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財団法人 日中医学協会

理事長 中島 章 殿

研究室で撮影した本人のスナップ写真、及び発表論文のコピーを添付

1．研究者氏名 龔 倩

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研究テーマ 中国における糖尿病ハイリスク者に対する運動療法

2．本年度の研究業績

(1) 学会・研究会等においての口頭発表 有 ・ (無) (学会名・内容)

(2) 学会誌等に発表した論文 有 ・ (無) (雑誌名・論文名)

3．今後の研究計画

1. 今年5月以降。本研究の中間結果を収集して分析する。

2. 上記の結果を評価し、1日から効果のよくない対象者に対し、北京医科大学第3附属病院の運動医学部と提携して、更に強化運動指導を行う予定。

3. 12月以降、味の素(株)の新プロジェクト(薬物臨床試験)を同病院と協力して中国に展開する予定。

4．研究指導者の意見

筆者はほとんど独立で北京における臨床応用研究(糖尿病に対する運動療法)を立案し、施設の交渉、協力者の教育を含め実施を精力的に進めております。

私も1998年5月と11月に北京を訪れ、ほぼ予定通りに研究が進んでいることを確認しております。研究の現状からすると筆者が取りくんでいる課題を超える研究となっておりますが、本人の努力に期待しております。

研究の成果としては、論文を発表するには到っておりませんが、1999年3月までには研究中間の報告、1999年内には成果の公表が可能と考えております。

研究指導者氏名　大磯幸雄　㊞

5．研究報告

別紙形式を参考に、報告本文4000字以上で報告して下さい（枚数自由・ワープロ使用）

タイトル・要旨等は日本語で、KEY WORDS以下は日本語或いは英語で記入して下さい。

研究成果の発表予定がある場合は発表原稿・抄録集等を添付して下さい。

論文発表に当っては、日中医学協会－日本財団補助金による旨を明記して下さい。

糖尿病の生活方式介入研究要旨

研究の内容と背景：

本研究は、インスリン非依存型糖尿病(NIDDM)患者の生活方式介入により、NIDDM の予防と治療の重要な治療法である運動療法について定量的に分析･評価する。適度の運動が血糖コントロールには重要と有効であることが報告されているが､実験条件管理下で検討された成績は多く見られる。今まで運動を定量化して評価しえた報告は認められない。患者に運動療法を実践してもらう場合、患者が自分なりの方法で行っている運動について、その種類と運動に費やす時間から運動量を考慮し、助言を与えている場合が多いが、客観的に運動量を評価することは難しい。また、実際に運動指導を行うに当たって必要な運動処方の作成、すなわち個人に合わせた運動強度の決定法に一定の基準がなく、経験的な指導がなされている。

研究の特徴：

本研究は上記の問題を考慮し、運動を継続させるために、運動の効果が自己測定により観察させることと､運動量の記録が残ることを試みた。６ヶ月の追跡期間の中に、日常生活で簡単に運動量を知るための方法のひとつに歩数計を用いて定量性を実現することにした。歩数計による数字に基づいて、運動量をチェック、記録し、運動量増加の可能性、増加幅による効果への影響について検討した。同時に、NIDDM のハイリスク人の性格傾向と（食事、運動などの）自己管理能力、HbA1c 値、体重及び運動量の増減などとの定量的な関係を研究した。

また、生活方式介入時に、対象者の心理要因及び社会的要因が運動と食事指導に影響する重要な要因として認識し、対象者が指導の通りよくやっている人とやっていない人が性格面でどのような特徴がもち、これによりどのように対応すべきかについて研究した。

以 上

AIM

To evaluate the efficacy of exercise therapy

To evaluate the contribution of pedometer

To evaluate the relationship of characteristics and compliance

METHODS

Selection of Participants

Participants were recruited through clinical centers of one dwells district, one institution and six universities. Eligible requirements for participation in the study were as follows:

Table 1 : The study inclusion and exclusion criteria.

Inclusion Criteria

1. Aged 35 to 65 years old.
2. FPG concentration was between 5.0 and 7.0 mmol/dl, and had at least one parameter of the high-risk of diabetes:
   - Resting blood pressure exceeding 140/90 mm/Hg
   - BMI >= 23 kg/m^2
   - Triglyceride concentration >= 150 mg/dl
   - HDL-c concentration =< 35 mg/dl
   - Diabetic family history
3. FPG concentration was between 7.0 and 7.6 mmol/dl.
4. FPG concentration was between 7.6 and 8.9 mmol/dl and no drug treatment.
5. HbA1c concentration more than 4.6mmol/dl.
6. Willing to participate in the trial for 1 year.
7. Informed consent.

