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DIABETES: MEDICATIONS, LIFE STYLES, STRESS AND MANAGEMENT-REVIEW

ABSTRACT

Type 2 diabetes mellitus is increasingly common, primarily because of increase in the prevalence of a sedentary lifestyle and obesity. Whether type 2 diabetes can be prevented by interventions that affect the lifestyles of subjects at high risk for the disease is not known. Since I am mellitus type 2 suffering and hence understand the reverse influence of the diabetes. I have been experiencing the high systolic and disistolic blood pressure and worried to realize it to be, 170 /90-100 mmHg. As a curiosity I questioned my physician about these elevations but he could not satisfy me. I use to notice the diagnosis report very closely and always wanted to check my food habits. I with this mellitus could be in a position to make it realize that how important it is to be cautious about this. The mellitus has a great influence on the biochemistry of the metabolism. Unmonitored check on this could be fatal to the sufferer.

KEYWORDS: diabetes mellitus, hyperlipidimia, hypertension, Hb_{1Ac}

1. INTRODUCTION

The main focus of the review would be that the glycolytic enzyme glucokinase is expressed only in liver and pancreatic beta cells and has a key role in the regulation of glucose homeostasis. In hepatocytes, the phosphorylation of glucose by glucokinase facilitates the uptake and metabolism of glucose by maintaining a gradient for glucose transport into these cells. Diabetes mellitus is increasing in prevalence worldwide and is currently estimated to affect more than 6.5 percent of the population of the United States. Diabetes is the most common cause of end-stage renal disease in this country, accounting for 40 percent of cases. Although the inhibition of the effects of angiotensin II has a beneficial effect in patients with nephropathy caused by type 1 diabetes, no published study with definitive renal outcomes has addressed the issue of Reno protection in patients with type 2 diabetes a population that differs substantially from patients with type 1 diabetes in terms of demographic characteristics, metabolic features, and potential mechanisms of glomerular disease. Several studies have addressed the positive effects of specific antihypertensive agents on cardiovascular morbidity and mortality within this population. [1-2]

Diabetes is a chronic, genetically determined, debilitating disease that affects every organ system. There are two major types of diabetes: Type I and Type II. Type I or insulin dependent diabetes mellitus (IDDM), is caused by the autoimmune destruction of the insulin producing cells of the pancreas and is usually, but not always diagnosed in childhood. People with type I diabetes must take insulin shots in order to survive. Type II diabetes or non-insulin dependent diabetes mellitus (NIDDM), are usually diagnosed in adulthood. They produce insulin, but their bodies do not use it effectively or properly. While many modern diseases plague society, diabetes has been known for many centuries (Juvenile Diabetes Foundation).[1-3] Type I diabetes is usually diagnosed in children and young adults and was previously known as juvenile diabetes. In type I diabetes, the body does not produce insulin. Insulin is necessary for the body to be able to use sugar. Sugar is the basic fuel for the cells in the body, and insulin takes the sugar from the blood into the cells. When sugar builds up in the blood instead of going into cells, it can cause two problems: cells may be starved for energy, and over time, high blood sugar levels may hurt your eyes, kidneys, nerves, or heart. Type II diabetes is the most common form of diabetes. In type II diabetes, either the body does not produce enough insulin or the cells ignore the insulin. Insulin is necessary for the body to be able to use sugar. 90 to 95% of diabetes accounts for Type II. Type II diabetes is nearing epidemic proportions, due to an increased number of older Americans, and a greater prevalence of obesity and sedentary lifestyles.[1-3]

Insulin dependent diabetes mellitus (IDDM) is accompanied by long term micro vascular, neurologic and macro vascular complications. Its daily management is not an easy task and retinopathy, nephropathy, neuropathy, and cardiovascular diseases have caused the most morbidity and mortality since the inception of insulin therapy. The prevention and control of these complications have

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been the major goals of recent research and medical practice. Sulfonylurea drugs have been the only oral therapy available for patients with non-insulin- dependent diabetes mellitus (NIDDM) in the world. Recently, however, metformin has been approved for the treatment of NIDDM. Combination therapy is logical for patients with non-insulin-dependent (type II) diabetes mellitus, because they often have poor responses to single-drug therapy. We studied the efficacy and physiologic effects of metformin and troglitazone alone and in combination in patients with type II diabetes. Angiotensin-converting–enzyme inhibitors improve the outcome among patients with left ventricular dysfunction, whether or not they have heart failure. We assessed the role of an angiotensin converting– enzyme inhibitor, ramipril, in patients who were at high risk for cardiovascular events but who did not have left ventricular dysfunction or heart failure.[3-4]

