THE ROLE OF LIFE EVENTS IN SHORT TERM METABOLIC CONTROL OF NON - INSULIN DEPENDENT DIABETES MELLITUS

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ABSTRACT

For present study 2 groups were first chosen, each consisting of 50 NIDDM patients with matched age, sex and social class. One group (i.e. Group A) had patients with poor metabolic control while other group i.e. Group B had patients with adequate metabolic control. Investigators found that female Group A patients had experienced higher mean number of life events in the one month period proceeding the date of study when compared with Group B females. Similar comparison in males showed increased experience of life events during the six month period. Regardless of sex, Group B patients were not found to differ from matched chronic disease patients (i.e. Group C) regarding the mean number of life events experienced during six month period. Male Group B patients, unlike females, experienced higher number of life events during past six months when compared with male matched disease free subjects (i.e. Group D). Adverse events seemed to have predominant role in diabetes control.

Key Words : Metabolic control, diabetes, NIDDM, life events

Role of psychosocial factors in diabetes remains a controversial issue. Most recent researches on this issue concentrates on the role of psychological stress in metabolic control (i.e. blood glucose level control) of diabetes mellitus. Since it is generally accepted that satisfactory metabolic control of diabetes mellitus helps to prevent acute and chronic complications of diabetes (Malins, 1968), research on this issue has important therapeutic implications.

Presently studies on role of psychological stress often use the concept of life events occurring in the diabetes patients as elicited by using various life events check list or interview methods. Chase & Jackson (1981) found that life stress as defined by a list of events requiring psychosocial readjustment is correlated with both glycosylated haemoglobin (HbA_{1c}) and fasting blood glucose, which suggested that psychological stress has impact on both long term (HbA_{1c}) and short term (fasting blood glucose) indices of glycaemic control. However strongest corroboration came when Rubinstein et al. (1993) showed that diabetic patients (both IDDM and NIDDM) in the Tel - Aviv city showed poor metabolic control during the Gulf war.

However most of the research work was performed using IDDM patients who were fewer in number than patients of NIDDM. Thus it is difficult to conduct controlled study with IDDM patients. Metabolic control in IDDM is much more seriously affected (often dramatically) by therapeutic noncompliance than NIDDM. Psychological factors also influence compliance (Helz & Templeton, 1990), thus studies that have not been controlled for compliance

(difficult in IDDM patients in our country due to high cost of insulin) needs to be interpreted with caution. Famous clinicians like Osler (1892) had concluded that NIDDM subjects were more responsive to psychological stress, thus study using such subjects is clinically worthwhile.

Taking these issues into consideration the present study aimed to compare the mean number of life events (total and adverse separately) in NIDDM patients maintaining adequate metabolic control with the patients showing poor metabolic control. Comparisons were also intended to be made with chronic disease (excluding diabetes) patients and normal subjects. All subjects chosen were needed to be free from psychiatric ailment or any disease related complication which might act as a confounding factor (Llyod et al., 1991) and had good therapeutic compliance.

MATERIAL AND METHOD

Diabetic subjects for the study were obtained from Medicine Department, through inter departmental liaison. The study was conducted over the period from 2nd January, 1996 to 3rd April, 1997. The diabetic patients were referred to Psychiatry Department provided they were suffering from NonInsulin Dependent Diabetes Mellitus (NIDDM) for a period more than six months but less than two years. The patients needed to have shown adequate diabetic control on last monthly visit and also in for at least five months period prior to the last month's visit. The patients were also needed to be compliant with therapeutic regimen (oral hypoglycaemic medication and diet control), not requiring insulin, between age group 41-55 years, literate and able to understand Bengali Questionnaire. They also needed to be free from past history of psychiatric illness, no other major disease at the moment except diabetes and have no complication of diabetes. They also needed to have been on regular follow up for at least last six months with regular (monthly) fasting sugar estimate record. Blood sample for fasting sugar estimate were taken at nearly same time of the day with patient in similar physical and mental condition and without the influence of factors that might alter sugar level (i.e. no physical exertion, no infection mediated disease before and during the collection of blood sample). The patient's current fasting sugar level was estimated on the same date but was kept secret at present from the patient. Investigators also kept themselves unaware of the sugar level. Patients did not know about the aim of the present study. Each subject (173 in total) was interviewed, and was screened by GHQ-60 (Goldberg, 1972; Sarkar, 1990, for Bengali version) to exclude psychiatric cases from the study. The patients that remained (142), were then requested to fill up the Life Events scale for Life events during last six months (Paykel et al., 1971; Bengali Version Sarkar, 1990), after explaining its use. After the patients completed the questionnaire they were interviewed as to the exact timing of the events reported and its nature as per subjects opinion (i.e. adverse or not). The patients answers were corroborated from their relative and if severe discrepancy was noted investigators rejected that subject from the study (3 were thus excluded). The demographic characteristics of the 139 remaining subjects were recorded (i.e. age in years, sex, social class (Kuppuswamy, 1962) and each subject was numbered serially on first come basis. Now the present fasting sugar level of the patients were recorded and those whose fasting sugar level were found to be greater than or equal to 150mg/100ml (10mg% higher than normal cut off for control level) were considered to be having poor metabolic control and assigned to Group A (59 subjects) while those with fasting sugar level 60-130 mg/100 ml were considered to have acceptable diabetes control and assigned to Group B (76 subjects). Subjects with sugar levels 131-149 mg/100 ml were not assigned to any group and dropped from the study (4 dropped). Now attempt was made to match the 59 Group A subjects with 76 Group B subjects, matching was done first on basis of social class and sex then according to age (i.e. closest age match was sought). If close age matching appeared to be impossible in a given patient ±3 years period was taken as matching age for that case. Thus 59 A and B group pairs remained. 50 pairs of subjects