Excluded Criteria

1. Severe diseases: uncontrolled congestive heart failure, uncontrolled hypertension, unstable dysrhythmia, unstable angina, coronary heart disease.
2. Clinical evidence of diabetes.
3. Treated with oral hypoglycemic agents
4. Medication use likely to interfere with lipid metabolism.
5. Exercise-limiting concurrent condition.
6. To refuse sign informed-consent documents to participate in the protocol, which was approved by the Ethics Committee of the study.

Screening

In early screening period the age-eligible high-risk population of diabetes were recruited and approximately 3570 people screened from June to September in 1998. Only 112 eligible participants were eventually entered into the trial. Because screening for high-risk group of diabetes was more difficult than expected, we decided to select IGT patients(1285 on total) by scanning 5805 patients' case reports in the clinical centers. As a result, 1228 patients receipted the screening test. The recruitment period was extended for 3 months.

Baseline Investigations

401 eligible participants according to the screening test took part in the baseline investigation in November 1998. At the baseline, informed consent was obtained, eligibility was determined, and data were collected on a series of the interview survey of questionnaire included questions on demographic characteristics, smoking habits, alcohol consumption, medical history, family history, treatment of medicine, diet habits and exercise behavior and other risk factors for diabetes, health status and functional capacity, and socio-demographic. FPG, HbA1c, FPI, TC, TG, HDL-c were measured. 256 participants were eligible for the study.

Patient Evaluation

Patient's situation were evaluated on baseline, and at 3 months, 6 months and one year after the study beginning. Table 2 summarizes the participants evaluation schedule.

Table 2 Patient Evaluation Schedule

	evaluation			
	(1) Initial	(2) 3 months	(3) 6 months	(4) 12 months
Demographic	○		○	○
Medical history	○		○	○
Physical activity questionnaire	○		○	○
Diet questionnaire	○		○	○
Physical exam				
Weight	○	○	○	○
Height	○		○	○
Blood pressure	○		○	○
Serum blood measures				
Fasting plasma glucose	○	○	○	○
Hemoglobin A1c	○	○	○	○
Fasting plasma insulin	○		○	○
Total cholesterol	○		○	○
Triglycerides	○		○	○
HDL-cholesterol	○		○	○
Tokyo University Egogram	○			
Treatment compliance			○	○
Pedometer measures	everyday			

Demographic data

At the initial evaluation, the participant's eligibility was assessed. As part of t He eligibility determination, detailed information was collected regarding the participant' fasting blood glucose, family history of diabetes and other risk factor of diabetes. Demographic data collected at the initial evaluation included sex, age, highest educational levels achieved, occupations.

Medical history

At the initial investigation, information was obtained on participants regarding their medical history of the heaviest body weight, history of babies over 4kg, history of

pregnancy diabetes, medical history of diabetes, coronary heart disease, hypertension, hyperlipidemia, stroke, severe disease of liver and kidney and other, condition of smoking alcohol consumption, medication use data were interviewed.

Leisure time physical activity questionnaire have been shown to possess good reliability and validity in MONICA study was developed and used. The kinds and time of the activities were interviewed. The daily quantity of leisure time physical activity was evaluated.

The food frequency record advocated by diabetes clinic of the third hospital of Beijing Medical University was used. Nutrition ingredients were analyzed by nutritionist of the Beijing Medical University.

Personality characters were evaluated by TEG, that was a 60 items self-administered questionnaires, developed by research group of Tokyo University. TEG aimed to assess ego state, through five ego states: CP(Critical Parent), NP(Nurturing Parent), A(Adult), AC(Adapted Child) and FC(Free Child). TEG scores were calculated an questionnaire were displayed by a line graph of the profile of the five subscales: CP, NP, A, FC, AC. According the classification of the graph the personality characters could be assessed by authors.

Blood pressure was recorded with a sphygmomanometer after a 15 min rest while sitting on a chair. Two successive recordings were taken, and the mean was used in the analysis with adjustment for inter-observer variation.

Body mass index calculated as weight(kg)/{height $(m)^2$} was used as an index of relative weight.

Daily physical activity were evaluated with the pedometer made by Suzuken Company. in Japan. The reliability and validity were tested by the pilot survey.

