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IMPACT OF INSULIN, BIGUANIDE AND SULFONYLUREA TREATMENT ON HbA_1C IN DIABETIC PATIENTS: AN INTERVENTIONAL STUDY IN RAJSHAHI, BANGLADESH

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Abstract

Proper management and selection of a single drug or multiple drugs for the treatment of diabetes is very important. The choice of treatment depends on a number of factors. With the proper treatment, the state of diabetes can be managed very smoothly. The main objective of this study was to compare the efficacy of insulin, biguanides and sulfonylurea on HbA_1C in diabetic patients. This interventional type of study was carried out among 102 diabetic patients attending at different hospitals in Rajshahi of Bangladesh. In this case purposive sampling technique was followed and data revealed that mean age of the patients was 45.98±11.23 years and most of them (35.30) were housewife. Among the insulin receiving group, 41.18% were male and 58.82% were female. In case of the biguanide receiving taking group 44.12% were male and 55.88% were female while for the sulfonylurea receiving group 35.29% were male and 64.71% were female. Regarding body mass index (BMI) among the respondents, it was found that 0.98% had BMI <18.50 kg/m^2, led sedentary lifestyle (65.7%), most of them were from urban area (67.6%) and non-smoker (86.0%) with family history of type 2 diabetes mellitus (T2DM) (17.0%). In the insulin receiving group, 82.35% had desired glycemic control; in the biguanide receiving group, 73.53% had desired glycemic control; and in the sulfonylurea receiving group, 64.71% had desired glycemic control. Data shows that the insulin receiving patients had relatively better glycemic control as compared to the other two mendicant receiving groups at 6^{th} month. This finding suggests that the selection of the best drug is the most key part of the treatment of T2DM. Therefore, this study would help to select the best choice of drug for the treatment of diabetes in Bangladesh.

***Key words*:** Insulin, Biguanide, Sulfonylurea, HbA_1C, Diabetes

Introduction

The metabolic condition type 2 diabetes mellitus (T2DM), which progresses over time, is being more recognized as having global epidemic potential (Hossain et al. 2021a & b). Preventing long-term problems is the main objective of diabetes care. The maintenance and improvement of glycemic control throughout time is an essential strategy for achieving this goal. Due to the disease's progressive nature, which necessitates prompt treatment optimization and typically results in insulin therapy, this is a difficult assignment. Sulfonylureas, glinides, thiazolidinediones (Derosa et al. 2009, Derosa and Maffioli 2011), biguanides (Cicero et al. 2012), and -glucosidase inhibitors are only a few of the several anti-diabetic medications that are currently available to treat type 2 diabetes mellitus (Derosa and Maffioli 2012). Despite the abundance of anti-diabetic medications on the market, sulfonylureas continue to be the most popular medication for treating people with type 2 diabetes (Bressler and Johnson 1997).

Individuals with diabetes display variable degrees of diminishing beta cell activity, insulin resistance, and an inability to control postprandial glucagon release. Diabetes is a degenerative multisystem disease. There are

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numerous co-morbidities and potentially fatal consequences connected with it (Hossain et al. 2022). The problem of diminishing beta cell function is not sufficiently addressed by the treatments that are now available. Yet, treatment with biguanides and insulin sulfonylureas is known to improve glycemia in patients with diabetes; however, it is unknown which medication most commonly achieves the target HbA1C below 7% (Winkler and Gerô 2011). One of the main types of anti-diabetic medications is biguanides, of which metformin is most frequently used as the initial treatment for diabetes mellitus (Holman 2007).

Sulfonylureas, second-line medications frequently used to treat T2DM in patients who are not excessively obese, work by directly blocking ATP-sensitive K+ channels on islet cells to increase insulin production (Ashcroft and Rorsman 2013). Whether used alone or in combination with other anti-hyperglycemic medications, they stay effective until they reach their intended objectives (Tripathi and Srivastava 2006), but they are reliant on the presence of an adequate number of cells with an adequate functional reserve. According to Phung et al. (2013), the main acute side effect of sulfonylureas is an increased rate of hypoglycemia, especially in older persons with impaired renal function, hepatic dysfunction, and those who have inadequate oral intake, alcohol misuse, calorie restriction, and other conditions (Scheen 2005).