Diabetes is associated with a marked increase (by a factor of two to four) in the risk of coronary heart disease. Clinically established coronary heart disease itself is associated with an increase in mortality from coronary heart disease by a factor of three to seven, depending on the mode of presentation. The plasma cholesterol level is a strong predictor of the risk of cardiovascular events both in patients with diabetes and in patients with coronary heart disease. The high-risk statuses of these groups of patients and their need for more aggressive lipid-lowering therapy have been recognized by both the National Cholesterol.[4-5]

1.1 Education Program and the American Diabetes Association

The reduction in plasma lipids recommended by the National Cholesterol Education Program is greater for patients with coronary heart disease than for patients with diabetes. However, there were differing opinions among members of the National Cholesterol Education Program panel, with some suggesting that diabetic patients should have the same intensity of cholesterol-lowering therapy as patients with coronary heart disease. Thus, there is controversy about how aggressively to treat cardiovascular risk factors in patients with diabetes. It has been suggested that such patients should be treated as if they had established coronary heart disease. [5-6]

Additional interest has focused on the role of lipid- lowering therapy in reducing coronary heart disease in patients with diabetes since data on the efficacy of lipid-lowering therapy with simvastatin and pravastatin in patients with both diabetes and pre-existing coronary heart disease were published by the Scandinavian Simvastatin Survival Study and the Cholesterol and Recurrent Events study. In the Scandinavian Simvastatin Survival Study, lipid-lowering therapy produced a greater reduction in the rate of coronary events in diabetic subjects than in nondiabetic subjects (55 percent vs. 32 percent). However, in the Cholesterol and Recurrent Events study, there were similar reductions in diabetic and nondiabetic subjects (27 percent and 25 percent, respectively). [6-7]

One way to assess whether patients with diabetes and patients who already have clinical coronary heart disease have a similar risk of cardiovascular events is to compare the risk of such events in diabetic subjects with and without prior coronary heart disease with that in nondiabetic subjects with and without prior coronary heart disease. In previous reports, the excess risk of coronary events in patients with prior myocardial infarction (a six-to-sevenfold difference) was higher than the excess risk in diabetic patients (a two-to-fourfold difference). However, comparisons across populations are difficult. Furthermore, diabetic patients are overrepresented among patients with myocardial infarction, and diabetic patients with myocardial infarction have a worse prognosis than nondiabetic patients with myocardial infarction. Little information is available on mortality from coronary heart disease in diabetic patients without prior myocardial infarction as compared with nondiabetic patients with prior myocardial infarction. [6-7]

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2. MATERIALS AND METHODS

Protocol 1

A total of 289 obese patients who were treated with diet alone were assigned to protocol 1. After an eight-week phase during which the patients were counselled about the consumption of a hypo caloric diet, 143 patients were randomly assigned to receive metformin and 146 to receive placebo. The base-line characteristics of the two groups of patients are shown in Table 1. [7-8]

Protocol 2

A total of 632 patients with NIDDM were assigned to protocol 2: 210 were assigned to receive metformin, 209 to receive glyburide, and 213 to receive both metformin and glyburide (combination therapy). The base-line characteristics of the three groups are also shown in Table 1. The diagnosis of NIDDM was based on clinical history and the finding of a fasting plasma glucose concentration above 140 mg per decilitre (7.8 mmol per litre) on two occasions. To be included in the study all patients had to lack acceptable glycemic control (fasting plasma glucose,140 mg per decilitre) after eight weeks of dietary therapy (protocol 1) or at least four weeks of dietary therapy plus 20 mg of glyburide per day (protocol 2). Other inclusion criteria included a weight that was 120 to 170 percent of ideal (on the basis of 1983 Metropolitan Life Insurance tables), an age of 40 to 70 years, normal renal function (serum creatinine, 1.4 mg per decilitre [124 *m* mol per litre] in men and 1.3 mg per decilitre [115 *m* mol per litre] in women; and proteinuria), and normal liver function. Patients were excluded if they had any of the following: symptomatic diabetes (polyuria, polydipsia, and weight loss), symptomatic cardiovascular disease, diastolic blood pressure above 100 mm Hg during antihypertensive- drug treatment, or any concurrent medical illness. They were also excluded if they had received insulin therapy within the previous six months, used medications known to affect glucose metabolism, drank three or more alcoholic drinks per day (3 oz of alcohol per day), used illicit drugs, or had previously received metformin therapy. Therapy with estrogens and a progestin and chlorthalidone or a thiazide was permitted in patients already taking these drugs as long as the dosage was not changed during the study. The protocols were approved by the institutional review board of each participating centre, and all patients gave written informed consent for the study. [7-8]

