Journal Homepage: -www.journalijar.com
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)
Article DOI:10.21474/IJAR01/6454
DOI URL: http://dx.doi.org/10.21474/IJAR01/6454

RESEARCH ARTICLE

FIXED-DOSE IRBESARTAN-HYDROCHLOROTHIAZIDE TREATMENT ADHERENCE IN ESSENTIAL HYPERTENSION PATIENTS: REGIONAL, MULTICENTER, NON-INTERVENTIONAL, NON-CONTROLLED, 3 MONTHS COHORT STUDY, PROSPECTIVE REGISTRY IN THE GULF REGION.

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Manuscript Info

Manuscript History

Received: 05 December 2017
Final Accepted: 07 January 2018
Published: February 2018

Keywords:-
Antihypertensive therapy, fixed-dose combinations, hypertension, Irbesartan-hydrochlorothiazide, treatment adherence.

Abstract

Hypertension persists as a major public health challenge worldwide and is predominantly caused by treatment non-adherence. Assessments of adherence and barriers to antihypertensive therapies in the Gulf region are needed. We aim to assess adherence to – and the tolerability, safety, and efficacy of – fixed-dose irbesartan-hydrochlorothiazide in hypertensive patients across several countries in the Gulf region. Essential hypertension patients for whom fixed-dose irbesartan-hydrochlorothiazide was prescribed at physicians' discretion were followed for three months. Treatment adherence (using The Morisky Medication Adherence Scale (MMAS-8)), tolerability, safety, and efficacy were assessed throughout the study period. Barriers preventing treatment adherence were also identified. We found that 70.9% of patients (n=681) were adherent to fixed-dose irbesartan-hydrochlorothiazide therapy following three months of treatment. An adverse event rate of 0.4% (n=4) was reported; 0.1% (n=1) of patients experienced serious adverse events. Following three months of treatment, 73.3% of patients (n=704) reached their target Blood Pressure (BP). Achievement of target BP was more prevalent in non-diabetic hypertensive patients (75.5% vs. 69.1%; p=0.033). Inconvenience of daily treatment was the most commonly reported barrier to adherence; 60.4% (n=169). In conclusion, Fixed-dose irbesartan-hydrochlorothiazide treatments can aid patients – including diabetics – correct elevated BP. High tolerability andtreatment effectiveness and a convenient dosing schedule are likely contributors to high antihypertensive treatment adherence.

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Introduction:-

In spite of recent drug developments and the surplus availability of antihypertensive therapies, hypertension persists as a major public health challenge worldwide. Defined as systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg, hypertension is often chronic and asymptomatic during the early stages of the disorder (Mancia et al., 2013, Krousel-Wodd et al., 2009). Hypertension is a major and modifiable contributor to the global burden of disease, accounting for the majority of cardiovascular disease (CVD)-related deaths every year (WHO, 2013).

Several investigations – including observational studies and randomized controlled trials of antihypertensive therapies – have demonstrated that adequate BP control can effectively reduce CVD-related morbidity and mortality (Collins and MacMahon 1994). Provided that monotherapies are seldom sufficient or effective for achieving target BP, the European Society of Hypertension – European Society of Cardiology (ESH – ESC) advocate the employment of aggressive treatment combinations when attempting to restore normotension – particularly in high risk patients and those with markedly elevated baseline BP (non-grade 1 hypertension) (Mancia et al., 2013, Rochlani et al., 2017, Carrao et al., 2010). Patients with resistant hypertension are likely to receive at least four antihypertensive drugs daily and that there is some evidence to suggest that fixed combinations bolster treatment adherence (Bangalore et al., 2007). Consequently, several guidelines have recommended use of such combinations to reduce the pill burden and improve adherence to treatment (Myat et al., 2012).

