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EMPAGLIFLOZIN SAFETY AND EFFICACY IN SOUTH INDIAN POPULATION

Diabetology

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ABSTRACT

Aim of this study to establish the safety and efficacy of empagliflozin. It's a Longitudinal observational study conducted in Medical college on 140 Type 2 Diabetes patients. The patients who where already in other OADs and started to take Empagliflozin 25mg within one week of initiation was taken into the study. The baseline value of FBS, PPBS, Weight, LDL, HDL, Sr.Electrolytes was noted. The patients will be followed up in 1st , 3rd , 6th month in each follow up visit physical examination will be done and clinical characteristic regarding adverse effects are noted. The laboratory investigations are repeated at the end of 6th month.The results are mean reduction in FBS & PPBS at the end of 6th month are 43mg/dl and 47mg/dl respectively. On observing the adverse events the incidence of hypoglycemia is 4.2%, hyponatremia is 7.5%, hypokalemia is 2.1% and Urinary tract infection is 2% . The serious adverse event is observed in one patient with a episode of DKA. There was mild increase in LDL and electrolyte imbalance. Empagliflozin 25mg OD shown better efficacy with lesser side effects.

KEYWORDS

I. INTRODUCTION

Diabetes mellitus have rapidly increased to 72.9 Million patients in India. Increase in Diabetes prevalence not only resulted in an increase in complication of diabetes but also increases health care cost and decreases QALY(1). Indians with diabetes have more body fat compared with Caucasians these body composition features worsens Insulin resistance(2). So the treatment for Indians been evolving based on this. SGLT 2 is Sodium Glucose Transporter present in Proximal tubule of nephron which accounts for 90% of glucose reabsorption. Inhibition of this can reduce glucose reabsorption and excretion in Urine. SGLT 2 Inhibitors like Empagliflozin is currently placed as a second line drug after failure glycemic control with metformin therapy particularly for Obese patients as per ADA 2022. Extra glycemic benefits like reduction in Body weight(3), decrease in Blood pressure(4) is been promising. EMPA-Reg trial showed that when compared with placebo, Empagliflozin reduces the rate of deaths from Cardiovascular causes(5).Adverse events is consistent with UTI and genital infection reported in greater proportion in empagliflozin (6). Since SGLT 2 independent of beta cell function there is an low risk of hypoglycaemia"(7). Empagliflozin increases the afferent arteriolar resistance without an alteration in efferent arteriolar leading to a reduction in glomerular hyperfiltration thus decrease in e GFR is hemodynamic in nature(8). Increase in HDL & LDL were observed in some trial which is due to Hemoconcentration(8). As the observational studies of SGLT 2 increases there is an increase in finding out of newer and rare adverse effect like recently FDA warned of Fournier's gangrene (9). So Post marketing surveillance and observational studies for safety is needed. The current study aims to analyse the efficacy and safety of empagliflozin on type 2 diabetes mellitus patients.

II. MATERIALAND METHODS

This Longitudinal observational study was carried out on patients of Department of Diabetology, Government medical college, Chennai, Tamilnadu from June 2019 to November 2019. A total 140 adult subjects (both male and females) of aged ≥ 18 years were for in this study.

Study Design: Longitudinal observational study

Study Location: This was done in tertiary care teaching hospital in Chennai.

Study Duration: June 2019 to November 2019

Sample size: 140 patients.

Sample size calculation: The sample size was estimated based oon prevalence. We assumed that confidence level of 95% ,Significance level(α)5%, & Tolerable level of error(L)= 5%. The sample size actually obtained for this study was 128 patients. We planned to include 140 patients with 10% drop out rate.

Subjects & selection method:

The study population was drawn from Kilpauk medical college who are attending Diabetology Out Patient department having uncontrollable diabetes and started on Empagliflozin from the period of June 2019 to December 2019.

Inclusion criteria:

1. Patients with Type 2 Diabetes Mellitus on Empagliflozin for less than <1 week.
2. Age >18 years.

Exclusion criteria:

1. Genetic mycotic infection.
2. Recurrent Urinary tract infection.
3. Pyelonephrities.
4. Acute Illness.
5. Type 1 Diabetes Mellitus.
6. e GFR < 45.
7. Pregnant women.
8. Lactating women.
9. Electrolyte Imbalances.

METHODOLOGY

After written informed consent was obtained, a questionnaire consisting of details of patients including sex, age, height, weight, duration of type 2 diabetes mellitus, duration of taking medications and pre-existing condition was given. Patients who were on oral medications were advised for insulin treatment, those refused are only included in this study and patient who has been initiated with SGLT2 inhibitor Empagliflozin 25mg OD less than 1 week are included. All patients were evaluated and screened for complications of diabetes as per standard of care. All patients were subjected to the following investigations: Fasting plasma glucose (FPG), Lipid profile, renal function tests and urine analysis at the start of study.

The patients will be followed up in 1st , 3rd , 6th month in each follow up visit physical examination will be done and clinical characteristic regarding adverse effects are noted. The laboratory investigations are repeated at the end of 6th month. All ADRs will be noted and analysed, they will also be reported to the Regional Pharmacovigilance centre by the CDSCO ADR reporting form. Based on the severity of ADR the drug will be withdrawn by the treating diabetologist.

Statistical analysis:

Datas were collected in Excel sheet. Statistical analysis were done in SPSS 23.0. Mean , Standard deviation and Standard error of mean were calculated. Data at start of the study and at end of 6th month were compared by Paired t test.