3. RESULTS AND DISCUSSION

The studies have found substantial evidence of linkage between the glucokinase locus and maturity onset diabetes of the young but not between this locus and late onset NIDDM. 16 mutations were identified in 18 of the 32 families with maturity onset diabetes of the young; none were found in families with late onset NIDDM. They included 10 mutations that resulted in the synthesis of a truncated protein and 3 that affected RNA processing. The affected subjects with glucokinase mutations usually had mild hyperglycemia that began during childhood whereas in subjects with maturity onset diabetes of the young not due to glucokinase mutations, hyperglycemia usually appeared after puberty (figure 1).[8-9]

3.1 Adherence and metabolic control

The entire cohort study of 1441 patients was followed for a mean of 6.5 years. For sometime during the trials due to study unavailability or the investigator's decision that continuation of their treatment would be hazardous. The adherence to assigned treatment and the effectiveness of the intensive therapy in lowering blood glucose (figure 2) concentrations were reflected in the substantial difference over the time between the Glycosylated haemoglobin values of the intensive therapy group and those of the conventional therapy group. Glycosylated haemoglobin reached a nadir at six months in the patients receiving intensive therapy. Statistically significant difference in the average Glycosylated haemoglobin value was maintained after base line between the intensive therapy and conventional therapy groups in both cohorts ($p<0.001$). Although, 44 percent of the patients receiving intensive therapy achieved the goal of a Glycosylated haemoglobin value of 6.05 percent or less, at least once during the study, less than 5 percent maintained an average value in the range. [8-9]

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3.2 Metformin Dose

At the end of the five-week titration phase 78 percent of the patients assigned to metformin were taking the maximal dose (2550 mg per day), and 85 percent eventually took this dose. At week 29 the mean (±SE) fasting plasma metformin concentrations were 742±182 and 872±99 ng per millilitre in the patients taking 1700 and 2550 mg of metformin per day, respectively. During the active-treatment phase, the patients in the metformin group lost 0.6±0.3 kg of weight and those in the placebo group lost 1.1±0.2 kg (P=0.21). [9-11]

It was Studied that by week 29 the fasting plasma glucose concentration had decreased by 525 mg per decilitre (2.9±0.3 mmol per litre) to 189±5 mg per decilitre (10.6±0.3 mmol per litre) in the metformin group and increased by 6±5 mg per decilitre (0.3±0.3 mmol per litre) to 244±6 mg per decilitre (13.7±0.3 mmol per litre) in the placebo group (P<0.001). The respective changes in Glycosylated haemoglobin were -1.4±0.1 percent and 0.4±0.1 percent (P=0.001). At week 29, 22 percent of the patients treated with metformin had fasting plasma glucose concentrations of 140 mg per decilitre or less, as compared with 6 percent in the placebo group (P=0.001). The fasting plasma glucose and Glycosylated haemoglobin values during the active-treatment phase respectively. In the metformin group, the fasting plasma glucose concentration declined progressively during the metformin-titration phase, reaching a nadir that was about 55 mg per decilitre (3.1 mmol per litre) below base line between weeks 5 and 9, and remained at this level until the end of the study. The magnitude of the decline in fasting plasma glucose was correlated (r=0.551, P<0.001). [11-15]

3.3 Body Weight and Adverse Events

The study found no significant changes in body weight during either monotherapy or combination therapy. Intermittent diarrhoea developed in one patient soon after metformin was added to troglitazone. She subsequently withdrew from the study. No other adverse events were ascribed to either monotherapy or combination therapy. The mean plasma lactate concentration was normal at all times in both groups, and no patient had any abnormalities on liver-function tests during the study. [15-20]