The burden of hypertension, and subsequent adverse cardiovascular effects, has been especially heavy in the Arab states of the Persian Gulf and the Middle East in general; hypertension prevalence rates for this region range from 25.2% in Oman to 37.3% in the United Arab Emirates (UAE) (Tailakh et al., 2014). This phenomenon has been attributed to the widespread adoption of sedentary lifestyles, increasingly unhealthy diets, and obesity that followed the rapid urbanization in this region over the last few decades (Gehani et al., 2014). Comprehensive assessments of antihypertensive treatment adherence and the present barriers for adherence in this region are currently scarce. The primary objective of our investigation was to ascertain adherence to fixed-dose combinations of hydrochlorothiazide (HCTZ) and the angiotensin II receptor antagonist irbesartan (IRB) in essential hypertension patients residing in the Gulf region. The secondary objectives were to assess the efficacy, safety, and tolerability of fixed-dose IRB-HCTZ, and to identify barriers preventing treatment adherence.

Materials and methods:-

Study design and ethical considerations:-

This regional, multicenter, non-comparative non-controlled and non-interventional study aimed to recruit 1000 patients with essential hypertension through public and private healthcare facilities across several countries in the Gulf region (namely UAE, Kuwait, Qatar, Bahrain, and Oman). Consecutive recruitment was considered to limit bias of patient selection. Recruitment only commenced following a review and approval/ favorable opinion by Dubai Health Authority (DHA) and Al Qassimi Clinical Research Centre, Research Ethics Committee, United Arab Emirates. The other four countries did not require a prior approval for observational studies.

The study procedures were conducted according to all applicable local laws and regulations and the principles established by the 18th World Medical Assembly (Helsinki, 1964). Written informed consent was obtained from all participants involved in this investigation prior to the conduct of any study-related activities.

This study included three visits spanning a total of three months (Figure 1). Investigators determined subject eligibility during the baseline/screening visit. Once eligibility was confirmed, enrolled participants attended two follow up visits 30 (conducted on-site or via telephone) and 90 days (on-site) following their recruitment. Demographic data, vital signs (including SBP and DBP), patient medical history, as well as history of prior antihypertensive therapies and treatment adherence were among the data collected during the baseline visit. Treatment adherence, tolerability, safety, and effectiveness of fixed-dose IRB-HCTZ were assessed during follow up.

Study participants:-

Participating subjects included male and female adult patients (18 years of age and over) with essential hypertension who had provided written informed consent and were prescribed fixed-dose IRB-HCTZ (150/12.5 mg, 300/12.5 mg, or 300/25 mg, CoAproval, Sanofi Aventis) at the sole discretion of their physicians, as per the summary of product

characteristics and/or the ESH-ESC2013 guidelines. Patients were excluded if they presented with impaired renal function, secondary hypertension, current pregnancy, breast-feeding, and any contraindications or hypersensitivity towards the investigational product.

Study objectives:-
The primary objective of our investigation was to assess treatment adherence in hypertensive patients prescribed fixed-dose IRB-HCTZ for three months. The Morisky Medication Adherence Scale (MMAS-8) – a scale with proven reliability for adherence assessments in hypertensive patients – was utilized to measure self-reported antihypertensive medication adherence during the final follow up visit. Using this eight-item scale, an integer score ranging from zero to eight was calculated. A score of six was used as the cut-off point for adherence (non-adherent: MMAS-8 < 6; adherent: MMAS-8 ≥ 6).

The secondary objectives for this study were as follows: 1) to assess the safety and tolerability of fixed-dose IRB-HCTZ; 2) to determine the proportion of patients achieving target BP, as per the definitions in the 2013 ESH-ESC guidelines; 3) to ascertain the relationship – if any – between treatment adherence and blood pressure reduction following a three-month treatment regimen; 4) to identify barriers leading to treatment non-adherence.

Safety assessments:-
All participating patients enrolled in the study, and for whom written informed consent was obtained, were included in the safety analyses. Abnormal reactions, side effects, intercurrent diseases, unexpected events, or abnormal laboratory findings, regardless of relatedness to prescribed therapy, were defined as adverse events (AE). The severity of such events and their relationship to trial medication was determined by the investigators. Any untoward medical occurrence that following the administration of any dose of the drug resulted in death, was life threatening, required inpatient hospitalization or caused a prolongation of an existing hospitalization, , results in persistent or significant disability/incapacity or; is a medically important event was defined as serious adverse events (SAE)

Efficacy assessments:-
All enrolled patients with at least one evaluable primary endpoint (MMAS-8 score) who had not committed any protocol violations were included in the efficacy analyses. The target BP (SBP and DBP) for patients enrolled in this investigation were in accordance with the 2013 ESH-ESC guidelines for blood pressure control rates.[1]The unified target SBP for treatment was considered at< 140 mmHg for patients with either low or high cardiovascular risk. The unified target DBP was < 90 mmHg for patients with low-high cardiovascular risk factors, and < 85 mmHg for diabetic patients. SBP and DBP were recorded on three separate occasions for each patient throughout the study period (once during each study visit).

