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A STUDY ON ASSESSMENT OF GLYCEMIC CONTROL OF ORAL HYPOGLYCEMIC DRUGS AND INSULIN IN TYPE 2 DIABETES MELLITUS PATIENTS

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ABSTRACT

Introduction

Insulin will be preferred as add-on therapy while the oral hypoglycemic (OHG) drugs are most often failed to control hyperglycemia in patients with chronic diabetes mellitus. The present study assesses the glycemic control in diabetes patient used Insulin and OHG drugs.

Methods

This prospective observational study was conducted in Chennai with a total of 129 diabetes mellitus patients. The patients with fasting blood sugar (FBS) >110 mg/dl and /or random blood sugar (RBS) >150 mg/dl and/or urine sugar level >50 mg/dl were enrolled. The patient's biochemical and vital physiological parameters were checked at every 30±3th day over 6 months excluded the first day of patient enrol. The average values were compared by use of paired sample't' test and statistical significance was set at $p<0.05$.

Results

Among all, except body temperature all parameters were exhibited significant in both groups ($p<0.05$). The FBS and RBS were not showed significant changes though a combination therapy with Metformin and Glipizide, Glibenclamide and Glimepiride in OHG drugs treated patients than Insulin treated patients. The changes in characteristics in both study groups over 6 months were shown oscillating. The treatment outcome measures were showed similar non significant improvement in patients treated with OHG drugs.

Conclusion

This study results showed the treatment outcome measures were not significantly improved in OHG drugs patients than Insulin treated patients. It reveals that addition of Insulin could have been better in poorly controlled hyperglycemia in combination with Metformin to achieve higher reduction in long term hyperglycemia control so that the hyperglycemia symptoms would have been improved.

KEYWORDS : : Oral hypoglycemic drugs, Insulin, Metformin, Glipizide, Glibenclamide, Glimepiride

INTRODUCTION

Diabetes mellitus is a chronic endocrine disorder characterized by insulin deficiency and insulin resistance associated with micro and macrovascular complications. The ways to achieve optimal glycemic control is necessary to reduce these complications [1-6]. The failure in glycemic control causes increased hospital stay decreased the quality of life, elevated cardiovascular and stroke complications. The optimum glycemic level shall be augmented sometimes with add-on therapy of Insulin to OHG drugs; in fact, several beneficial metabolic effects are also reviewed [7]. Hence, the glycemic control is challenging task [8] especially in non hospitalized patients where factors like age, sedentary life, stress, changes in antidiabetes drugs regimen [9] would play as hidden threats prone to treatment failure. The present study assesses the comparison of glycemic control in diabetes patient used Insulin and OHG drugs.

METHODOLOGY

This prospective observational study was carried out in non hospitalized type 2 diabetes mellitus patients in Chennai, Tamil Nadu. The patients of age 20-60 of both sexes, used only Insulin and OHG with FBS>110 mg/dl, RBS >150 mg/dl and/or urine sugar level >50 mg/dl for a cumulative of last 2 months were enrolled. The study protocol was reviewed and approved (Protocol id: 1058/IEC/2015, Version-1). The patients on steroid therapy, pregnant and lactating women, diabetic nephropathy, diabetic neuropathy, diabetic microangiopathy, underwent surgical procedures <90 days, hypertensive crisis, hypertensive nephropathy were excluded. Each patient was interviewed, for their past medical history of diabetes before participation in the study. Patients included in the study were those their Diabetes was not adequately controlled by dietary restrictions, physical activity and were under treatment with single OHG. The patients were followed standard diabetic diet throughout the period of 6 months. The demographic parameters, body weight, height, waist and hip measurements were assessed manually and BMI and WHR were calculated on every 30±5 days for 6 months except the day of enrolling. The average ± standard deviation (SD) values of each parameter have been calculated. The statistical interpretation was carried out by using paired sample't' test in SPSS 20.