Adding troglitazone to metformin significantly increased the rate of glucose disposal to 337 mg per square meter per minute (18.7 mmol per square meter per minute), a mean increase of 24 percent over the three-month value (P=0.04). In contradistinction, when metformin was added to troglitazone, the rate of glucose disposal increased to 304 mg per square meter per minute (16.9 mmol per square meter per minute), a mean increase of only 15 percent from three months (P=0.30). The mean increase in the rate of glucose disposal between base line and six months was 40 percent (P<0.001) in the patients who received metformin first, with troglitazone added for the second three months, and it was 77 percent (P<0.001) in those initially treated with troglitazone, with metformin added for the second three months. [20-23]

Diabetic status and history of myocardial infarction at baseline Physicians showed that, in the overall population type2 diabetes was associated with older age, higher body-mass index, a greater prevalence of hypertension, higher triglyceride levels, and lower levels of low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol. In the overall population, prior myocardial infarction was associated with male sex, smoking, older age, hypertension, obesity, higher total and LDL cholesterol and triglyceride levels, and lower HDL cholesterol levels. They also mention that the seven-year incidence of cardiovascular events in relation to diabetic status and history of myocardial infarction at base line. In both diabetic and nondiabetic subjects, a history of myocardial infarction at base line was significantly associated with an increased incidence of myocardial infarction (fatal and nonfatal), stroke (fatal and nonfatal), and death from cardiovascular causes. [20-23]

Previous research has suggested that thiazide diuretics and beta-blockers may promote the development of type 2 diabetes mellitus. However, the results of these studies have been inconsistent, and many studies have been limited by inadequate data on outcomes and by potential confounding. The association between the risk of diabetes and use of beta-blockers did not appear to be confounded by heart rate, since the mean (±SE) base-line heart rate among the 84 initially untreated subjects with hypertension who went on to

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receive beta-blockers was similar to that among the 334 initially untreated subjects who went on to receive other antihypertensive agents (70.4±1.1 and 70.2±0.5 beats per minute, respectively). Weight gain did not appear to mediate the excess risk of diabetes associated with beta-blocker use in subjects with hypertension: from base line to the six-year follow-up visit, this subgroup had a mean gain in body-mass index that was virtually identical to that in subjects with hypertension who were taking no medication (0.20±0.08 and 0.20±0.05, respectively), and this gain was less than that in subjects taking any other antihypertensive medication (0.43±0.04). [24-26]

The mean (±SD) amount of weight lost between base line and the end of year 1 was 4.2±5.1 kg in the intervention group and 0.8±3.7 kg in the control group; the net loss by the end of year 2 was 3.5±5.5 kg in the intervention group and 0.8±4.4 kg in the control group (P<0.001 for both comparisons between the groups). The cumulative incidence of diabetes after four years was 11 percent (95 percent confidence interval, 6 to 15 percent) in the intervention group and 23 percent (95 percent confidence interval, 17 to 29 percent) in the control group. During the trial, the risk of diabetes was reduced by 58 percent (P<0.001) in the intervention group. The reduction in the incidence of diabetes was directly associated with changes in lifestyle. [24-26]

Pioglitazone lowers glycated haemoglobin values and has been shown to preserve beta-cell function, leading to long-lasting glycemic control. Moreover, its favourable effects on the lipid profile and reported associated reductions in rates of death, myocardial infarction, and stroke make Pioglitazone a well-validated treatment option. Furthermore, the lack of data on long-term cardiovascular safety and the need for parenteral administration of GLP-1 agonists (which were suggested as subsequent therapy for the patient described in the vignette) lead us to advise Pioglitazone as the next therapeutic step, after metformin, in this young patient. They also recommend the addition of Pioglitazone as a third agent to the regimen. Although this approaches, is not contraindicated and given the adverse effects of weight gain. The risk of fractures of long bones and the possibility of bladder cancer with long term use of Pioglitazone in young person, favour other therapeutic options. [24-28]