Statistical considerations:-
The safety population included all patients who had signed an informed consent form. Patients in the eligible population (i.e. those satisfying all inclusion/exclusion criteria) were included in the baseline descriptive analyses. Of those, patients who had not committed any major protocol violations and had at least one evaluable primary endpoint were included in the efficacy analyses.

Previous studies involving a large pool of hypertensive patients have demonstrated good adherence (91.1%) to a one-year IRB treatment regimen (Brunier et al., 2005). For this study, the predicted adherence to a three-month fixed-dose IRB-HCTZ regimen was 90% with a 95% confidence interval (CI) of 2%. A target of 1000 patients was set, considering the target sample size (n=864) and an anticipated drop-out rate of 10%.

Descriptive summary statistics were provided for quantitative data; andwere summarized using count, mean with 95% confidence interval (CI), standard deviation (SD), median, minimum, and maximum. The chi-square test was employed to compare patients achieving their target BP levels to those who had not. Potential correlations between drug adherence scores and BP reduction at three months were identified using Spearman's Rho correlation coefficient. The statistical significance of differences in age and baseline grade of hypertension for non-adherent and treatment-adherent patients were determined using the student t-test and chi-square test, respectively. All statistical tests were performed at a 5% level of significance, using SPSS version 21[1].

[1] IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.

Results:-

Patient Disposition:-

A total of 1000 patients with essential hypertension were recruited from 56 sites in UAE (30.1%), Kuwait (19.5%), Bahrain (17.1%), Oman (16.7%), and Qatar (16.6%). Of those, 980 (98.0%) fully met inclusion/exclusion criteria and were included in the descriptive analyses; excluded patients included 17 who had received concomitant antihypertensive interventions besides IRB-HCTZ and three with alterations to their initial IRB-HCTZ treatment. By study end (month 3), 961 (96.1%) participants had an evaluable MMAS-8 score, allowing for their inclusion in the efficacy analyses (Figure 2).

Baseline Characteristics:-

Patient characteristics are summarized in table 1. The mean (SD) age of enrolled participants was 47.55 (9.53) years.Most patients were men (72.8%), of Asian ethnicity (57.0%), and a previous family history of hypertension (75.3%). The most common cardiovascular risk factors associated with hypertension in our patient population included dyslipidemia (47.7%), diabetes mellitus (34.3%), and obesity (19.3%). Most patients had been treated with antihypertensives prior to enrollment (73.4%), and most reported satisfactory adherence to previous regimens (74.5%). At baseline, around half of our patients (53.8%) were following a dietary control regimen to mitigate the effects of hypertension. A minority reported being "highly active" (5.2%) and "currently smoking" (17.1%) at baseline.

Adherence to fixed-doseIRB-HCTZ therapy:-

All enrolled subjects were prescribed IRB-HCTZ therapy, including the 150/12.5 mg (55.3%), 300/12.5 mg (42.1%), and 300/25 mg (2.7%) formulations. On the basis of MMAS-8 assessments and subsequent scores following a three-month treatment, 306 (31.8%) patients exhibited high adherence, 375 (39.0%) were moderately adherent, and 280 (29.1%) had low adherence to their respective fixed-dose IRB-HCTZ regimens. In total, 681 (70.9%) patients adhered to their prescribed treatment (Figure 3).The extent of adherence to IRB-HCTZ regimens did not significantly differ when comparing diabetics to non-diabetics (adherent, 68.5% vs. 72.1%; p=0.234; Table 2).