RESULTS

A total of 129 patients were successfully completed the study with all 6 months review. The results were categorized in to 3; 1) demographic characteristics, 2) vital and biochemical parameters and 3) diabetes mellitus symptoms. Figure 1 shows the distribution of study subjects; in which, 75 patients used Insulin (41.86%) and 54 patients (58.13%) used OHG. The average age of Insulin treated patients was 42.54±9.14 and OHG treated patients was 39.29±5.84. Metformin has been used in all patients treated with OHG drugs either as single or in combination as shown in figure 2. As obvious, the Insulin treated patients showed significant decrease ($p<0.05$) in vital, biochemical (Table 1) as well as

diabetes symptoms (Table 2) parameters. The other features of treatment glycemic control were FBS, RBS and HbA1C were also seemed positively responded to Insulin treatment. Except body temperature all characteristics were exhibited significant in both groups (Table 1). The progress of changes in the levels of characteristics in both study groups over 6 months were shown significant perhaps oscillating. Blood pressure and heart rate were shown similar changes in both groups. Even with non significant elevation of systolic blood pressure, heart rate was showed significant increase ($p<0.05$) in both groups (Table 1, Table 2); could be the hyper osmolarity delayed ventricular filling pressure. The glycemic control parameters FBS, RBS and HbA1C were also not improved though a combination therapy with Metformin and Glipizide, Glibenclamide and Glimepiride. The treatment outcome measures were showed similar non significant improvement in patients treated with OHG drugs as shown in Table 4 but Insulin treated group were improved (Table 3) even though no significant glycemic control as showed in Table 2.

DISCUSSION

The purpose of this prospective observational study was to assess the therapeutic efficacy of OHG drugs and Insulin in diabetes mellitus. From the most of our included studies, we observed that the baseline vital and biochemical parameters are slightly high in OHG drugs used patients than Insulin other than Metformin. However, the mathematical values were showed variations, the statistical significance was little explainable. One finding of our study was the association of treatment outcome and use of Insulin against OHG drugs; response to OHG drugs has been reduced while comparison over 6 months reviews period. Traditionally, Insulin has more anti hyperglycemic activity [10], hence used in conditions where OHG drugs fail to control glycemic level. The BMI were reduced in OHG treated groups which was indicated the diminished response level to Insulin resistance. The results of our study direct to the findings of fluctuations in HbA1C, BMI and WHR over the review period which might include multiple co factors could not be identified. This suggests that use of insulin is associated with higher control over glycemic level, even after adjusting for severity of illness. However, these data might fit into the clinical perspective [11] that insulin should be delayed until OHG drugs failed to maintain glycemic control. The current trends of India; selection of a précised perhaps targeted anti diabetes agent is a topic of debate [12] due to varied treatment outcomes of OHG drugs and even Insulin preparations. The importance of individualized therapy target to optimum dosage regimen ought to address key perspectives of risks and benefits [13] to achieve durable glycemic control as well as minimized post treatment complications. The majority of diabetes mellitus patients receive therapy either Insulin with Metforminmin and dietary management or both. However, a significant number of patients require multiple drugs [14] even dietary management is advised. This could be quite debatable even Consensus exists [15] about; acceptability of OHG drugs is also to be considered.

The present study observed that significantly more individuals used Metformin as combination with other OHG drugs than alone; thought to be switched over to OHG drugs than vice versa. Glipizide was the mostly used combined drug with Metformin than with Pioglitazone and Glimepiride. The rationale of use of Insulin secretagogues is still under evaluation; might be the negative perceptions [16] from patient's responses and non evidence based treatments also could contributed to decide the practitioners away from Pioglitazone. Sometimes patients develop anxiety, discomfort, fear [17] may cause decreased adherence to medicines and thus might produced negative feedback.

The treatment outcomes measures were the important finding of our study; thus choices of physical symptoms of diabetes mellitus are convinced to explain. We expected several key findings including that patients placed on Metformin with Glimepiride, Glibenclamide and Glipizide to have more treatment outcome equivalent to Insulin treated patients. This was strongly predicted when the patients instructed not to follow else other treatments than advised during the review period. But this was not true observed in OHG drugs treated patients; there RBS had shown lesser improvement than Insulin treated patients where the diagnosis strongly predicted placement of Insulin as add-on therapy. These findings on short and long term glycemic control were an element of conflict [18, 19] with many investigators that have found [20] Insulin to be the best and most effective hypoglycemic agent. While expanding the body of literature had also suggested the importance of Insulin even for Type 2 diabetes mellitus [21, 22] patients to be initiated in earlier stage.

