ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Effect of Glimepiride on Health Related Quality of Life in Type 2 Diabetes Mellitus.

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ABSTRACT

Diabetes treatment regimens often require changes of lifestyle and behaviour that influence patients' daily functioning and well-being. Therefore, 'health-related quality of life' (HRQoL) is a valuable outcome indicator alongside traditional biomedical measures. Glimepiride is one of the commonly used sulfonylurea oral anti-diabetic drug in type 2 diabetes mellitus patients. This community based cross sectional study was carried out on 424 type 2 diabetes mellitus patients on different oral anti-diabetic drugs to assess the influence of glimepiride on HRQoL. Short-Form 36 (SF-36 of the Medical Outcome Study Group) was used to measure the 'health-related quality of life' (HRQoL). Inter group comparison of the mean SF-36 scores was done using independent samples 't' test in SPSS version 16.0. SF-36 score was lower in patients being treated with gimepiride along with other oral anti-diabetic drugs (54.29 ± 22.43) as compared to those treated without glimepiride (69.09 ± 20.57). SF-36 and its eight domain scores had significant association with the treatment option along with other key factors like duration of the disease, comorbidity, coexisting complications, and habitual physical activity. The choice of the oral anti-diabetic drug influences the 'health-related quality of life' in patients of type 2 diabetes mellitus. HRQoL was higher in patients using oral anti-diabetic drugs that had better tolerability and less fear of hypoglycemia.

Keywords: Glimepiride**,** health-related quality of life, short form – 36, type 2 diabetes mellitus

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ISSN: 0975-8585

INTRODUCTION

Diabetes mellitus is one of the most common chronic diseases across the world and number of diabetic patients is on rise. Globally, the number of people is expected to rise to 552 million by 2030. Most people with diabetes live in low- and middle-income countries like India, and these countries will also see the greatest increase over the next 19 years [1]. The recently published ICMR-INDIAB national study reported that there are 62.4 million people with type 2 diabetes (T2DM) and 77 million people with pre-diabetes in India[2]. These numbers are projected to increase to 101 million by the year 2030 [1]. There is an apparent epidemic of diabetes, which is strongly related to lifestyle and economic change [3]. Type 2 diabetes mellitus constitute about 90% of all cases.

The conventional outcome assessment for diabetes treatment relies on laboratory indicators and complications of the disease. The exclusive reliance on clinical outcomes, however, does not necessarily reflect patients' perceptions of their health [4,5]. Moreover, diabetes treatment regimens that require changes of lifestyle and behavior can influence patients' daily functioning and well-being. Therefore, 'health-related quality of life' (HRQoL) is a valuable outcome indicator alongside traditional biomedical measures.

'Health-related quality of life' (HRQoL) is a subjective assessment of health status that includes relevant aspects such as general health, physical, emotional, cognitive, and role functioning, as well as social well-being and functioning[6]. 'Quality of life' (QoL) has been defined by W.H.O as 'individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. 'Quality of life' evaluation has emerged as an important outcome measure for chronic disease management. In this context, a large variety of generic [7] and disease specific [8] quality of life assessment tools have been validated and evaluated in diverse population settings.

Most of the existing QoL studies have been developed in western population, which are socially, culturally and economically different from Indian participants and work from India on the subject is scarce. Further, very few studies have been done in India to study the influence of one of the commonly used sulfonylurea oral anti-diabetic drug, glimepiride on HRQoL in type 2 diabetes mellitus patients. With this background this study was initiated to assess the influence of glimepiride on HRQoL in patients with type 2 diabetes mellitus and to compare the changes in HRQoL, in patients treated with and without glimepiride.

MATERIAL AND METHODS

Study design and setting

This is a community based cross-sectional study that was carried out among the patients attending the diabetic check-up camps in Berhampur town, in the state of Odisha from April 2013 to June 2014.

Sample size and sampling techniques

The study population was patients attending the diabetes checkup camps. Assuming the prevalence of use of sulfonylureas in type 2 diabetes mellitus to be 40% in the Indian population from available literature, an absolute precision of 5% at 95% confidence level, the sample size was estimated to be 369. The response rate was expected to be 87% from similar studies done earlier. So, the final sample size was calculated to be 424. Systematic sampling method was employed to select the patients from each diabetic check up camp. For a patient turnout of 130 in each camp and prevalence of type 2 diabetes of 95%, for a sample size to be 424, the sampling interval was calculated to be 3. So, every 3^{rd} patient with type 2 diabetes mellitus confirming to the inclusion and exclusion criteria was included in the study from 10 diabetes check-up camps during the study period. The first patient interviewed was determined in each camp from the camp register using simple random sampling method. The next patient selected was identified systematically $(H/h)^{th}$ All the patients participating in the study were explained clearly about the purpose and nature of the study in the local language (odia) or in any other language they could understand. Written informed consent was obtained before including them in the study. All the included patients were interviewed only once and their prescriptions were checked individually for the necessary information to fill up the case record forms. During selection of the patients in the diabetes check-up camps, the inclusion criteria included definite diagnosis of type 2 diabetes mellitus, absence of ketosis or other severe stresses in the past 6 months, on treatment with

one or more oral anti-diabetic drug for at least 3 months, aged 18 years and above as well as willing to participate in the study.