Safety and tolerability:-

Data from the safety population (n=1000) was included in this analysis. The total treatment exposure period was 90 days. Overall, a 0.4% (N=4) adverse event rate was observed throughout the study period (Table 3). Reported events included hyperuricaemia, maculopapular rashes, gastritis, and a road traffic accident. All but one event were mild-moderate in nature (hyperuricaemia, maculopapular rash, and gastritis); the road traffic accident was serious in nature with a fatal outcome. Patients experiencing hyperuricaemia and maculopapular rashes required corrective actions/treatments. Prescribed IRB-HCTZ treatments were discontinued in the two instances of gastritis and maculopapular rashes. All reported AEs, with the exception of the maculopapular rash, were deemed unrelated to IRB-HCTZ treatment by the study investigators.

Blood pressure target achievement:-

Following a single month of IRB-HCTZ antihypertensive therapy, over a third (40.8%) of patients achieved their blood pressure target as per the ESH-ESC 2013 recommendations. By the third month of treatment, marked improvements in SBP and DBP were observed in the majority of patients with 73.3% meeting their BP targets (Figure 4). Superior treatment outcomes were observed in non-diabetics when compared to their diabetic counterparts; the proportion of diabetic patients achieving their target BP was significantly lower (75.5% vs. 69.1%; p=0.033; Table 2).

The proportion of patients who had reached their BP target was similar in both the treatment adherent and non-adherent subgroups (73.3% vs. 73.2%; p=0.985; Table 4). However, significant differences in target BP achievement rates were noted when comparing patients reporting low (73.2%), moderate (78.4%), and high (67.0%) treatment adherence(p=0.004; Table 4); a larger proportion of patients in the high adherence subgroup did not meet their BP endpoint when compared to those reporting moderate treatment adherence (33.0% vs. 21.6%; p=0.001; Table 4). No significant correlations between MMAS-8 scores and a reduction in both SBP and DBP were observed (r=+0.005; p=0.886 and r=+0.032; p=0.319, respectively).

Barriers to treatment adherence:-

During the MMAS-8 treatment adherence assessments, additional information regarding the barriers to adherence was collected.Reasons provided by patients for non-adherence to their prescribed anti-hypertensive therapy included the inconvenience of having to take the medicine every day (169/280; 60.4%), the inconvenience of having to take the medicine outside their homes (167/280; 59.6%), feeling like the symptoms are under control (103/280; 36.8%), and feeling worse following treatment (84/280; 30.0%).