Like in all observational studies, we also had certain limitations. The study could have been conducted in large population. There were few unmeasured variables in both study groups which would have been considered. The physical activity status of the patients over study duration was not accounted consistently. It was quite possible but patient's resistance was critical factor, this could have been an unpredictable impact on treatment outcome and thus failure to complete the study period successfully.

CONCLUSION

The study reveals that Insulin and OHG drugs are less effective in glycemic control in diabetes mellitus non hospitalized patients. Insulin was found not enough in controlling hyperglycemia but comparatively produced good glycemic control over OHG drugs. This study also reveals that addition of Insulin could have been better in poorly controlled hyperglycemia in combination with Metformin to achieve higher reduction in long term hyperglycemia control so that the hyperglycemia symptoms would have been improved.

Acknowledgement

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Conflict of interest

None declared

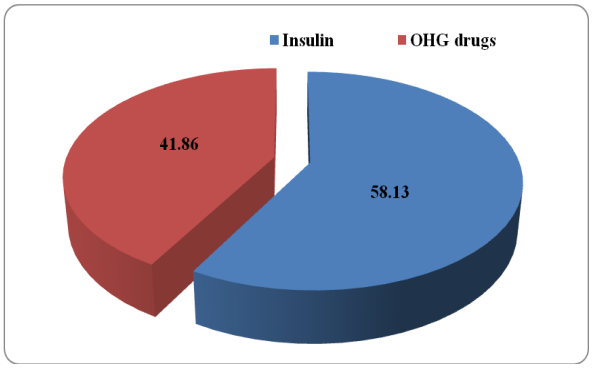

Figure 1 shows the distribution of patients. Values expressed as %

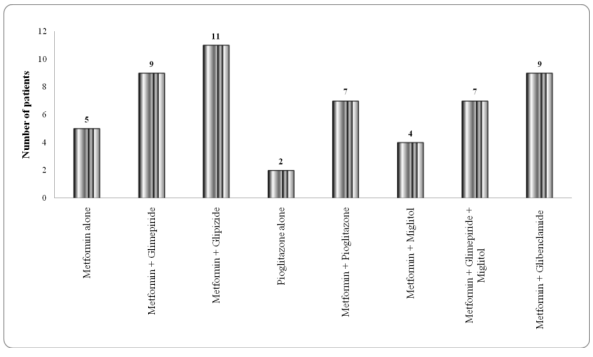

Figure 2 shows the OHG drugs used by the patients. Values expresses as number.

Table 1 shows the comparison of vital and biochemical parameters in Insulin consumed patients. Values expressed as average ±SD

Parameters	Frequency of review					
	I	II	III	IV	V	VI
FBS	149.24±14.7*	129.12±19.4	159.49±12.9	105.71±18.7	104.54±17.4	109.12±11.2
RBS	110.55±24.04	104.24±19.37*	150.67±14.37*	130.99±54.02*	120.02±35.33	140.44±24.74

HbA1C	4.8±0.19	5.1±.07	2.5±0.17*	5.2±0.11	4.9±0.09	7.1±0.05
SBP	160.09±21.04	180.22±13.19	170.27±14.24	140.75±12.99*	130.14±09.54*	150.19±15.15*
DBP	94.55±13.44*	92.34±08.57*	104.14±11.27	100.87±08.22*	90.97±11.05*	95.99±13.99*
HR	70.09±4.33	84.22±06.11*	72.15±10.42*	94.24±5.95	74.12±13.14	73.15±5.92
RR	20.41±2.42*	21.74±2.91	24.02±5.32	15.74±3.67	20.12±3.62*	16.83±2.19
Body temp.	98.9±0.11	96.4±0.42	99.2±0.18	98.6±0.24	98.9±0.01	98.9±0.17
BMI	21.29±2.15*	22.31±1.02	24.2±2.01	24.77±1.09	21.14±2.09	21.03±3.52*
WHR	0.82±0.02*	0.99±0.17	0.71±0.15*	0.74±0.89*	0.75±0.12	0.71±0.09*
Serum urea	65.01±09.24*	72.01±2.15*	94.09±9.04*	30.33±3.99*	110.1±9.37*	97.99±12.78*
WBCs	5734.04±37.01	7237.04±230.1	7404.22±230.11*	8468.01±240.88*	10504.11±410.21	9747.09±340.11