Blood sample collection and measurement

Blood sampling was performed at 8 AM after an overnight fast (10 to 12 hours). For total cholesterol, HDL-cholesterol, triglycerides, fasting plasma glucose concentration were determined by the methods of the enzymatic method, insulin by the radio-immuno-diffusion method. The instrument remained "standardized" according to the criteria of the Ministry determining center. For HbA1c determination, blood was drawn under EDTA, then measured by chromatographic method (turbidimetric inhibition immunoassay method) standard according to the criteria of the Boehringer Mannheim Systems with the BM/Hitachi7170. The reference range is 2.9-4.6%. (in Japan it was determined by conventional HPLC method, the reference range is 4.3-5.8%). An alter formula between the two measurement methods

is %HbA1c=o.81*HbA1c(g/dl)*100/Hb(g/dl) +2.39.

Design and randomization

At the end of the baseline investigation, eligible participants were classified into three groups: one group treated with diet alone (control group=C1), other group treated with diet and wore pedometer (pedometer control group=E1), another group treated with diet, wore pedometer and intervened by increasing 30% exercise (intervention group=E2).(E1 and E2 groups were named pedometer groups).

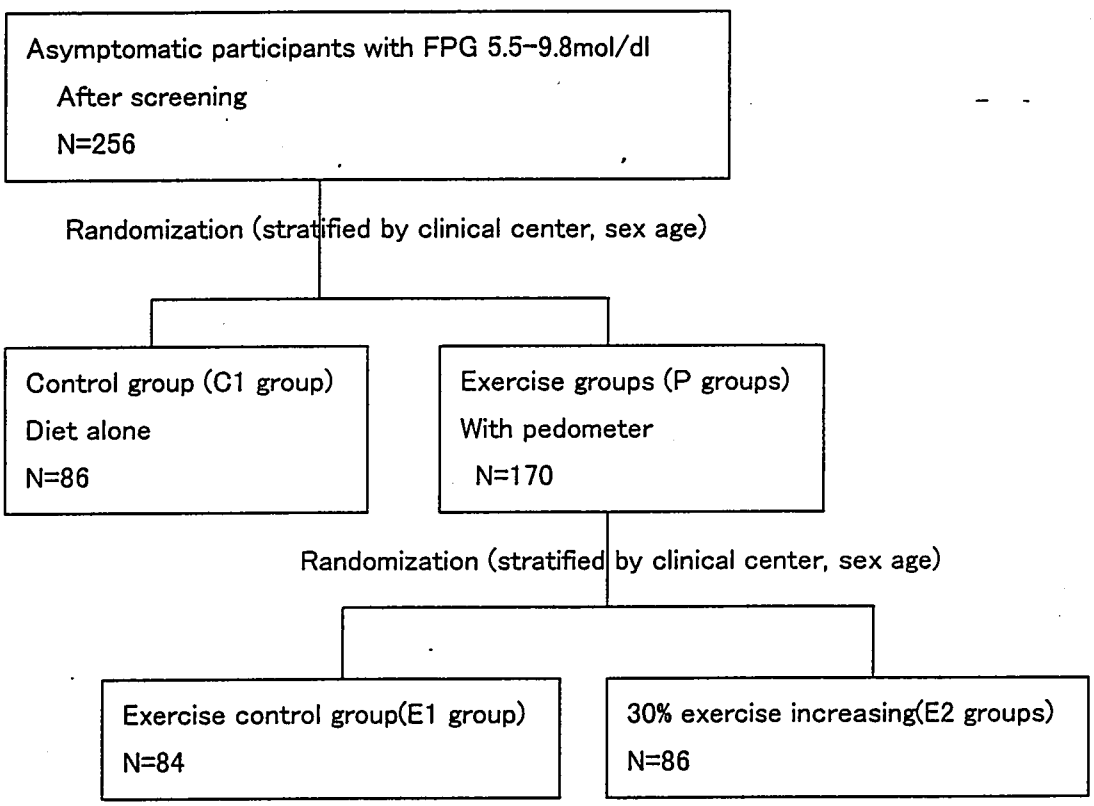

Figure 1. A flow diagram of randomization. The main analysis compares participants assigned to C1 group with participants assigned to E2 group with using pedometer and increasing exercise.

At the first randomization each participants had a 33.3% chance of being allocated into C1 group and 66.7% into P groups. The randomization was stratified by their clinical center, sex, age, FPG.

170 participants were allocated into P groups and were asked to wearing pedometer and recording the number of the steps everyday for a month.

The secondary randomization was done in the P groups, Randomization was stratified

by the average of the steps, clinical center, sex, age. 170 Participants were assigned with equal probability to the E1 group and E2 group.