Figure 1:- Study design

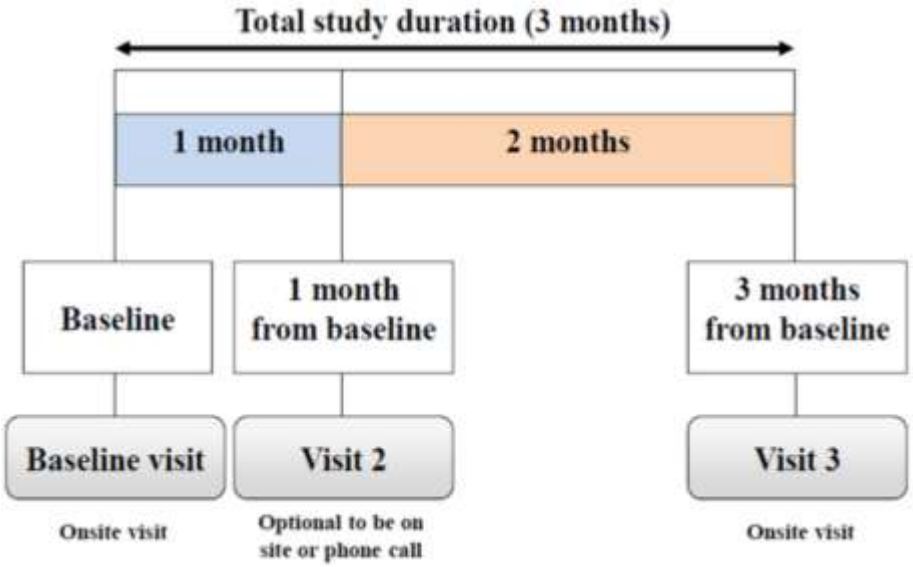

Figure 2:- Flowchart of patient enrollment

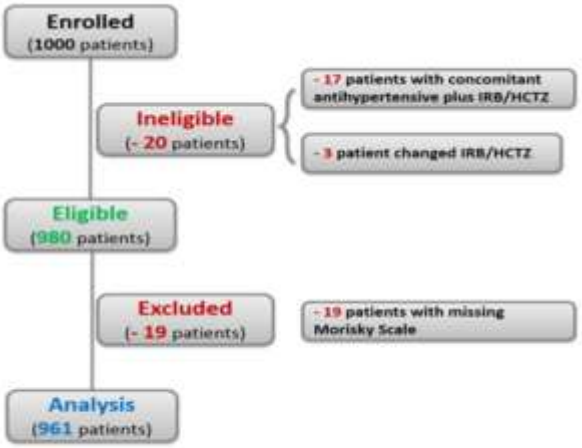

Figure 3:- Adherence to prescribed Irbesartan-hydrochlorothiazide fixed dose combination