The exclusion criteria included ketoacidosis or hyperosmolar coma, severe cerebrovascular diseases, severe hepatic or renal insufficiency, progressive, systemic diseases like end stage renal disease, psychiatric disorders, pregnant (gestational diabetes) or lactating women, history of allergy to oral anti-diabetic drugs or sulfa drugs, history of alcoholism or drug abuse, patients on insulin therapy and patients unwilling to participate in the study.

Data collection procedures

The data was collected by trained data collectors who were supervised daily. The patients, who were not able to give time in the first visit, were revisited for two more times.

Data processing and analysis

The data gathered through the structured case record form were entered and analyzed using SPSS version 16.0. Besides, the data were checked and cleaned for their completeness and errors in data entering. To explain the study population in relation to the relevant variables, descriptive statistics were used. Independent samples 't' test was used to compare the mean SF-36 scores. p value ≤ 0.05 was taken to be statistically significant.

Study instrument

A predesigned, semi-structured interview schedule was used. At interview, data was collected on personal details, treatment history, and relevant clinical history. A standardized questionnaire – the Medical Outcome Study Groups' SF-36 v2 (English/local language - oriya translated version), was used to measure 'health-related quality of life' (HRQoL) of patients. This questionnaire has eight domains, viz. Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role Emotional (RE), and Mental Health (MH). The scoring manual of Rand - 36 item health survey (version 1.1) was used for calculating the scores[9,10].

Ethical consideration

Ethical clearance was obtained from the Institutional Ethics Committee of MKCG Medical College, Berhampur, Odisha. The data collectors obtained the information after obtaining verbal consent from each participant. The respondents were informed that they could refuse giving information at any time they wanted and they were also informed that they could ask anything about the study. The prospects of this study for improving understanding of diabetes mellitus were explained to the participants and informed consent was obtained from the interviewing subjects.

RESULTS

Out of the 424 respondents, 186 were females and 238 were males. The mean age of the respondents was 46.2 years (M = 47.5 years; F = 51.2 years). 76% of the respondents were more than 40 years. The mean duration of diabetes was 5.84 ± 4.23 (SD) years. 32% of the respondents had normoglycemia at the time of taking their SF-36 scores. Concomitant disease was seen in 67.9% patients. The most common comorbidity was hypertension (36.3%) followed by dyslipidemia. The most common complication present was neuropathy (21.4%). 45.6% of male and 58.4% of female respondents were either overweight or obese. 41.3% of study subjects undertook regular physical activity.

The average number of oral anti-diabetic drug prescribed per patient was 2.25. Most commonly prescribed oral anti-diabetic drug was metformin (44.5%), followed by sulfonylureas (38.9%), thiazolidinediones (20.3%), alfa gucosidase inhibitors (10.4%), and dipeptidyl peptidase - 4 inhibitors (6.03%). Multiple drugs were used in 71.1% patients. Out of the patients receiving multiple drugs, two drug therapies was common in 63.8% followed by three drugs in 24.2% and four drugs in 12%. Most common two drug combination was glimepiride + metformin, followed by vildagliptin + metformin. Most prevalent three drug

therapy was glimepiride + metformin + pioglitazone. Glimepiride + metformin + pioglitazone + voglibose was the most common four drug combination used. Glimepiride were being used by 38.4% of the patients along with other oral anti-diabetic drugs. For monotherapy metformin was most commonly used followed by glimepiride.

HRQoL was assessed using the SF-36 questionnaire (v2). 65.6% male and 59.3% female subjects reported that their health status had worsened or that there had been no changes as compared to that experienced one year back. Self-appraisal of current health status was better among males (92%) than among female (74%) respondents. The SF-36 score was 56.82 ± 23.47 in females and 67.65 ± 20.84 in males. Out of eight domains in the SF-36 questionnaire, the two most affected domains were 'general health' (GH) and 'vitality' (VT). The two domains that were least affected were 'social functioning' (SF) and 'role emotional' (RE). The SF-36 scores and its sub-domains had significant associations with parameters like treatment options, glycaemia, duration of diabetes, gender, age, regular physical activity, coexisting complications, comorbidity. (Table - 1) Patients being treated without glimepiride had higher HRQoL scores (69.09 ± 20.57) as compared to those treated with glimepiride along with other oral anti-diabetic drugs (54.29 ± 22.43). This difference was found to be statistically significant ($p \leq 0.05$). (Table - 2) All the SF-36 domains, other than 'general health' (GH), had significant association with the treatment option.