*p<0.05, paired sample 't' test, R1-29th day, R2-60th day, R3-92th day, R4-126th day, R5-156th day, R6-185th day, n-75, duration-06 months

Table 2 shows the comparison of vital and biochemical parameters in patients consumed OHG drugs. Values expressed as average ±SD

Parameters	Frequency of review					
	I	II	III	IV	V	VI
FBS	135.24±12.54*	129.12±10.4*	129.49±05.54	115.81±11.01	124.14±15.11*	112.12±11.22*
RBS	192.15±19.24	212.78±11.97	190.97±05.14	109.91±15.99	151.12±25.13*	210.14±14.94
HbA1C	5.8±0.15	4.9±0.71	2.5±0.07	3.02±0.02	3.09±0.91*	5.9±0.15
SBP	161.25±21.54	149.32±10.19	150.27±10.14	130.25±10.04*	120.44±08.04	150.79±12.95
DBP	90.15±11.14*	94.14±05.17	100.44±07.77	110.17±12.02*	90.02±14.15*	100.09±10.19
HR	80.09±2.13	80.12±03.01*	75.05±08.12	90.14±5.12	80.15±03.44	80.12±2.12
RR	18.11±2.12*	22.54±2.11	21.62±5.12*	19.44±5.97*	20.99±4.02	14.33±2.12
Body temp.	98.4±0.21	99.4±0.12	98.2±0.98	98.9±0.94	98.4±0.51	94.9±0.77
BMI	24.05±4.22	24.51±3.92	24.67±2.71	29.57±3.99*	27.54±3.79	29.53±4.22
WHR	0.84±0.01*	0.89±0.17	0.79±0.15*	0.82±0.89*	0.79±0.12*	0.74±0.09
Serum urea	45.21±03.94	51.71±3.54*	84.29±2.09	59.23±3.47	34.18±4.97	27.09±04.18
WBCs	5234.94±13.51	6937.24±240.55	8404.92±22.11	8098.51±21.11*	7904.51±24.04	8917.19±13.54

*p<0.05, paired sample 't' test, R1-29th day, R2-60th day, R3-92th day, R4-126th day, R5-156th day, R6-185th day, n-54, duration-06 months

Table 3 shows the comparison of symptoms of treatment outcomes in patients consumed Insulin. Values expressed as average ±SD

Parameters	Frequency of review					
	I	II	III	IV	V	VI
Polyuria	1.5±0.86	2.25±0.57*	2.25±0.89	3.0±0.0	2.25±0.86	3.0±0.0*
Polydipsia	2.5±0.87	2.25±0.89	2.75±0.97*	2.0±0.0*	2.0±0.0	2.75±0.87*
Fatigue	1.25±0.57	0	0	1.75±0.54	0	1.25±0.57*
Increased Thirst	3.0±0.0*	3.0±0.0	2.25±0.89*	1.25±0.57*	2.25±0.89*	3.0±0.0
Increased hunger	3.0±0.0*	2.0±0.0	1.0±0.0	1.75±0.89	0	0
Headache	0	0	2.0±0.0	0	0	0
Diff. concentration	2.0±0.0*	3.0±0.0*	2.0±0.0*	3.0±0.0	0	2.75±0.57*
Frequent Urination	3.0±0.0	2.75±0.97*	20.0±0.0*	3.0±0.0*	2.75±0.87*	1.0±0.0*
Tiredness	3.0±0.0*	2.0±0.0	3.0±0.0	2.75±0.87*	3.0±0.0	1.75±0.89*
Insensitivity of limbs	0	0	0	0	1.0±0.0*	2.25±0.87*
Slow healing of cuts/wounds	0	0	0	0	1.0±0.0*	0
Hair loss	2.0±0.0*	1.75±0.87*	1.75±0.87*	0	1.0±0.0	1.0±0.0*
Chronic /frequent constipation	0	0	0	0	1.0.±0.0	2.0±0.0
Diarrhea	0	0	0	0	0	0
Confusion	1.0±0.0*	1.0±0.0*	1.0±0.0	1.75±0.87	0	0
Dry mouth	2.25±0.87*	2.25±0.87*	1.75±0.89*	3.0±0.0*	2.5±0.67*	2.75±0.87
Nausea/vomiting	0	0	0	0	0	0
Trembling/ shaking of hands	2.25±0.87*	2.25±0.87*	2.0±0.0*	3.0±0.0	1.5±0.57*	0
Giddiness	0	0	0	1.0±0.0*	2.0±0.0*	0
Sweating	1.5±0.87	2.25±0.87*	1.0±0.0	0	1.0±0.0*	0