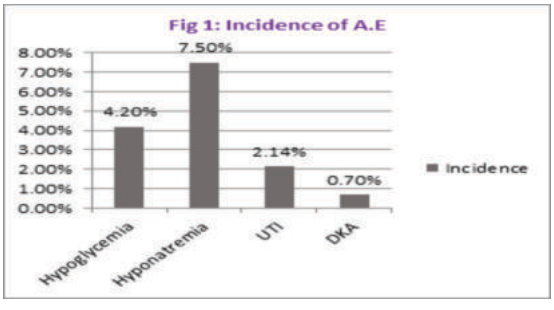
RESULT:

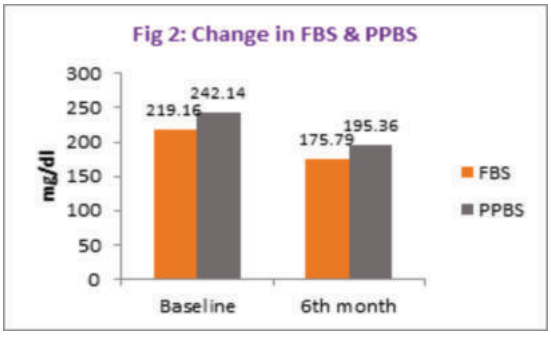
Demography:
Total of 140 patients was recruited after informed consent form. Out of 140 number of males are 50(35.7%) and number of females are 90(64.3%) the females were recruited more are due to in previous studies it had been shown that adverse event are more common among females. As far as age group is considered patients are divided into two group 40-50 years and 51-60 years. 55 patients are in 40-50 years and 85 patients are in 51-60 years group. Empagliflozin was used as 3rd line drug used after Metformin 1000mg and Glimepiride 2mg per day.

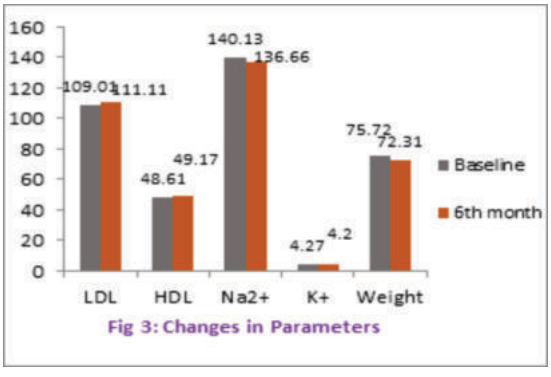
Efficacy end point:
The efficacy end points are FBS & PPBS. The mean FBS at the end of 6th month is 175.79mg/dl and the mean reduction in FBS from baseline is 43.37 mg/dl which was found to statistical significant p <0.0001. The mean PPBS at the end of 6th month is 195.36mg/dl and the mean reduction in PPBS from baseline is 46.78 mg/dl which was found to statistical significant p <0.01.

Other efficacy end points:
Mean LDL after 6 month of treatment was 111.11 mg/dl with mean change from baseline is significantly found to be +2.1mg/dl. Mean HDL after 6 month of treatment was 49.17 mg/dl with mean change from baseline is significantly found to be +0.57 mg/dl.

Safety end point:
6(4.2%) patients had atleast one episodes of Hypoglycemia i.e <70mg/dl during 6 months of duration, these episodes may be due to other OAD also. Mean reduction in Sr.Sodium level is found to be 3.47 mEq/L. 11 (7.5%) patient was diagnosed with Hyponatremia. Mean reduction in Sr.Potassium level is found to be 0.07 mEq/L. No patients experienced hypokalemia. 3(2.14%) patients was found to be culture positive urinary tract infection and was treated with oral antibiotics.1(0.7%) patient was admitted for DKA. Empagliflozin was stopped all 3 UTI patients and 1 DKA patient. Mean weight reduction after 6 month was 3.41 kg which was statistical significant.







Parameter	Start		6th month		p Value
	Mean	S.D	Mean	SD	
FBS	219.1	46.9	175.79	33.32	<0.01
PPBS	242.1	49.8	195.36	33.71	<0.01

Parameter	Start		6th month		p Value
	Mean	S.D	Mean	SD	
LDL	109.01	16.69	111.11	16.09	>0.05
HDL	48.61	5.37	49.17	5.12	>0.05
Weight	75.72	8.95	72.31	7.44	<0.01

Parameter	Start		6th month		p Value
	Mean	S.D	Mean	SD	
Na2+	140.13	2.95	136.66	2.57	<0.0001
K+	4.27	0.46	4.20	0.450	>0.05

DISCUSSION:
This study was a prospective observational study to evaluate the safety and efficacy of Empagliflozin 25mg in tertiary care hospital. Efficacy analysis showed mean reduction in fasting sugar was -43.37 mg/dl and post prandial sugars was -46.78 mg/dl in this study. J Rosenstock (10) et al demonstrated mean change in FBS to be -27mg/dl and HbA1C% as -0.55%. The change in PPG may be contributed by other OADs. Though there was mild increase in LDL but its not statistical significant, the raise in LDL may be due to decreased LDL turnover. The adverse event found in this study was hypoglycaemia (4.2%), hyponatremia(7.5%), hypokalemia (2.14%), and UTI in 3 patients. One patient had serious adverse event of Ketoacidosis and was hospitalised. Empagliflozin was discontinued in one patient. The above safety profile matches with Flippatos et al (11) showing electrolyte and kohei et al on hypoglycaemia, urinary tract infection which is due to increased secretion of glucose from SGLT 2 receptor.

CONCLUSION:
Patients with once daily Empagliflozin 25mg as add on to other OADs shown better efficacy with Fasting and post prandial glucose. It was well tolerated with some electrolyte imbalance and minimal episode of hypoglycaemia. Though the LDL is increased but the overall benefit in cardiovascular benefit is high.

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