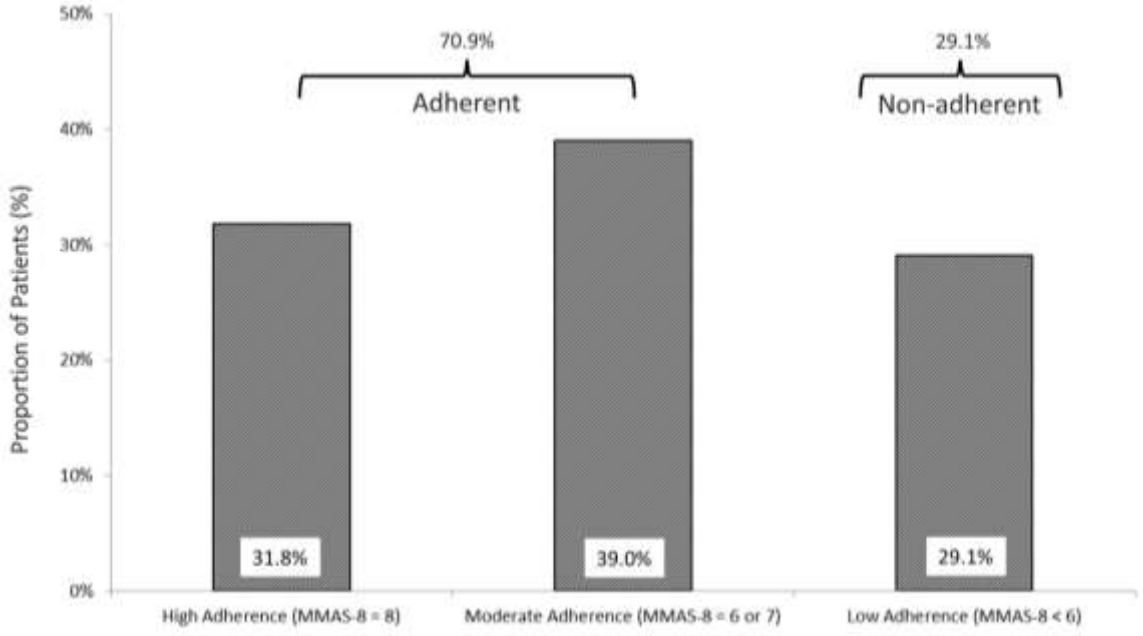

Figure 4:- Achievement of target BP levels at month one and three of treatment

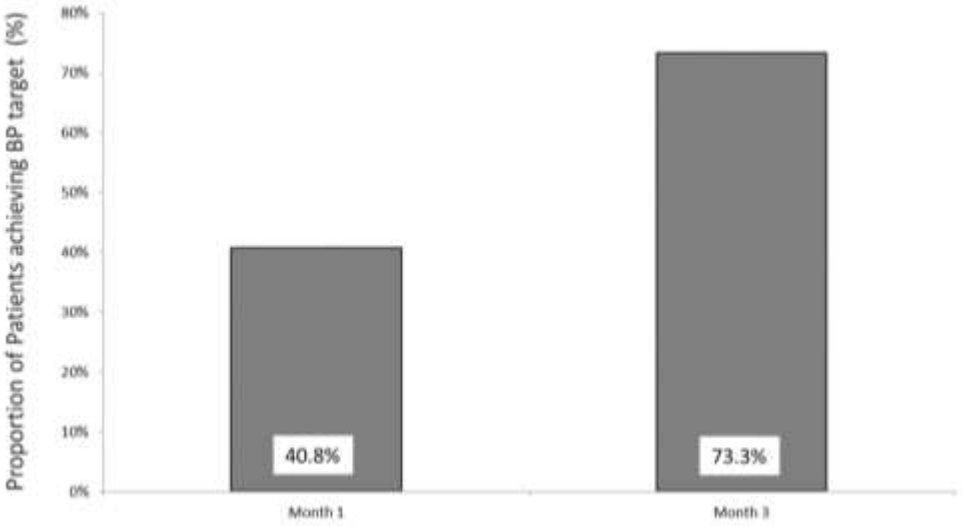

Table 1:- Patient Characteristics at Baseline (Eligible Patients)

Characteristic	Total Study Population (N = 980)
Demographics	
Age, mean (range), y	47.55 (23.7-85.5)
Men/Women, No. (%)	713/267 (72.8/27.2)
Ethnicity, No. (%)	
Asian	558 (57.0)
Arab	372 (38)
Caucasian	23 (2.3)
Black	19 (1.9)

Other	7 (0.7)
Weight, mean (range), kg	83.04 (48.2-186.0)
Smoking, No. (%)	166 (17.1)
Uneducated, No. (%)	27 (2.8)
Unemployed, No. (%)	185 (19.1)
Cardiovascular Status/History	
Heart rate, mean (range), bpm	79.76 (56-125)
SBP, mean (range), mmHg	156.36 (110.0-222.5)
DBP, mean (range), mmHg	96.61 (62.5-139.0)
Dyslipidemia, No. (%)	467 (47.7)
Diabetes Mellitus, No. (%)	336 (34.3)
Obesity, No. (%)	189 (19.3)
Duration of HPTN, mean (range), y	4.84 (0.0-115.6)
Family history of HPTN, No. (%)	730 (75.3)
Prior antihypertensive therapy, No. (%)	718 (73.4)
Compliant, No. (%)	540 (74.5)
Following dietary control plan, No. (%)	499 (53.8)
HCTZ hydrochlorothiazide; **bpm** beats per minute; **SBP** systolic blood pressure; **DBP** diastolic blood pressure	

Table 2:- Adherence to treatment and achievement of target BP according to diabetic status

Status at month 3	Diabetics (N = 333)	Non-diabetics (N = 628)	*P*
Adherence to IRB-HCTZ			
Adherent, No. (%)	228 (68.5)	453 (72.1)	0.234*
Non-adherent, No. (%)	105 (31.5)	175 (27.9)	
Achievement of BP Target			
Target Achieved, No. (%)	230 (69.1)	474 (75.5)	**0.033***
Target not achieved, No. (%)	103 (30.9)	154 (24.5)	
BP Blood Pressure ***** Pearson Chi Square test was utilized for comparisons between diabetics and non-diabetics.			

Table 3:- Incidence of adverse events

AEs. No. (%)	Safety Population (N = 1000)
Total	4 (0.4)
Hyperuricaemia	1 (0.1)
Rash (maculopapular)	1 (0.1)
Gastritis	1 (0.1)
Road Traffic Accident	1 (0.1)
Severity	
Mild	2 (0.2)
Moderate	1 (0.1)
Severe	1 (0.1)
Related to prescribed treatment	1 (0.1)
Requiring corrective action	2 (0.2)
Serious	1 (0.1)
Deaths	1(0.1)
Discontinuations due to AE	2(0.2)
AE adverse event	

Table 4:- Adherence to treatment according to achievement of target BP

Adherence	Target achieved (N = 704)	Target not achieved (N = 257)
Non-adherent*, No. (%)	205 (73.2)	75 (26.8)
*Low adherence***	205 (73.2)	75 (26.8)
Adherent total*, No. (%)	499 (73.3)	182 (26.7)
*Moderate adherence***	294 (78.4)	81 (21.6)
*High Adherence***	205 (67.0)	101 (33.0)

* Pearson Chi Square test to compare adherent and non-adherent groups revealed p = 0.985
Pearson Chi Square test to compare all three adherence groups revealed **p = 0.004
Post-hoc test to compare moderate and high adherence groups revealed **p = 0.001
**Relative risk of uncontrolled BP to controlled BP according to moderate and high adherence: 1.53 (95% CI = 1.19-1.96)