Banting and Best discovered insulin, the most powerful anti-hyperglycemic medication, in 1921. Since then, it has resulted in significant improvements in the management of T2DM. Even when oral anti-diabetic medications are insufficient, insulin therapy can still effectively manage blood sugar levels and help individuals with T2DM with many metabolic abnormalities. It was observed that insulin has been used to treat diabetes for a longer period of time than any other drug, and the volume of research demonstrating a favorable balance between its advantages and hazards keeps expanding.

Depending on the clinical details of each patient, the start of insulin therapy is appropriate at different stages of diabetes. When a form of diabetes with significant insulin shortage is present or when the diagnosis of diabetes is made during an acute illness or severe metabolic decompensation, use as the initial form of pharmacotherapy is required. Later, when oral medicines and lifestyle interventions are no longer totally effective, insulin is typically the preferred initial injectable therapy. The selection of the appropriate medicine is the most crucial component of T2DM treatment. The objective of the current study was to identify the most effective treatments for diabetes in Bangladesh.

Methodology

Setting and participants: This interventional type of study was carried out in all the diabetic patients attending in Rajshahi Medical College Hospital, Barind Medical College Hospital, Diabetic Association Hospital in Rajshahi, and Chapainawabganj Hospital, Bangladesh. Sample size was 102 and was selected purposively during the study period of 3 years (August 2018 to July 2021).

Inclusion / exclusion criteria: All the patients with diabetes (HbA_1C >7.0%) attending the mentioned areas during the study period was considered as inclusion criteria. Patients who were not interested to participate using intra uterine device (IUD) and sub-dermal contraceptive implants were excluded from this study.

Data collection procedure: The researchers himself collected data from all the diabetic patients attending of the mentioned study areas in Bangladesh. Data were collected through a partially structured questionnaire. Baseline information on socio-demographic characteristics and impact of insulin, biguanide, 2nd generation sulfonylurea among them was collected from the study participants through interviewer administered questionnaire by face-to-face interview. For clinical assessment and monitoring random blood sugar (RBS), fasting blood sugar (FBS), 2 hours plasma glucose and HbA_1C were measured in the laboratory. For confirmation of diabetic condition HbA_1C was rechecked within 3 months interval. All efforts

were made to collect data accurately. For open questions, the respondents were asked in such a manner so that they could speak freely and explain their opinion in a normal and neutral way. No leading questions were asked.

Outcome variable: Impact of insulin, biguanide and 2nd generation sulfonylurea among the diabetic patients.

Independent variables: Age, sex, residence, occupation, life style, smoking habit, family history of diabetes, BMI, HbA_1C, FBS, and PPBS.

Ethical approval and consent of the participants: Prior to the commencement of the study, the research protocol was approved by the ethical committee of Institute of Biological Sciences (IBSc), University of Rajshahi, Bangladesh.

Statistical analysis

The data were analyzed according to the objectives of the study by using IBM SPSS software (Version-23).

Results

The mean age of the respondents as shown in Table 1, was 45.98 ± 11.23 years. Among the respondents 12.75%, 22.55%, 24.51%, 32.35% and 7.84% were in 18-30, 31-40, 41-50, 51-60 and >60 years age group, respectively. Age distribution of the patients was matched among the groups ($p = 0.985$). In the insulin receiving group, 41.18% were male and 58.82% were female;, in the biguanide receiving group, 44.12% were male and 55.88% were female; and in the sulfonylurea receiving group 35.29% were male and 64.71% were female. The sex distribution of the cases was matched among the groups ($p = 0.752$).