Intervention

Dietary intervention

All of three groups were placed on diets provided with food scales for use during the study. The dietitian provided individual instruction on the keeping of food records at the beginning of the study. The food recording procedure was also documented in an information folder given to each subject. decreasing total energy intake from fat, with the remainder distributed between carbohydrates and protein. Diets were individually designed for each subject using the estimated energy intake food records performed during baseline. Compliance with the low-fat diet was assessed by 3 monthly interviews with the dietitian and completion of a food checklist.

Exercise Intervention

Participants in exercise groups were asked to wear the pedometer from getting-up till sleeping and record the steps numbers everyday.

The participants of intervention group were asked and encouraged to increase the amount of their leisure physical exercise by 30% steps/day. To this groups, counseling sessions were conducted monthly. The rate of increase depended on the baseline steps, and types of exercise recommended were jogging, walking.

Follow-up Visits

During the intervention phase of the phase of the trial, follow-up visits to the clinical center are scheduled every 3 month to assess and encourage compliance with study exercise treatment, and obtain outcome information.

Expected Outcome

Primary Expected Effected is 0.5% difference in change of HbA1c.

Secondary expected Effect is Decreasing in TC,TG,HDL-c FPI,BMI BP.

Discontinuation

The study treatment is discontinued but follow-up continued for the persons who develop any of the following conditions: severe syndrome diabetes or other any severe illness that may have study discontinued.

28% of 256 subjects.

· The participants' data on age, sex, duration of education, income (Ken), occupation in table 3 and the risk factors in table 4 at the start of the study did not differ between groups. These base line data and enables us to examine how effectively the randomization process produced three generally equivalent groups that were unaffected by participant preferences, investigator bias and other confounding factor.

Dietary intake measures were not significantly different for the three groups(table 7).

The average steps was 9821 steps (SD:3197) everyday. The median average daily steps was 9447 steps. Average daily steps recorded with pedometer correlated well with the questionnaire measurement.

DISCUSSION

The chance of finding participants through the method of screening the high risk population was lower, the likelihood became higher through the method of checking the medical case reports.

Although the FPG is the new ADA criteria for diagnosing type 2 diabetes, but it was known to be poorly reproducible. HbA1c level may be more convenient and a more better measure test.

Pedometer should be recommended for type 2 diabetic patients to monitor the physical activity.

Table3. Demographic characteristics of sample (n=254)

Characteristics	control group	pedometer control group	intervention group	p
Age(year)				
35-45	20	18	15	ns
46-55	26	23	28	ns
56-65	40	43	43	ns
Educaton(year)				
<5	5	10	6	ns
6-11	20	17	9	ns
11-15	20	15	18	ns
>=16	41	41	53	ns
Income(ken)				
<300	3	1	3	ns
300-999	37	38	43	ns
1000-2999	43	42	37	ns
>=30000	3	3	6	ns
Ocupation				
officer	18	20	21	ns
worker	20	16	15	ns
teacher	26	23	27	ns
business	1	0	0	ns
retired	20	22	23	ns
others	1	3	0	ns
Smokers	21	19	13	ns

Table4 :e of diabeteic risk factor

Risk Factor	control group (number)	pedometer control group (number)	intervention group (number)	p
history of pregnancy diabetes	0	1	0	ns
history of babies over 4kg	5	8	5	ns
History of hypertension	23	17	22	ns
History of CHD	9	11	10	ns
History of DM	2	3	2	ns
History of hyperlipidemia	13	24	14	ns
History of stroke	1	3	0	ns
History of	0	1	2	ns
History of liver and kidney	1	1	1	ns
Family history				
paesent	17	17	14	ns
chidren	1	0	0	ns
sister and brother	8	15	10	ns
grandmother and father	3	2	4	ns
Systoelic blood pressure(mmHg)				
<140	58	61	61	ns
140-160	18	18	15	ns
>160	10	5	10	ns
Diastolic blood pressure(mmHg)				
<90	53	59	48	ns
90-100	18	19	26	ns
>100	15	6	12	ns
Total cholesterol(mg/dl)				
<200	37	34	32	ns
200-240	21	24	16	ns
>240	28	25	38	ns
Triglycerides(mg/dl)				
<150	45	46	42	ns
>=150	41	37	44	ns
HDL cholesterol(mg/dl)				
=<35	9	12	7	ns
35-50	12	13	11	ns
>50	65	58	68	ns
fasting plasma glucose(mol/l)				
95-110	35	46	35	ns
110-126	28	19	27	ns
126-140	16	7	14	ns
140-160	7	12	10	ns
fasting plasma insulin(mol/l)				
<9	9	12	12	ns
9-20	67	55	62	ns
>20	10	16	12	ns
hemoglobin a1c				
<2.9	30	30	32	ns
2.9-4.6	47	42	41	ns
>4.6	9	12	13	ns
Body mass index				
<23(normal)	8	6	12	ns
23-25(moderately obese)	25	30	26	ns
25-28(obese)	32	30	28	ns
>28(severely obese)	21	18	20	ns
Alcohol consumption(drinks per day)				
0(no alcohol in past 7 days)	59	58	67	ns
1-2	13	12	4	ns
3-4	5	2	3	ns
>=5	9	12	12	ns