Discussion:-

The limited data on adherence to and barriers preventing antihypertensive treatment therapy in the Gulf region merits further investigation. This multicenter observational study included a large sample of patients with essential hypertension across five countries. Adherence to – and the safety, tolerability and efficacy of – fixed-dose IRB-HCTZ regimens were assessed. Our chief findings included 1) over two thirds of enrollees (70.9%) reported self-administration practices in adherence with physician advice, 2) treatment with fixed-dose IRB-HCTZ was extremely well tolerated and adverse event rates were minimal (0.4%), 3) hypertensive patients exhibited a prompt response to treatment and the majority (73.3%) achieved target BP levels per ESH-ESC guidelines following three months of treatment, 4) non-diabetic hypertensive patients demonstrated a superior response to treatment when compared to diabetics, and 5) inconvenience of a daily treatment regimen was the most common barrier to adherence.

Poor adherence with prescribed antihypertensive treatments is the predominant cause of uncontrolled hypertension (Morisky et al., 2008). Fixed-dose combinations are convenient by design, encouraging treatment adherence and persistence by reducing the overall pill burden and simplifying patients' dosing regimens (Bramlage, 2009). As we expected, the vast majority of our patients reported moderate-to-high adherence to fixed-dose IRB-HCTZ treatments. These rates are concordant with previous reports for various fixed-dose treatments (Dickson, and Plauschinat, 2008). It should be noted that marginally higher IRB-HCTZ treatment adherence has been reported by other investigations, including an observational study that was conducted in hypertensive patients in Egypt for a similar duration (Leon, 2014). A recent study conducted by Mohd et al. (2016) to assess treatment adherence in adults with diabetes in this region reported age as a predictor of adherence; older patients were more treatment adherent (Mohd et al., 2016). Additionally, Caro et al. previously reported that older patients and women were more likely to exhibit treatment persistence (Caro et al., 1999). The relatively lower adherence rates in this report may therefore be a consequence of the fact that our hypertensive cohort was younger (47.55 vs. 52.84 years) and included a greater proportion of male patients (72.8% vs. 58.2% males) (Leon, 2014).

Tolerability is one of several critical factors that often influences adherence in patients receiving long-term therapies for chronic conditions. Our safety/tolerability assessments indicate that low (150/12.5 mg) and high dose (300/12.5 mg and 300/25 mg) IRB-HCTZ treatments have outstanding safety profiles and are well tolerated in hypertensive patients residing in the Gulf region. The aforementioned observations are consistent with previous reports from short- and long-term studies (Kochar et al., 1999, Coca et al., 2003, Neutel et al., 2009). The majority of reported events were mild and unrelated to the prescribed treatment. AEs that typically occur following initiation of IRB-based therapies – including dizziness, fatigue, and musculoskeletal pain – did not manifest in enrolled participants (FDA, 1997). One event was serious in nature; one of our patients was involved in a fatal road traffic accident, an event that was not related to the prescribed treatment. All non-serious events were recovered by the end of the investigation. The low adverse event rate in our study reinforces the notion that fixed-dose IRB-HCTZ is highly safe and tolerable, and likely contributed to the favorable adherence rates that were observed.

The cumulative efficacy of combined IRB-HCTZ in hypertensive patients has been demonstrated in several studies, with reported response rates over 80% following 2-12 months of treatment (Kochar, 1999, Weir et al., 2007). Furthermore, previous investigations have also demonstrated that IRB-HCTZ can effectively elicit favorable BP responses in both treatment-naïve and –experienced patients (Weir et al., 2007, Bobrie et al., 2005). The present

analysis indicates that a daily fixed-dose of IRB-HCTZ facilitates an expedited reduction of BP; almost half of our patients reached their BP targets within one month of treatment, echoing response rates reported by Neutel et al. for patients with severe hypertension following 5 weeks of therapy (Neutel et al., 2006). The number of patients achieving ESH-ESC BP goals rose to 73.3% by the third month of treatment. Given the observational nature of our study, the aforementioned rates indicate that IRB-HCTZ therapies produce clinically meaningful SBP/DBP reductions in real-world clinical settings in the Gulf region.