Regarding BMI among the respondents, it was found that 0.98% had BMI <18.50 kg/m^2, 52.94% had BMI between 18.50-24.99 kg/m^2 and 46.08% had BMI >25 kg/m^2. BMI status of the patients was matched among the groups ($p = 0.621$). It was observed that insulin receiving patients had relatively better glycemic control than biguanide receiving group than sulfonylurea receiving group at 3rd month. In insulin receiving group 82.35% had desired glycemic control, in biguanide receiving group 70.59% had desired glycemic control and in sulfonylurea receiving group 64.71% had desired glycemic control. Insulin receiving patients (88.24%) also had a relatively better glycemic control than the biguanide (76.47%) and sulfonylurea receiving group (73.53%) after 6th month.

In insulin receiving group 67.60% were urban resident and 32.40% were rural resident, in biguanide receiving group 64.70% were urban resident and 35.80% were rural resident and in sulfonylurea receiving group 58.80% were urban resident and 41.20% were rural resident. Resident history of the cases were matched among the groups ($p = 0.743$) (Fig. 1). Out of 102 diabetic cases 12.70% were government employee, 14.70% were non-government employee, 17.60% wee businessman, 35.30% were housewife, 9.80% had others profession and 9.80% were unemployed (Fig. 2). Among the respondents 65.70% had sedentary life style and 34.30% had active life style. Life style of the cases was also matched among the groups ($p = 0.337$) (Fig. 3). Regarding smoking status, it was revealed that 86% were non-smoker and 14% were smoker. Smoking habit of the patients was also matched among three groups ($p = 0.207$) (Fig. 4). Out of 102 DM cases 17% had positive family history of DM. Family history of DM was also matched among the groups ($p = 0.932$) (Fig. 5).

Table 1: Distribution of the respondents with different drugs.

Variables		Insulin	Biguanides	Sulfonylureas	Total	p-value
		(n = 34) %				
Age (years)	18-30	04 (11.76)	05 (14.71)	04 (11.76)	13 (12.75)	0.985
	31-40	06 (17.65)	07 (20.59)	09 (26.47)	23 (22.55)	
	41-50	09 (26.47)	08 (23.53)	09 (26.47)	25(24.51)	
	51-60	12 (35.29)	12 (35.29)	09 (26.47)	33 (32.35)	
	>60	03 (08.82)	02 (5.88)	03 (8.82)	08 (7.84)	
Mean age	45.98 ± 11.23 yr					
Sex	Male	14 (41.18)	15 (44.12)	12 (35.29)	41 (40.20)	0.752
	Female	20 (58.82)	19 (55.88)	22 (64.71)	61 (59.80)	
BMI	<18.50	01 (2.94)	00 (00)	0 (00)	01 (0.98)	0.621
	18.50-24.99	17 (50)	17 (50%)	20 (58.82)	54 (52.94)	
	>25	16 (47.06)	17 (50%)	14 (41.76)	47 (46.08)	
Glycemic control of the patients at 3rd month follow up (n = 102)						
HbA_1C	< 7	28 (82.35)	24 (70.59)	22 (64.71)	0.252	
	≥ 7	06 (17.65)	10 (29.41)	12 (35.29)		
FBS	< 7.2	30 (88.24)	26 (76.47)	25 (73.53)	0.284	
	≥ 7.2	04 (11.76)	08 (23.53)	09 (26.47)		
PPBS	<10	28 (82.35)	25 (73.53)	26 (76.47)	0.675	
	≥ 10	06 (17.65)	09 (26.47)	08 (23.53)		
Glycemic control of the patients at 6th month (n = 102)						
HbA_1C	< 7	30 (88.24)	26 (76.47)	25 (73.53)	0.284	
	≥ 7.0	04 (11.76)	08 (23.53)	09 (26.47)		
FBS	< 7.2	31 (91.18)	27 (79.41)	27 (79.41)	0.323	
	≥ 7.2	03 (8.82)	07 (20.59)	07 (20.59)		
PPBS	<10.0	29 (85.29)	27 (79.41)	28 (82.35)	0.817	
	≥ 10.0	05 (14.71)	07 (20.59)	06 (17.65)		