The lack of exercise, a poor diet, current smoking, and abstinence from alcohol were all associated with a significantly increased risk of diabetes even after adjustment for the body-mass index. The inverse association between physical activity and the risk of diabetes was much stronger without body-mass index in the model (the relative risk of diabetes for women who exercised for seven or more hours per week as compared with women who exercised for less than half an hour was 0.48; 95 percent confidence interval, 0.38 to 0.61). Analyses stratified according to the body mass index showed that the associations between diabetes and diet, physical activity, smoking status, and alcohol use were generally similar among women with a normal body-mass index, those who were overweight, and those who were obese. Further adjustment for the body-mass index as a continuous variable in each stratum did not substantially alter the results. In addition, the individual components of the dietary score were independently and significantly associated with the risk of diabetes when they were entered into the same model. [24-28]

It was disclosed that a total of 327 patients in the losartan group reached the primary end point, as compared with 359 in the placebo group (risk reduction, 16 percent; P=0.02). Losartan reduced the incidence of a doubling of the serum creatinine concentration (risk reduction, 25 percent; P=0.006) and end-stage renal disease (risk reduction, 28 percent; P=0.002) but had no effect on the rate of death. The benefit exceeded that attributable to changes in blood pressure. The composite of morbidity and mortality from cardiovascular causes was similar in the two groups, although the rate of first hospitalization for heart failure was significantly lower with losartan (risk reduction, 32 percent; P=0.005). The level of protein urea declined by 35 percent with losartan (P<0.001 for the comparison with placebo). Diabetic nephropathy is the leading cause of end-stage renal disease. Interruption of the rennin angiotensin system slows the progression of renal disease in patients with type 1 diabetes, but similar data are not available for patients with type 2, the most common form of diabetes. We assessed the role of the angiotensin-II–receptor antagonist losartan in patients with type 2 diabetes and nephropathy.[24-28]

Diabetic type 2 patients with irbesartan was associated with a risk of the primary composite end point that was 20 percent lower than that in the placebo group (P=0.02) and 23 percent lower than that in the amlodipine group (P=0.006). The risk of a doubling of the

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serum creatinine concentration was 33 percent lower in the irbesartan group than in the placebo group (P=0.003) and 37 percent lower in the irbesartan group than in the amlodipine group (P<0.001). Treatment with irbesartan was associated with a relative risk of end-stage renal disease that was 23 percent lower than that in both other groups (P=0.07 for both comparisons). These differences were not explained by differences in the blood pressures that were achieved. The serum creatinine concentration increased 24 percent more slowly in the irbesartan group than in the placebo group (P=0.008) and 21 percent more slowly than in the amlodipine group (P=0.02). There were no significant differences in the rates of death from any cause or in the cardiovascular composite end point. [24-28]

Glycemic change in the first year, there was a similar reduction in the mean fasting plasma glucose values in the metformin and lifestyle-intervention groups, whereas the values rose in the placebo group. The values rose in parallel in all three groups in subsequent years. There was a similar temporal pattern in the values for Glycosylated haemoglobin, except that the values in the metformin group were in between those in the lifestyle-intervention and placebo groups. Figure 4 shows the percentage of participants who had normal glucose concentrations (fasting values, post-load values, and both) at each annual examination. Metformin and the lifestyle intervention were similarly effective in restoring normal fasting glucose values, but the lifestyle intervention was more effective in restoring normal post-load glucose values.[24-28]

The mean fasting glucose level decreased more in the low-carbohydrate group than in the low-fat group at six months (–9±19 percent vs. –2±17 percent, P=0.02). This difference remained significant after adjustment for base-line variables (P=0.004). However, the greater reduction in serum glucose levels in the low-carbohydrate group was limited to diabetic subjects, with no significant change in the levels in no diabetic subjects on either diet. Assignment to the low-carbohydrate diet was no longer a significant predictor of a decrease in glucose levels after adjustment for the amount of weight lost (P=0.12). There was a trend toward a greater decrease in mean Glycosylated haemoglobin values in diabetic subjects on the low-carbohydrate diet, as compared with those on the low-fat diet (P=0.06). By six months, seven subjects in the low-carbohydrate group had had dose reductions in oral hypoglycaemic agents or insulin. In comparison, one subject in the low-fat group had a dose reduction in insulin and one subject became oral therapy. Insulin sensitivity was measured only in subjects weight-loss strata demonstrated a uniformly, but non significantly, greater improvement in insulin sensitivity among those on the low-carbohydrate diet within each stratum. [24-30]