were chosen to be included in the final study by the use of random number table (Kirkwood, 1988). After this 50 chronic disease patients i.e. Group C (any chronic medical disease except diabetes) were chosen from a sample of 80 chronic disease patients (on long term medication) attending medicine OPD to match Group A subjects. Group C consisted of 30 hypertensive, 7 asthmatics, 5 hypothyroid patients and 8 patients suffering from ischaemic heart disease. Lastly physically normal patients (i.e. Group D) were chosen to match Group A from a sample of 80 normal subjects chosen among relatives and volunteers. Group C and D subjects were also subject to similar exclusion and inclusion criteria as described from Group A and B except that Group C and D subjects did not have diabetes. Life events were recorded for Group C and D subjects in the same way as for Group A and B. It may be noted that study date or date of study was the date when a particular patient was examined by us and all time periods for that patient was evaluated with that date as reference.

Mean number of total life events during the six month period prior to the date of examination by investigators were compared between Group A and Group B, Group B and Group C and Group B and Group D. Then the analysis was repeated for mean number of adverse life events during past six month period. Lastly Group A and B subjects (not C and D Group as no clinically relevant change was expected) were compared with regard to mean number of life events (total and adverse separately) during past one month period. All the comparisons were done using paired t-test. Since difference of less than one life event is not clinically relevant, investigators used this as cut off for Confidence Interval Analysis. No comparison was attempted between Group C and Group D because - i) present study did not intend to show whether experience of life events in chronic disease patients differed from normal subjects. ii) such comparison would increase the number of t-tests with associated problems (explained in results section). Indeed for similar reasons investigators avoided comparing Group A with Group C and D. Group B Subjects were taken

as a representative of diabetic population which can be used as baseline for comparison with non-diabetics. Lastly, each group was subdivided into three subgroups on the basis of sex of subjects i.e. male subgroup, female subgroup and overall subgroup (male & female subjects) and above mentioned comparisons was repeated for each subgroup individually.

RESULTS

Subjects in Group A (N=50) (diabetic patients showing poor metabolic control at present) were matched with Group B (Diabetic patients showing adequate metabolic control at present), Group C (Patients suffering from chronic medical disorders except diabetes) and Group D (Normal subjects i.e. with no major physical disease) subjects. Matching was done with respect to sex, social class and age (within ±3 years). The mean age of Group A subjects was 45.66±4.46 years, for males in Group A mean age was 45.48±4.24 years, while for female it was 45.90±4.24 years.

The demographic profile of Group A subjects (which due to design of the present study was identical of Group B, C and D subjects) has been shown in table 1. Since Chi-square test was not significant hence the variation of number of male and female subjects in different social classes was due to chance variation and not due to any specific demographic trend in our sample.

Table 2 and table 3 shows comparison of experience of life events between different groups. For all comparisons paired t-test was used. For present study data, 24 separate t-test

TABLE 1
DEMOGRAPHIC PROFILE OF GROUP A (ALSO OF B,C,D AS THESE ARE MATCHED WITH A)

Social class	Male (N=29)	Female (N=21)	Total (N=50)
Upper socioeconomic class,	6	3	9
Middle socioeconomic class,	8	5	13
Lower socioeconomic class	15	13	28

$X^2 = 0.57$, d.f. =2, N.S.