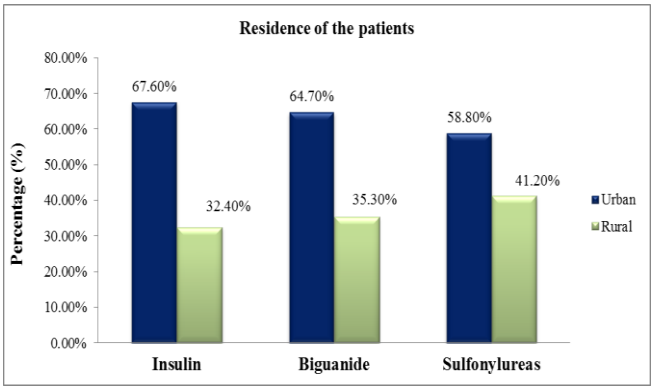

Fig. 1: Distribution of the respondents by residence.

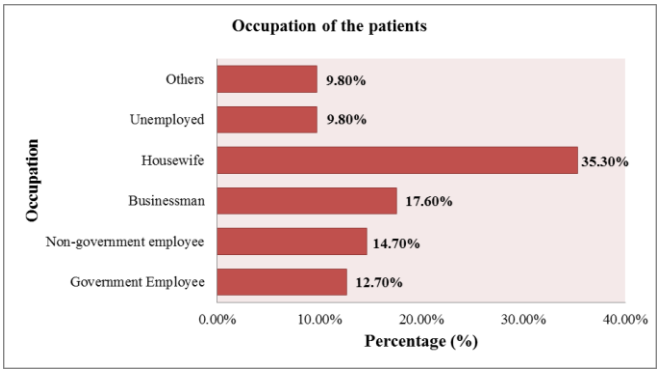

Fig. 2: Distribution of the respondents by occupation.

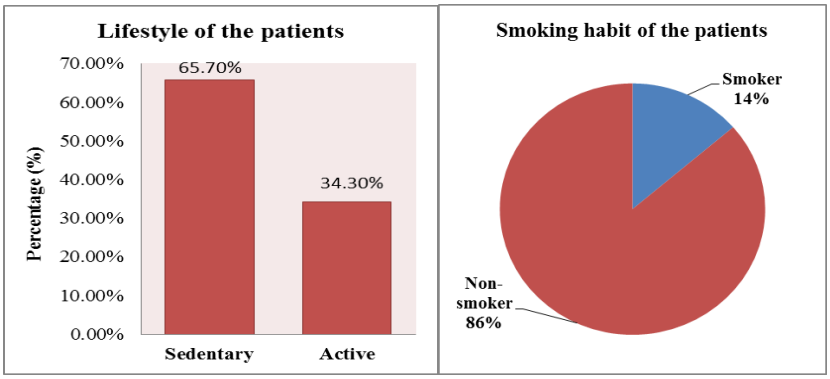

Fig. 3, 4: Distribution of the respondents by lifestyle and smoking habit.

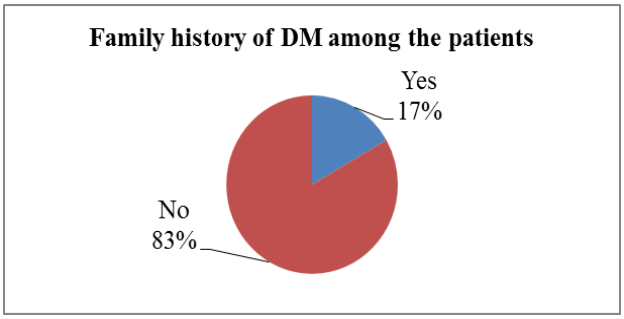

Fig. 5: Distribution of the respondents by family history of DM.

Discussion

We learned about the efficacy of diabetes medication and its effects on human health from this interventional type of investigation. This study was conducted among diabetic patients who were enrolled in several medical schools and hospitals in Rajshahi and its surrounding areas in Bangladesh. In our study, men made up 41.18% of the insulin receiving group, while women made up 58.82% of the biguanide receiving group, and men made up 44.12% of the sulfonylurea receiving group. The cases' sex distribution was balanced between the groups (p = 0.752). Similar to our findings, a study by Adeniyi et al. (2016) found that the majority of participants were females (70.3%) and resided in rural areas (88.7%). Regarding BMI of the respondents, the present study found 0.98% had BMI <18.50 kg/m^2, 52.94% had BMI between 18.50-24.99 kg/m^2 and 46.08% had BMI >25 kg/ m^2. BMI status of the patients was matched among the groups (p = 0.621). Nearly 90% of diabetic patients develop T2DM mostly relating to excess body weight according to the World Health Organization (WHO 2011). Furthermore, obesity is strongly inherited (Walley et al. 2006). It was assessed that insulin receiving patients had relatively better glycemic control than biguanide receiving group than sulfonylurea receiving group at 3rd month.