*p<0.05, paired sample 't' test, R1-29th day, R2-60th day, R3-92th day, R4-126th day, R5-156th day, R6-185th day, n- 75, duration-06 months

Table 4 shows the comparison of symptoms of treatment outcomes in patients consumed OHG drugs. Values expressed as average ±SD

Parameters	Frequency of review					
	I	II	III	IV	V	VI
Polyuria	2.1±0.12	2.2±0.01*	1.14±0.11	2.0±0.01*	1.25±0.01	2.25±0.01
Polydipsia	1.15±0.04	1.25±0.09	2.25±0.02	2.15±0.01	1.15±0.09	2.25±0.09
Fatigue	2.15±0.5	2.15±0.15*	1.15±0.09	2.25±0.05*	2.5±0.09	1.15±0.05*
Increased Thirst	2.0±0.0	1.25±0.09	1.25±0.05*	2.25±0.05	1.15±0.01	2.0±0.0
Increased hunger	2.15±0.25	2.0±0.0	3.0±0.0	2.75±0.89	1.15±0.09	0
Headache	3.0 ±0.0*	2.5±0.05*	2.15±0.05	2.5±0.05	1.15±0.89*	2.25±0.05
Diff. concentration	2.0±0.0	3.0±0.0	2.0±0.0	3.0±0.0	0	2.75±0.57
Frequent Urination	3.0±0.0*	2.75±0.97	20.0±0.0	3.0±0.0	2.75±0.87*	1.0±0.0*
Tiredness	3.0±0.0	2.0±0.0	3.0±0.0	2.75±0.87*	3.0±0.0	1.75±0.89*
Insensitivity of limbs	1.14±0.11	0	1.15±0.01*	1.25±0.57	1.0±0.0*	2.25±0.87*

Slow healing of cuts/wounds	2.25±0.02	0	1.15±0.09*	3.0±0.0*	1.0±0.0*	0
Hair loss	1.15±0.09	1.75±0.87	1.15±0.89	3.0±0.0*	1.0±0.0	1.0±0.0*
Chronic /frequent constipation	1.25±0.05	0	1.15±0.01	1.25±0.57	2.75±0.87*	1.0±0.0*
Diarrhea	3.0±0.0	0	2.75±0.87	3.0±0.0	2.1±0.12	3.0±0.0
Confusion	1.0±0.0	1.0±0.0	1.0±0.0	1.75±0.87	0	1.0±0.0*
Dry mouth	2.25±0.87	1.5±0.57*	1.75±0.89	3.0±0.0	2.5±0.67	2.75±0.87
Nausea/vomiting	0	2.0±0.0*	0	2.0±0.0*	2.1±0.12	1.25±0.57
Trembling/shaking of hands	2.25±0.87	1.0±0.0*	2.0±0.0	1.0±0.0*	1.5±0.57	3.0±0.0*
Giddiness	0	1.5±0.57*	0	1.0±0.0	2.0±0.0	3.0±0.0*
Sweating	1.5±0.87	2.0±0.0*	1.0±0.0	0	1.0±0.0	1.25±0.57

*p<0.05, paired sample 't' test, R1-29th day, R2-60th day, R3-92th day, R4-126th day, R5-156th day, R6-185th day, n- 54, duration-06 months

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