Table 1: Association of SF-36 scores with different parameters in type 2 diabetes mellitus

Variable	Sub-classification	SF-36 domain								SF-36
		PF	RP	RE	BP	GH	VT	SF	MH	
Treatment option	With G, Without G	*	*	*	*		*	*	*	*
Glycaemia	Normo, Hyperglycemia	*	*	*	*	*		*		*
Duration of diabetes	< 5 years, > 5 years		*	*	*		*		*	*
Gender	Male, Female	*	*	*	*	*	*	*	*	*
Age group	< 40 years, > 40years	*	*	*	*		*	*	*	*
Regular physical activity	Regular, nil/irregular	*	*	*	*	*	*	*	*	*
Complications	Present, Absent	*	*		*			*	*	*
Co-morbidity	Present, Absent	*								*

(* boxes represent statistically significant relationship i.e. $p \leq 0.05$) Physical Functioning(PF), Role Physical(RP), Role Emotional(RE), Bodily Pain(BP), General Health(GH), Vitality(VT), Social Functioning(SF) , Mental Health(MH), G - Glimepiride

Table 2: Comparison of SF-36 scores in type 2 diabetes mellitus treated without Glimepiride and with Glimepiride

SF-36 domain	Without glimepiride	With glimepiride
Physical functioning	76.84±24.53	57.93±25.97
Role physical	70.54±26.74	52.27±27.25
Role emotional	75.47±25.93	64.01±27.96
Bodily pain	68.52±24.52	55.13±22.76
General health	55.61±18.12	41.89±14.56
Vitality	58.46±18.46	44.27±17.88
Social functioning	78.95±23.59	62.85±24.85
Mental health	68.35±14.96	55.95±19.24
SF-36 score	69.09±20.57	54.29±22.43

values are in mean ± SD

DISCUSSION

In the present study, the HRQoL score in subjects with more than 5 years' duration of diabetes, was lower in all domains except in 'physical functioning' (PF), 'general health' (GH) and 'mental health' (MH). The better scores in these three domains may be due to adaptation to diabetic lifestyle. As the duration of diabetes increases, the physical health deteriorates but patients may feel better as they come to terms with their diabetic condition. Sparring *et al* have reported that the differences in HRQoL between individuals with

diabetes and control individuals tend to increase with longer disease duration [11]. The SF-36 score was significantly lower among respondents with complications as compared to respondents without complications. SF-36 domains like 'physical functioning' (PF), 'role physical' (RP), and 'role emotional' (RE) were affected more and the differences were statistically significant. Woodcock *et al* also observed better scores in all domains (except RP and BP) in those without complications [12]. Males had higher scores than females in all eight domains. Chittleborough *et al*, Gulliford *et al* and Schunk *et al* have reported similar findings in their studies in Australia, Trinidad and Germany respectively [13-15]. Factors that lead to relatively poor quality of life in women with type 2 diabetes mellitus need to be researched more thoroughly. In the U.K. Prospective Diabetes Group study and in a recent review it has been observed that in type 2 diabetes mellitus, interventions like severe dietary restriction and daily self-administration of oral medications or insulin may adversely affect an individual's health-related quality of life [16].

The pattern of prescription of oral hypoglycemic agents observed in our study was similar to the findings in other studies by Khan *et al* and Kanan *et al* [17,18]. In this study, patients being treated without glimepiride had higher HRQoL scores as compared to those treated with glimepiride along with other oral anti-diabetic drugs. Use of sulfonylureas was associated with an elevated risk of hypoglycaemia [19]. In one observational study it has been found that the annual risk for a first hypoglycemia diagnosis associated with sulfonylurea use was 1.8% (1,800 per 100,000 person years)[20]. In another randomized, double-blind study by *Ahren et al* on 3,059 subjects it was found that the hypoglycemia risk was significantly higher in patients receiving glimepiride 2mg/day but was lower in patients on vildagliptin with similar results unadjusted or adjusted for last HbA1c [adjusted hazard ratio (HR) = 0.06 (95% CI 0.03, 0.11)]. The risk of hypoglycemia with glimepiride 2 mg/day increased with lower HbA1c [21].

There are studies which show that episodes and fear of hypoglycaemia and of long-term consequences may have a substantial impact on health status thus affecting the health-related quality of life[22,23]. In a study by Pollack *et al* done on 2074 participants in United States it was observed that tolerability issues like signs and symptoms of hypoglycemia, constipation, diarrhoea, headache, weight gain and water retention have a significant association on the likelihood of non-adherence and reduced treatment satisfaction in type 2 diabetes mellitus [24]. In the present study, better HRQoL scores in patients of type 2 diabetes mellitus on treatment without glimepiride may be due to better tolerability and less fear of hypoglycemia.

CONCLUSION

'Health-related quality of life' in type 2 diabetes mellitus patients is affected significantly by the oral anti-diabetic drugs used in the treatment along with other key factors like, duration of diabetes, gender, age, glycaemia, body mass index, regular physical activity, coexisting complications, comorbidity. Though, larger studies in this regard are required in the Indian population, the findings of this study reinforce the importance of choosing an oral anti-diabetic drug in type 2 diabetes mellitus that improves the 'health-related quality of life' of the patient rather than only achieving euglycemia. The study has few limitations like, compared to the magnitude of the problem of diabetes mellitus the sample size was small, non-diabetics were not included as a comparison group, lack of data on diet and eating pattern of the participants and a generalized scoring system for HRQoL was used rather than a disease specific scoring system.

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