In insulin receiving group 82.35% had desired glycemic control, in biguanide receiving group 73.53% had desired glycemic control and in sulfonylurea receiving group 64.71% had desired glycemic control. Insulin receiving patients had relatively better glycemic control than biguanide receiving group than sulfonylurea receiving group at 6th month. In insulin receiving group 88.24% had desired glycemic control, in biguanide receiving group 76.47% had desired glycemic control and in sulfonylurea receiving group 73.53% had desired glycemic control. Patients treated with combinations of insulin secretagogues and biguanides at enrolment showed a significantly higher yearly mortality rate when compared with the rest of the sample (3.6% vs. 6.2% yearly; p<0.05); this was confirmed at multivariate analysis (OR [95% CI] 1.618 [1.044; 2.512]) (Monami et al. 2008).In insulin receiving group 67.60% were urban resident and 32.40% were rural resident, in biguanide receiving group 64.70% were urban resident and 35.80% were rural resident and in sulfonylurea receiving group 58.80% were urban resident and 41.20% were rural resident.

Resident history of the cases was matched among the groups (p = 0.743) (Fig. 1). The rural communities lack functional health facilities; there is a regular stock-out of medications and lack of doctors and nurses. Further access to quality healthcare becomes unattainable due to poverty (Longo et al. 2011, Adeniyi et al. 2015). In the present study the 102 diabetic cases 12.70% were government employee, 14.70% were non-government employee, 17.60% wee businessman, 35.30% were housewife, 9.80% had others profession and 9.80% were unemployed (Fig. 2). Among the respondents 65.70% had sedentary life style and 34.30% had active life style. Life style of the cases was also matched among the groups (p = 0.337) (Fig. 3).

Regarding smoking status, it was revealed that 86% were non-smoker and 14% were smoker. Smoking habit of the patients was also matched among three groups (p = 0.207) (Fig. 4).

A wide variety of lifestyle factors are also of great importance to the development of T2DM, such as sedentary lifestyle (Zimmet et al. 2001), physical inactivity (Hu et al. 2001), smoking (Manson et al. 2000). Out of 102 DM cases, 17% had positive family history of DM. Family history of DM was also matched among the groups (p = 0.932) as shown in Fig. 5. Insulin, biguanide and second-generation sulfonylurea their well-established glycemic efficacy, safety and tolerability support their use as an integral part of diabetes treatment. Given the fact that many of the clinical concerns associated with the use of insulin, biguanide and sulfonylurea are agent-specific, and do not pertain to the class as such, a careful choice of specific diabetic drug should be considered beneficial. Proper patient selection, choice of drug and dose, patient education and empowerment, and physicians training help ensures effective and safe use of this important class of drugs. People with no education, lower socio-economic status, and those who lived in disadvantaged regions in terms of education and economic profile (North-western part of Bangladesh) were found lacking of diagnosis, treatment, and control of diabetes.

From the findings of our study, we can conclude that substantial improvements of diabetes detection and treatment are needed in Bangladesh especially among the disadvantaged populations. These can be tackled by (i) reforming the health system based on disease burden, the Government of Bangladesh should give top priority to NCDs especially diabetes prevention and control in their health promotion programs; (ii) implementing universal health insurance or other risk pooling mechanisms in health financing system to ensure access and affordable care for all citizen from poor to rich; and (iii) creating diabetes awareness, changing lifestyle and dietary habits through well-designed public education and mass media campaigns.

Conflict of interest: the authors hereby declare no conflict of interest regarding the publication of this article.

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