Effect of Metformin in HbA1C in Nepalese Type 2 Diabetes

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ABSTRACT

Introduction: Up to now a limited number of studies compared metformin with other OHA directly and some of their results are still controversial.[1] The study which compared metformin and other OHA, the ADOPT study, the U.K. Prospective Diabetes Study (UKPDS), did not include Nepalese diabetic patients . Therefore, the aim of study was the comparative evaluation of metformin and other OHA influence on glycemic control(HbA1c) in Nepalese patients with diagnosed type 2.

Methods: A prospective cross sectional database of patients treated at diabetic clinic, TUTH, were analyzed. Patients with type 2 diabetes with HbA1c (A1C) data and treated with metformin and other OHA, for at least three visits were included (n = 115). Analysis by HbA1c and the type of oral agent was performed.

Results: In the analyzed group of patients, the mean duration of therapy was for 9 months. Metformin was given to 48 patients and 57 patients were on other OHA. In the metformin group mean HbA1c level (from 7.8 ± 1.8 at baseline to 6.7 ± 0.8 at the end of analysis period; $p<0.05$). The highest mean HbA1c at baseline (7.8 ± 1.8) was observed in the group treated with metformin; the same group experienced the highest drop in HbA1c levels (by .7, from 7.8 ± 1.8 to7.1 ± 0.9). The comparable decrease in HbA1c (by .5 from 7.6 ± 2.1 to 7.1 ± 1.2) was also found in the group treated with other OHA.

Conclusion: We conclude that metformin is as efficacious and is a good agent of chice to reduce HbA1c. Our study provides evidence-based data to support metformin use in Nepalese individuals with type 2 diabetes.

Key words: HBA1c, Metformin, Type 2 Diabetes

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INTRODUCTION

Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by the presence of hyperglycemia due to either a deficiency in the production or secretion of insulin, diminished tissue response to the actions of insulin, or both.[1,] Prevalence data indicate that diabetes has reached epidemic proportions worldwide, particularly in developed countries and emerging nations.[3, 4] The Nepal Diabetes Association reported that diabetes affects approximately 15% of people over 20 years and 19% of people over 40 years of age in urban areas of Nepal. According to WHO, diabetes affects more than 436,000 people in Nepal, and this number will rise to 1,328,000 by 2030.[6] The percentage of diabetic patients has increased from 19.04% in 2002 to 25.9% in 2009 in Nepal.[7].

For every 1% increase in glycosylated hemoglobin (HbA1c) above 5%, there is a 20% epidemiological increase in cardiovascular risk (Khaw et al., 2004). Metformine, a medication that can significantly lower hemoglobin A1c, body weight, and postprandial glucose excursions in humans and significantly improve â -cell function. This paper comprehensively analyzes and compares metformine to other medications that treat diabetes mellitus type II. Many studies have consistently shown that strict glycemic control significantly reduced long-term complications of diabetes.[8,9] A 1% change in glycated hemoglobin (HbA_{1c})signifies about a 10% change in risk of CAD, which is responsible for almost half the deaths in this population.[10,11,12] Hyperglycemia has been shown to be one of the potentially modifiable risk factor for CAD in patients with type 2 diabetes.[11]

METHODS

A prospective cross sectional analysis following approximately 115 patients in the outpatient and inpatient setting between January - October 2010. Both male and female patients aged 18 and above, on metformin and other OHA were included in the study. The two groups of subject were, Nepalese diabetic patients on metformin and Nepalese diabetic patients on other OHA. The information collected were Name, age, sex, weight, height, HbA1c. HbA1c will be documented at zero, three, six and nine months after metformin and other OHA use. A mean HbA1c was calculated and compared among different groups.

Frequencies and percentage distribution were obtained for each variable. SPSS version 17.0 for windows was utilized to analyze the data. T test was utilized to detect the level of significance. P-value was calculated and value <0.05 was considered significant.

Patient included were Diabetic males and females aged >18 years those only on OHA without Insulin, Patients attending the outpatient clinic and inpatient at TUTH, Duration: January, 2010 and October, 2010. Patient excluded were, Patients on Metformin for less than 3 months, Patients on medications other than oral anti- diabetic medications known to interfere with glucose metabolism. These medications include oral corticosteroids, estrogen or birth control pills, nicotinic acid, anti-retroviral therapy, phenytoin, anti-psychotics and SSRIs, patients with conditions that may interfere with HbA1c such as cancer, HIV, thyroid disturbances, growth hormone secreting pituitary adenomas, acromegaly, cushing'ssyndrome, pheochromocytoma, anemia, congestive heart failure and renal failure, non-compliant patients and Diabetes with insulin therapy.

RESULTS

Total Patients: 115. Mean Age of Patients: 48.53 ± 8.5 years (Range: 26 – 69 Years)

Table 1: Mean HbA1c Distribution (With Standard Deviation)

	Ideal Weight	Overweight	Obese	Total	p-value
Patients on Metformin	8.25 ± 3.22	7.85 ± 1.49	7.60 ± 1.51	7.80 ± 1.8	<0.05
Patients on other OHAs	7.84 ± 2.4	7.39 ± 1.5	7.63 ± 2.3	7.67 ± 2.1	
Total	7.90 ± 2.5	7.60 ± 1.5	7.61 ± 1.6	7.73 ± 2.03	

Table 2: Gender distribution and Mean HbA1c Levels at Presentation (with Standard Deviation)

Subject Class	Sex	Mean	No. of Patients
Patients on Metformin	Females	7.91 ± 2.1	24
	Males	7.69 ± 1.4	24
	Total	7.80 ± 1.8	48
Patients on other OHAs	Females	7.77 ± 2.13	34
	Males	7.57 ± 2.29	33
	Total	7.67 ± 2.1	67
Total	Females	7.83 ± 2.1	58
	Males	7.62 ± 1.9	57
	Total	7.73 ± 2.03	115