They found that one subject on the low-carbohydrate diet was hospitalized with chest pain, which was ultimately determined to be unrelated to myocardial ischemia. One subject on the low-carbohydrate diet died from complications of hyperosmolar coma, which was thought to be due to poor compliance with drug therapy for diabetes. There was no clinically significant change in the uric acid level in either group. [24-30]

The multicenter double-blind, randomized Bergamo Nephrologic Diabetes Complications Trial (BENEDICT) was designed to assess whether angiotensin converting enzyme inhibitors and non-dihydropyridine calcium-channel blockers, alone or in combination, prevent microalbuminuria in subjects with hypertension, type 2 diabetes mellitus, and normal urinary albumin excretion. Persistent micro albuminuria developed in 17 of the 300 subjects receiving trandolapril plus verapamil (5.7 percent), as compared with 30 of the 300 subjects receiving placebo (10.0 percent). Kaplan–Meier curves for these two treatment groups clearly separated at three months. The estimated acceleration factor when we controlled for predefined baseline variables was 0.39 (95 percent confidence interval, 0.19 to 0.80; P=0.01) in the trandolapril-plus-verapamil group as compared with the placebo group. Thus, the combination of trandolapril and verapamil significantly delayed the onset of micro albuminuria, by a factor of 2.6. [30-31]

The unadjusted comparison provided similar results. After separate adjustment for systolic and diastolic blood pressure at follow-up visits, the acceleration factor accounting for systolic blood pressure was 0.46 (95 percent confidence interval, 0.22 to 0.93; P=0.03) and that accounting for diastolic blood pressure was 0.46 (95 percent confidence interval, 0.22 to 0.95; P=0.04).[30-33]

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4. CONCLUSIONS

Intensive therapy effectively delays the onset and slows the progression of diabetic retinopathy, nephropathy, and neuropathy in patients with IDDM. Metformin and troglitazone have different mechanisms of action, yet are equally effective in lowering plasma glucose concentrations in patients with type II diabetes. Combination metformin and troglitazone therapy results in further improvement in glucose control, without stimulation of insulin secretion and with reversal of the two principal path physiologic abnormalities in this disorder. Patients with type 2 diabetes who have not had a myocardial infarction have a risk of infarction similar to that among nondiabetic patients who have had a prior myocardial infarction. This observation, combined with the results of previous studies showing the efficacy of lipid-lowering therapy in diabetic patients with coronary heart disease and the high mortality (including pre hospital mortality) after myocardial infarction, suggests that all persons with diabetes could be treated as if they had prior coronary heart disease. The best way to answer this question more definitively would be to conduct a clinical trial comparing the effect of different levels of lipid-lowering therapy on coronary heart disease in diabetic subjects. Clinical trials, however, are very expensive and take many years to complete. In the short term, further confirmation of our findings may come from other observational studies.

Results have three main implications. First, the association between hypertension and the development of diabetes should prompt research on shared risk factors and alert clinicians that there is an easily identified group at high risk for diabetes. Second, concern about increasing the risk of diabetes should not discourage physicians from prescribing thiazide diuretics for the treatment of hypertension in adults. Third, the use of beta-blockers appears to increase the risk of diabetes, but this adverse effect must be weighed against the proven benefits of beta-blockers in reducing the risk of cardiovascular events. Type 2diabetes can be prevented by changes in the lifestyles of high-risk subjects.

In subjects with type 2 diabetes and hypertension but with normoalbuminuria, the use of trandolapril plus verapamil and trandolapril alone decreased the incidence of microalbuminuria to a similar extent. The effect of verapamil alone was similar to that of placebo.

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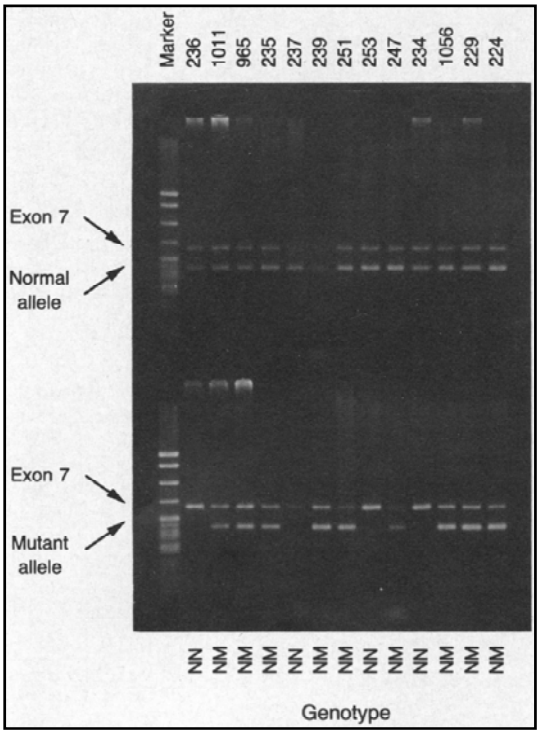

