)	-2.9 (-5.8, -0.0)	0.05
	Year 1	29	20.4 (10.2)	37	14.7 (6.3)	6.5 (2.2, 12.8)	0.003
	Year 2	27	22.4 (10.0)	32	16.3 (6.8)	6.1 (2.1, 10.0)	0.004
Activity (score/day)	Year 0	37	91.6 (8.3)	52	101.5 (16.7)	-8.9 (-13.4, -3.5)	0.002
	Year 1	33	99 (12.8)	26	98.5 (14.0)	0.1 (-6.9, 7.07)	0.99
	Year 2	31	100 (12.4)	18	95.1 (14.1)	6.0 (-1.8, 13.8)	0.13

Table 4: *Presents data of standard deviation (SD) values of secondary outcomes: comparison of sustained beneficial change with no sustained beneficial change groups in each study year.*

Discussion

Main findings

T2DM can be prevented or delayed by interventions designed to change the lifestyles of participants with IGT the overall incidence of diabetes was reduced by 55% in the Intervention group compared with the Control group, a magnitude of effect similar to that seen in the other main diabetes prevention trials [5]. However, this study was designed as part of a larger study and was not powered for statistical significance. The baseline differences in diet and physical activity measures suggest that those with the greatest capacity for beneficial change at baseline (because they were furthest from the healthy targets) were most able to sustain and to benefit from the changes made. The annual changes (means and distributions) in the groups that did and did not sustain beneficial change, demonstrate that small amounts of sustained change are effective in reducing risk.

Whilst the control treatment was 'minimal intervention', it involved an annual clinical review and annual food intake and physical activity diaries. It has been recognised that a diagnosis of IGT, together with annual clinical reviews, constitute rather more than 'usual care' [15]. The motivational effect of monitoring needs to be assessed separately and considered in future pragmatic trials.

The problem of identifying persistent IGT for trial recruitment has been partly addressed since we commenced this trial by the development of prospective diabetes risk scores, such as FINDRISC [16]. Risk scores could also reduce the potential for selection bias when participants are recruited through primary care. Large trials, where the participants have been recruited on the basis of risk scores, are underway [17]. However, risk scores do not diagnose T2DM nor monitor progression, so the OGTT is likely to remain the diagnostic test of choice in future trials.

Future pragmatic trials of the efficacy of lifestyle intervention in T2DM prevention should address: achieving higher levels of recruitment; acceptable, ethical and efficient data collection tools; and acceptable, safe and efficient monitoring schemes to evaluate trial progression. This may involve investigating more convenient times and locations for intervention delivery, including workplaces. Refining the physical activity and dietary advice within T2DM prevention interventions to maximise initiation, magnitude and maintenance of change remains a continuing challenge and should be the subject of further investigation.

Conclusion

Type 2 Diabetes (TYPE II DIABETES) can be not only delayed but prevented by lifestyle modification in adults with IGT. In explanatory analysis, we showed that small sustained beneficial changes in secondary outcome measures: weight loss, increase in physical activity, reduction in dietary energy intake, reduction in percentage fat intake and increase in percentage fibre intake, were associated with reduction in T2DM incidence.

Bibliography

1. International Diabetes Federation. IDF diabetes atlas. Brussels, Belgium: International Diabetes Federation (2013).

2. UK Prospective Diabetes Study (UKPDS) Group. "Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33)". *Lancet* 352.9131 (1998): 837-853.

3. Harris MI and Eastman RC. "Early detection of undiagnosed diabetes mellitus: a US perspective". *Diabetes/Metabolism Research and Reviews* 16.4 (2000): 230-236.

4. The Diabetes Prevention Program Research Group. "The Diabetes Prevention Program: design and methods for a clinical trial in the prevention of type 2 diabetes". *Diabetes Care* 22.4 (1999): 623-634.

5. Tuomilehto J., *et al*. "Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance". *New England Journal of Medicine* 344.18 (2001): 1343-1350.

6. Knowler WC., *et al*. "Preventing non-insulin-dependent diabetes". *Diabetes* 44.5 (1995): 483-488.

7. Sørensen M., *et al*. "Health promotion interventions in type 2 diabetes". *Annali dell'Istituto Superiore di Sanità* 51.3 (2015): 192-198.

8. Tataranni PA and Bogardus C. "Changing habits to delay diabetes". *New England Journal of Medicine* 344.18 (2001): 1390-1392.

9. Nelson MAM and Meyer J. "Food Portion Sizes". London: MAFF (1997).

10. Hays RD., *et al*. "The RAND 36-Item Health Survey 1.0". *Health Economics* 2.3 (1993): 217-227.

11. Rose GABH., *et al*. "Cardiovascular Survey Methods". *Monograph series No 56, Geneva: World Health Organization* (1968).

12. Rollnick S., *et al*. "Health Behaviour Change". *Edinburgh: Churchill livingstone* (1999).

13. Ha TK and Lean ME. "Recommendations for the nutritional management of patients with diabetes mellitus". *European Journal of Clinical Nutrition* 52.7 (1998): 467-481.

14. Penn L., *et al*. "Participants' perspective on maintaining behaviour change: a qualitative study within the European Diabetes Prevention Study". *BMC Public Health* 8 (2008): 235.

15. Lindstrom J., *et al*. "The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity". *Diabetes Care* 26.12 (2003): 3230-3236.

16. Lindstrom J and Tuomilehto J. "The diabetes risk score: a practical tool to predict type 2 diabetes risk". *Diabetes Care* 26.3 (2003): 725-731.

17. Schwarz PEH., *et al*. "The European perspective of type 2 diabetes prevention: diabetes in Europe--prevention using lifestyle, physical activity and nutritional intervention (DE-PLAN) project". *Experimental and Clinical Endocrinology and Diabetes* 116.3 (2008): 167-172.

Volume 4 Issue 4 May 2017