A substantial proportion of hypertensive patients present with comorbid diabetes mellitus, and the coexistence of both disorders escalate the risk of macrovascular and microvascular complications (Sowers 2004, King et al., 1999). While restoration of normotension can markedly reduce the prevalence of cardiovascular and renal disorders, some reports suggest that this is more difficult to achieve in diabetic patients presumably due to the adverse impact of diabetes on the cardiovascular system (Mallat et al., 2014, Shelley et al., 2011). Indeed, Weir et al. previously reported a notably diminished attainment of target BP (<140/90 mmHg) in patients with type 2 diabetes compared to those without (35.4% vs. 45.5%) (Weir et al., 2007). Our results – namely the significantly diminished target BP achievement in diabetics – corroborate the aforementioned observations, though it is interesting to note that target BP achievement rates in our diabetic cohort were notably higher (69.1% vs. 35.4%. Based on our analyses, treatment with fixed-dose IRB-HCTZ is a convenient and effective approach to treat hypertensive patients, including those with comorbid diabetes for whom initial therapy with multiple agents is recommended (American Diabetes Association, 2002).

The relatively low response rates in in the high adherence cohort was interesting to note and surprising. These seemingly discrepant observations resonate with those made by Breaux-Shropshire et al. and are likely a byproduct of inaccurate patient recall or patients reporting an overly optimistic – and socially desirable – approximation of adherence to their physicians (Breaux et al., 2012). While the MMAS-8 has been previously validated, the potential biases of self-report measures allude to the relative benefits of more objective adherence assessments that are based on medication possession ratio (MPR) (Ho et al., 2009). Conversely, the reliability MPR is similarly questionable provided that medication refill history does not necessarily provide an accurate account of patients taking their treatments as prescribed.

On the basis of the administered MMAS-8 assessments, enrolled patients reported several barriers to adherence that included treatment- and condition-centered factors. Despite the once-daily dosing schedule for fixed-dose IRB-HCTZ, inconvenience of a daily treatment plan was identified as the predominant barrier to adherence in our hypertensive cohort. The asymptomatic nature of hypertension was also a prevalent contributor. Provided that a missed - or even mistimed - dose can adversely impact BP control, our analysis suggests a need for additional interventions – alongside reducing the number of daily doses – to further augment treatment adherence (Zannad, 1995). The benefits of educational sessions (about the disease and importance of adherence) for patients with chronic conditions in this region have been previously demonstrated (Khalil and Elzubier, 1997, Al-Qasem et al., 2011). Complex interventions that encompass treatment simplification, educational sessions, and motivational strategies (daily reminder charts, training in self-administration, electronic medication adherence aids/smart caps, and telephone follow-up/counseling) will likely enhance treatment adherence in hypertensive patients (Domino, 2005).

There are several limitations to the current study that should be addressed. Given the observational nature of this investigation, the lack of a control arm means it is difficult to conclusively ascertain the efficacy and safety of fixed-dose IRB-HCTZ in enrolled patients. However, our reported adherence rates are likely an accurate representation of rates in general practice. The assessment period for this study was relatively short (a total of 90 days). While this design permitted an investigation of initial responses, the long-term adherence, tolerability, and effectiveness of fixed-dose IRB-HCTZ were not evaluated. Considering the chronic nature of hypertension, such assessments can provide additional and valuable insights to physicians and guide local and regional healthcare policies.

In conclusion, our study represents an initial step towards identifying adherence and barriers to antihypertensive therapies in the Gulf region. Fixed-dose IRB-HCTZ treatments (150/12.5, 300/12.5, and 300/25 mg) can aid patients – including those who are diabetic – correct elevated BP. While some patients achieve their target BP within a month, most will require treatment for at least a few months to reach their goal.Superior tolerability, high effectiveness and a convenient dosing regimen are likely contributors to high IRB-HCTZ treatment adherence.

Acknowledgments:-

This investigation was conducted by investigators in private and public hospitals (totaling 56 centers) in the UAE, Kuwait, Qatar, Bahrain, and Oman. We thank all participating centers for their valuable involvement in this study. Editorial support for this article was provided by DataClin CRO. This study was funded by Sanofi-Aventis UAE which took no part in the analysis/ interpretation of the presented data.

Disclosure of conflict of interest:-

The authors have no conflicts of interest to declare.

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