Figure 1Allele specific amplification of the Glu-Gln mutation at Codon 300 in 13 members of the third generation of family F51[3]

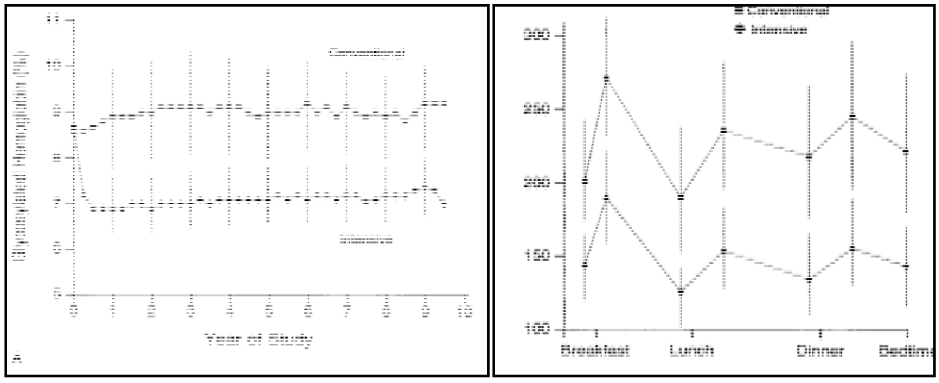

Figure 2 Measurement of glycosylated hemoglobin and blood glucose in patients with IDDM receiving intensive or conventional therapy[3]

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Country	No. of Papers			% Share of Papers			Rank		
	99-08	1999	2008	1999-08	1999	2008	99-08	1999	2008
USA	74503	4813	9547	29.61	30.48	27.48	1	1	1
UK	21124	1335	2895	8.4	8.45	8.33	2	2	2
Japan	16277	1239	2042	6.47	7.85	5.88	3	3	3
Germany	14178	1033	1793	5.64	6.54	5.16	4	4	4
Italy	11196	660	1633	4.45	4.18	4.70	5	6	6
France	10093	820	1290	4.01	5.19	3.71	6	5	7
China	7413	125	1747	2.95	0.79	5.03	7	14	5
Spain	7202	359	1084	2.86	2.27	3.12	8	8	8
Sweden	6035	467	819	2.86	2.96	2.36	9	7	11
Netherlands	5832	342	895	2.86	2.17	2.58	10	9	9
India	4824	215	838	2.86	1.36	2.41	11	12	10
Switzerland	3624	220	474	2.86	1.39	1.36	12	11	16
Turkey	3436	120	558	2.86	0.76	1.61	13	16	14
Belgium	3287	244	442	2.86	1.55	1.27	14	10	17
Brazil	3231	105	672	2.86	0.66	1.93	15	18	12
South Korea	3061	111	606	2.86	0.70	1.74	16	17	13
Poland	2864	142	383	2.86	0.9	1.10	17	13	18
Taiwan	2831	125	475	2.86	0.79	1.37	18	15	15
Russia	758	61	108	2.86	0.39	0.31	19	19	20
South Africa	697	31	110	2.86	0.2	0.32	20	20	19
World	251590	15790	34744	100	100	100			

Table 1Global publication output, publication share and top 18 most productive countries in diabetes research [1]

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Period	TP	TC	ICP
1999	215	715	15
2000	227	871	18
2001	276	1027	22
2002	390	1654	39
2003	426	1862	54
2004	469	2883	59
2005	543	3260	70
2006	652	3840	75
2007	788	3295	114
2008	838	1271	120
1999-08	4824	20678	586

TP=Total papers; TC=Total citations; ICP=International collaborative papers

Table 2 Publication output and impact of Indian research output in diabetes[1]

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