TABLE 2
LIFE EVENTS (TOTAL AND ADVERSE) EXPERIENCED DURING THE PAST SIX MONTH PERIOD BY GROUPS A,B,C,D (OVERALL, MALE, FEMALE SUBJECTS SEPARATELY)

Groups	Number of subjects	Mean number of life events (total and adverse) experienced during the past six month period ±SD	Difference between mean of respective category (i.e. overall, male, female) A-B, B-C, B-D	S.E.	d.f.	t	p	CI-95
Group B	50	0.32±0.62	-	-		-	-	-
Overall		0.18±0.48	-	-		-	-	-
Group B	29	2.03±1.12	-	-		-	-	-
Male		1.48±1.06	-	-		-	-	-
Group B	21	2.00±1.48	-	-		-	-	-
Female		1.38±1.40	-	-		-	-	-
Group A	50	3.70±1.82	1.68	0.31	98	5.35	<0.001*	1.06-2.3*
Overall		3.26±1.69	1.82	0.29		6.21	<0.001*	1.24-2.4*
Group A	29	3.69±1.63	1.66	0.37	56	4.52	<0.001*	0.92-2.4
Male		3.48±1.68	2.0	0.37		5.42	<0.001*	1.26-2.74*
Group A	21	3.71±2.10	1.71	0.56	40	3.05	0.002<p <0.005NS	0.58-2.84
Female		2.95±1.69	1.57	0.48		3.28	0.002<p <0.005NS	0.6-2.54
Group C	50	2.00±1.69	0.02	0.3	98	0.07	>0.9NS	-0.58-0.62
Overall		0.84±0.89	1.16	0.22		0.51	0.6<p <0.7NS	-0.36-0.6
Group C	29	1.97±1.76	0.06	0.39	56	0.15	0.8<p <0.9NS	-0.72-0.84
Male		1.34±1.26	0.06	0.31		0.46	0.6<p 0.7NS	-0.48-0.76
Group C	21	2.05±1.63	-0.05	0.48	40	-0.10	>0.9NS	-1.02-0.92
Female		1.29±1.06	0.09	0.38		0.23	0.8<p <0.9NS	-0.68-0.86
Group D	50	0.84±0.89	1.18	0.22	98	5.38	<0.001*	0.74-1.62
Overall		0.54±0.76	0.9	0.2		4.48	<0.001*	0.5-1.3
Group D	29	0.86±0.88	1.17	0.26	56	4.42	<0.001*	0.65-1.69
Male		0.55±0.78	0.93	0.24		3.81	<0.001*	0.45-1.41
Group D	21	0.81±0.93	1.19	0.38	40	3.12	0.002<p <0.005NS	0.42-1.96
Female		0.52±0.75	0.86	0.35		2.48	0.01<p <0.02NS	0.15-2.43

TABLE 3
LIFE EVENTS (TOTAL AND ADVERSE) EXPERIENCED DURING THE PAST ONE MONTH PERIOD BY GROUPS A & B(OVERALL, MALE, FEMALE SUBJECTS SEPARATELY)

Groups	Number of subjects	Mean number of life events (total and adverse) experienced during the past six month period ±SD	Difference between mean of respective category (i.e. overall, male, female) A-B	S.E.	d.f.	t	p	CI-95
Group B Overall	50	0.320±0.62 0.18±0.48	- -	- -	- -	- -	- -	· ·
Group A Overall	50	2.28±1.46 2.18±1.48	1.96 2.0	0.22 0.22	98	8.74 9.09	<0.001* <0.001*	1.52-2.4* 1.36-2.44*
Group B Male	29	0.34±0.67 0.21±0.56	- -	- -	- -	- -	- -	- -
Group A Male	29	2.21±1.37 2.14±1.41	1.87 1.93	0.28 0.28	56	6.6 6.85	<0.001* <0.001*	1.31-2.43* 1.37-2.49*
Group B Female	21	0.29±0.56 0.14±1.41	- -	- -	- -	- -	- -	- -
Group A Female	21	2.38±1.60 2.24±1.61	2.09 2.10	0.37 0.36	40	5.65 5.83	<0.001* <0.001*	1.34-2.84* 1.37-2.83*

were needed. With multiple comparisons the probability of a false positive result (Type 1 error) would be increased. Thus, it was necessary to make some adjustment for multiple comparisons to retain an over all type-1 error rate of 5% i.e. p<0.05. To do this, investigators used the Bonferroni method, i.e. dividing the overall type 1 error rate by number of comparisons and used the resultant p value as the level of probability for declaring statistical significance (Freeman & Tyrer, 1992).

For present study resultant 'p' value was 0.05/24=0.002083=0.0021 (approximately). Thus each separate test would be considered significant at 5% level if p<0.0021.