Table 3: Mean reduction in HbA1C following treatment in different subject classes

	Patients on Metformin	Patients on other OHAs	p-value
HbA1C (at the end of third month)	0.86 ± 1.39	0.8 ± 1.57	>0.05
HbA1C (at the end of sixth month)	1.03 ± 1.65	0.76 ± 1.73	>0.05
HbA1C (at the end of ninth month)	1.09 ± 1.69	0.58 ± 2.28	>0.05

Of the 115 individuals with complete demographic, anthropometric, A1C, and hypoglycemic medication data, had at least three visits to our Diabetes Centre. 41.73% were in the metformin group and 58.27% were in the other OHA group.

DISCUSSION

Of the 115 individuals with complete demographic, anthropometric, A1C, and hypoglycemic medication data, had at least three visits to our Diabetes Centre. 41.73% were in the metformin group and 58.27% were in the other OHA group.
In the analyzed group of patients, the mean duration of therapy was for 9 months. Metformine was given to 48 patients and 57 patients were on other OHA. In the metformine group mean HbA1c level (from 7.8 ± 1.8 at baseline to 6.7 ± 0.8 at the end of analysis period; $p<0.05$). The highest mean HbA1c at baseline (7.8 ± 1.8) was observed in the group treated with metformin; the same group experienced the highest drop in HbA1c levels (by .7, from 7.8 ± 1.8 to7.1 ± 0.9). The comparable decrease in HbA1c (by .5 from 7.6 ± 2.1 to 7.1 ± 1.2) was also found in the group treated with other OHA. The smallest effect of treatment was observed in other OHA group.

Reduction of HbA1c was similar between metformine and on patient on other OHA during the observation period. Although several studies have shown the advantage of metformin in diabetic patients, 12 the observation periods were relatively short. The reduction of HbA1c by metformin was not different between 303 ideal weight (0.9%, BMI < 25 kg/m2) and 300 overweight (1.0%, BMI ≥ 25 kg/m2) Japanese patients with type 2 diabetes mellitus according to a prospective study for 12 months. 12 It retrospectively showed a significant 0.79% reduction in HbA1c levels in 58 patients on metformine and 0.73% in 136 patients on other OHA in 12 months for type 2 diabetes mellitus.13 Clarke and Campbell reported that metformin monotherapy (*n* = 98) was equally effective as other OHA, on blood glucose control without HbA1c measurements, and that metformin was superior in the body weight control in type 2 diabetes mellitus according to a prospective study for 1 year. 14 Yajima *et al*. demonstrated the metformin administration at a dose of 500-750 mg/day to be more effective in patients with type 2 diabetes mellitus than in those treated with others OHA, in a crossover study conducted with 3-months treatment periods.15 Lund *et al*. described that the glycemic regulation was equivalent between metformin and other OHA, in a 4-month crossover trial in 96 European patients with type 2 diabetes mellitus.16 They also reported that the effect of metformin (*n* = 52) and other OHA(*n* = 49) was not significantly different when combined with insulin for the treatment, according to a randomized prospective study for 12 months.17 Donnelly *et al.* showed the glucose-lowering effect of metformin to be very similar with other OHA taking patients with type 2 diabetes mellitus according to a study covering a period ranging from 3-12 months.18 Ong *at al*. revealed that metformin was efficacious in subjects with type 2 diabetes mellitus (*n* = 136) according to a retrospective analysis of 16 years.19 This is the first report to show the long-term effect of metformin among patients with type 2 diabetes mellitus.

The efficacy of metformin has been well proven in the last several years.20 In our study metformin was effective in reducing BMI and lowering HbA1c.BMI decrease by 0.97 ± 1.18 and HbA1c fell by 1.09 ± 1.69, during the whole analyzed period. These results are in accordance with recent observations made by several authors. However, the duration of these prospective studies did not exceed 6 months, which is considerably shorter than the period we analyzed. Given the outcome of our analysis we suggest that the metformin is still efficacious, even though the maximum doses used in our patients did not exceed 2000 mg/day. We cannot comment, however, on any dose-response effect of metformin, since the subjects included in our study did not change their dosage. One may only assume that, as different patients require different doses (in our study from 500 to 2000 mg), the drug may have a clear dose-dependent effect on blood glucose control.

This study shows significant decrease in total serum calcium level in hypertensive patients than normotensive controls and the results are in close agreement with that of others who also found a significant decrease in serum calcium in patients with essential hypertension .[7,8] Though there are not enough study describing the relation of serum calcium and hypertension, but the findings of the present study are in agreement with that of Sudhakar, Sujhata, Babu, Padmanathi and Reddy.[28] Toyuz et al also reported reduced serum calcium level in hypertensive individuals.[9] However, Kosch et aldid not find any changes in serum calcium levels in hypertensive individuals.[10] In approximately two third of the studies based on this subject done by 1994, increase in calcium intake produced a mild antihypertensive response, with an average decrease of 4-7 mm Hg systolic and 2-4 mm Hg diastolic blood pressure .[11]

CONCLUSION

In this study, type 2 diabeticsubjects on Metformine have reduction in HbA1c. We found that treatment with metformin was able to significantlyimprove the HbA1c. In fact,the regimen may be a safeguard againstNepalese type 2 Diabetes.

This thesis demonstrated effectiveness of Metformine in Nepalese type 2 Diabetes as compared to other OHA. In conclusion, the result of our study provided that Metformine should be the first drug to be started in Nepalese type 2 diabetes.

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