Table5 sex-specific characteristics of 256 Participants in the study

Characteristic	men		women		
	Number	percent(%)	Number	percent(%)	p
Age(year)					
35-45	28	21.88	25	19.53	ns
46-55	27	21.09	50	39.06	ns
56-65	73	57.03	53	41.41	ns
Educaton(year)					
<5	5	1.95	16	6.25	ns
6-11	19	7.42	27	10.55	ns
11-15	25	9.77	28	10.94	ns
>=15	79	30.86	57	22.27	ns
Income(ken)					
<300	1	0.39	3	1.17	ns
300-1000	59	23.05	59	23.05	ns
>1000	61	23.83	61	23.83	ns
>3000	7	2.73	5	1.95	ns
Ocupation					
officer	25	9.77	34	13.28	ns
worker	27	10.55	24	9.38	ns
teacher	52	20.31	24	9.38	ns
bussiness	0	0.00	1	0.39	ns
retired	24	9.38	41	16.02	ns
others	0	0.00	4	1.56	ns

Table6 sex-specific prevalence of 256 Participants in the study

Risk Factor	men		women		
	Number	percent(%)	Number	percent(%)	p
smokers	46	18.04	7	2.75	*
history of pregnancy diabetes	0	0.00	1	0.88	ns
history of babies over 4kg	0	0.00	18	14.52	ns
History of hypertension	28	10.94	34	13.28	ns
History of CHD	14	5.49	16	6.27	ns
History of DM	6	2.35	1	0.39	ns
History of hyperlipidemia	24	9.38	27	10.55	ns
History of stroke	2	0.78	2	0.78	ns
History of liver and kidney	21	8.20	21	8.20	ns
Family history					
paesent	21	8.20	27	10.55	ns
chidren	0	0.00	1	0.39	ns
sister and brother	17	6.64	16	6.25	ns
grandmother and father	5	1.95	4	1.56	ns
Systoelic blood pressure(mmHg)					
<140	89	34.77	91	35.55	ns
140-160	30	11.72	21	8.20	ns
>160	9	3.52	16	6.25	ns
Diastolic blood pressure(mmHg)					
<90	70	27.34	90	35.16	ns
>= 90	35	13.67	28	10.94	ns
Total cholesterol(mg/dl)					
<200	60	23.53	43	16.86	ns
200-240	30	11.76	31	12.16	ns
>240	37	14.51	54	21.18	ns
Triglycerides(mg/dl)					
<150	64	25.10	69	27.06	ns
>=150	63	24.71	59	23.14	ns
HDL cholesterol(mg/dl)					
=<35	23	9.02	5	1.96	*
35-50	25	9.80	11	4.31	ns
>50	79	30.98	112	43.92	ns
fasting plasma glucose(mol/l)					
95-110	57	22.27	59	23.05	ns
110-126	34	13.28	40	15.63	ns
126-140	20	7.81	17	6.64	ns
140-160	17	6.64	12	4.69	ns
fasting plasma insulin(mol/l)					
<9	22	8.63	11	4.31	ns
9-20	85	33.33	99	38.82	ns
>20	20	7.84	18	7.06	ns
HbA1c					
<2.9	42	16.41	50	19.53	ns
2.9-4.6	66	25.78	64	25.00	ns
>4.6	20	7.81	14	5.47	ns
Body mass index					
<23(normal)	12	4.69	14	5.47	ns
23-25(moderately obese)	45	17.58	36	14.06	ns
25-28(obese)	46	17.97	44	17.19	ns
>28(severely obese)	25	9.77	34	13.28	ns

Table 7 Charactersistics of the diet at baseline(mean±std)

Characteristics	control group	pedometer control group	intervention group	p
Energy intake(kcal)	2038±644	1945±596	1970±638	ns
Carbohydrates(g)	577±191	540±186	552±189	ns
Protein(g)	90±31	85±24	89±31	ns
Fat(g)	74±31	76±32	77±36	ns
Alcohol(g)	52±146	29±93	44±148	ns