Investigators did not use ANOVA (which would have avoided such conservative type I error rate), due to heterogeneity of variance. Use of confidence intervals along with significance thus helped to clarify the results obtained.

Table 2 shows that Group A subjects (overall and male subgroup) experienced significantly higher number of life events (total and adverse) when compared to Group B subjects.

Confidence Interval Analysis upheld the result of significance test in all cases except in male Group A subjects for total life events. Females of Group A when similarly compared did not show any significant difference in experience of life events. Adverse life events showed higher significance levels during the comparisons. Group B and Group C where compared showed no significant difference in experience of life events irrespective of gender and event type under comparison.

Group B subjects when compared with Group D showed significantly higher experience of life events (total and adverse) for comparison between overall and male subgroup. However, this significant result was not upheld by Confidence Interval Analysis.

Table 3 which shows life events (total and adverse) experienced in past one month by Group A and B (Overall, male, female subjects i.e. three subgroups separately) indicates that -

Group A (overall) subjects experienced significantly higher number of total and adverse life events compared to Group B (overall). Confidence interval upheld the clinical relevance

of the observed differences. The difference was more prominent for adverse events.

Male subjects of Group A experienced significantly higher number of total and adverse life events when compared to male subjects of Group B. The difference was more prominent for adverse events. Confidence interval upheld the clinical relevance of the observed difference.

Female subjects of Group A experienced significantly higher number of total and adverse life events when compared to female subjects of Group B. The difference was more prominent for adverse events. Confidence interval upheld the clinical relevance of the observed difference.

It could also be seen that level of significance was more for males than in females.

DISCUSSION

Present study indicated marked genderwise difference regarding the role of life events experienced by diabetic subjects in influencing diabetes control. While females showed the relationship only in short term i.e. during the past one month period, males showed it in both short and long term i.e. during past six month period.

Effect of life events does vary with sex (Paykel, 1983). While Lloyd et al. (1991) found that effect of psychological stress on diabetes was independent of sex, Stenstorm et al. (1993) had found more negative life events in males alone. Perhaps in present study, female subjects were affected only in short term period or by very recent life events only. Alternatively females may have better adaptability to life events when they occur spaced within slightly longer periods (i.e. six month in the case of present study). Alternatively male diabetics were more responsive to life events.

Grant et al. (1974) had attempted to look into the role of life events and fluctuations in the course of diabetes mellitus in 15 IDDM and 22 NIDDM patients and found relationship with events (mainly, the events of negative nature) and had suggested that there may be two separate types of diabetic patients i.e. life event responsive and non-responsive.

Several studies have reported the effects of behavioural or psychosocial interventions on glucose level control in diabetic patients which may be interpreted as further evidence of interaction between emotional stress and metabolic control in diabetes. Surwit & Feinglos (1983) have shown improvement in blood glucose control using relaxation therapy in NIDDM but not in IDDM patients.

The major short coming of the present study was that it did not use the laboratory investigation considered to be most accurate measure of metabolic control by Western researchers i.e. glycosylated haemoglobin (HbA_{1c}). HbA_{1c} can give an idea of degree of metabolic control in at least last 6-12 weeks and thus serves as a measure of long term metabolic control. Investigators could not use this as being an expensive investigation, very few can afford to get it done. Hence physicians of institution to which investigators belong use fasting sugar level as guide to metabolic control (short term) and provided diet, physical and mental condition and the time of day at which blood sample is taken remains constant in a given patient, even this can give an accurate picture. Investigators had modified the cutoff sugar levels to avoid misplacing a patient as regards the metabolic control status. Cut off levels and statistical interpretation makes the results of the present study more reliable than that might be expected when not using HbA_{1c}. Hall & Besser (1989) had stated that fasting blood glucose concentrations in NIDDM patients correlates well with HbA_{1c} level. Considering that Barglow et al. (1985) had emphasised the importance of using several measures of diabetes control (including fasting glucose) to determine stress control relationship, the findings of the present study do have clinical relevance.

However, the present study consisted of subjects sent to the investigators by physicians and not self referred and bias was thus possible. Use of highly selective criteria to choose study subjects might have added to the bias. Small sample size, lack of follow up study, lack of event wise analysis were some other

shortcomings of the present study.

In conclusion, it may be stated that the present study indicated that patients suffering from poor control of diabetes experienced higher number of life events (specially adverse type) with significant gender wise difference. Gender related difference found needs further investigation. This study also indicated higher incidence of life events in chronic medical disorder patients than normals, thus separate studies may be contemplated about these diseases as well. Investigators hope that this will perhaps help in providing patients of chronic diseases like diabetes a comprehensive management that will also address the psychosocial issues.

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