COMPARISON OF DILTIAZEM AND METOPROLOL IN THETREATMENT OF ATRIAL FIBRILLATIONS: AN OBSERVATIONAL STUDY

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ABSTRACT

AIM: To compare the effectiveness of Diltiazem Versus Metoprolol in the treatment of Atrial fibrillation

INTRODUCTION: Atrial fibrillation is the commonest cardiac arrhythmia that accounts for more than one third of hospital admissions for the disturbance in cardiac rhythm. From the recent epidemiological data, it is reaffirmed that AF is a global epidemic and has adverse effect on long term morbidity and mortality.

METHODS: A prospective clinical study was conducted among 80 patients of atrial fibrillation admitted at Mandya Institute of Medical Sciences during a time period of 12 months. Further, according to the need of the patient and choice of the treating physician, 40 patients received Diltiazem while other 40 patients received Metoprolol. Later, ECG was taken at 5,10,15 and 20 min and the results were compared.

RESULTS: On comparing both the groups, the mean age was 56.53 years in Diltiazem group whereas 57.35 years in the Metoprolol group. Majority were suffering from hypertension, followed by ischemic heart disease, and diabetes mellitus. Further, the variation in heart rate from the baseline was observed on 4 more occasions which includes 5, 10, 15 and 20 minutes duration. The study also found statistically significant association with respect to number of doses required for management of the condition between two groups, thereby suggesting that just a single dose was enough in case of diltiazem, while 3 doses were required in case of metoprolol.

CONCLUSION: Although, both diltiazem and metoprolol reduced the heart rate of the participants below 100 bets per min over the period of time, diltiazem was more successful comparatively.

KEYWORDS: Atrial fibrillation, Effectiveness, Safety, Diltiazem, Metoprolol

INTRODUCTION

Atrial fibrillation (AF) is the commonest cardiac arrhythmia, and is increasing in frequency. Atrial fibrillation is an abnormal heart rhythm during which the upper chambers of the heart beat irregularly. Normally the pacemaker of the heart generates an electrical impulse, which is conducted or carried to the lower or pumping chambers of the heart via the electrical conducting tissues of the heart. In atrial fibrillation, the

heart's natural pacemaker, the sinus node, no longer generates an electrical impulse. Instead electrical activity occurs irregularly throughout both left and right atria. This irregular electrical impulse is conducted erratically to the ventricles, resulting in an irregular heartbeat which may be excessively fast and vary in volume from beat to beat.

The chief consequence of AF is an increased likelihood of stroke; this occurs in 1.5% of persons with AF in their 50s, to a 23.5% risk for those in their 80s. Mortality rates are doubled, in both sexes, due to stroke, heart failure, or myocardial infarction. Atrial fibrillation may cause chest pain, shortness of breath, dizziness, weakness or fatigue. In some patients there are no accompanying symptoms. Usually however symptoms are not that severe and the arrhythmia may be dealt with less acutely.

There are so many causes or risk factors which produces the risk of AF which includes cardiac causes like systemic hypertension,ischemic heart disease, rheumatic mitral valve disease, chronic obstructive pulmonary disease, congestive cardiac failure , diastolic dysfunction and heart failure ,pericarditis and myocarditis, post cardiac surgery ,sick sinus syndrome etc. The non cradiac causes invclude age , hyperthyroidism, excessive alcohol intake, obstructive sleep apnoea syndrome, diabetes mellitus, obesity,pulmonary hypertension ,pulmonary embolism,pneumonia,drugs, amyloidosis, smoking, exercise, genetic etc.

The major complications associated includes :

- Heart Failure

At rest approximately 20% of left ventricular stoke volume is by atrial contraction. It will be lost in AF, and will cause LV dysfunction and irregular rhythm of ventricles. Hence atrial fibrillation is a common arrhythmia in patients with heart failure, with a prevalence ranging from 10% in patients with New York Heart Association (NYHA) functional Class I up to 50% in Class IV patients.

- Stroke

The most common complication in AF is thromboembolism induced stroke. AF is associated with 5 fold increased risk of stroke.

Treatment

Acute management

Patients who present to the emergency department because of AF often have a rapid ventricular rate, and control of the ventricular rate is most rapidly achieved with intravenous diltiazem or esmolol.[1]If the patient is hemodynamically unstable, immediate transthoracic cardioversion may be appropriate. Cardioversion should be preceded by TEE to rule out a left atrial thrombus if the AF has been present for longer than 48 hours or if the duration is unclear and the patient is not already anticoagulated.[1] If patient is hemodynamically stable then management is based on several factors including symptoms, prior AF episodes, age, left atrial size, and current AAD therapy. If cardioversion is decided for a hemodynamically stable patient then two management decisions must be made: early versus delayed cardioversion and pharmacologic versus electrical cardioversion.[1]If AF is < 48 hrs

cardioversion have rapid relief of symptoms and avoidance of TEE and anticoagulation 3 weeks prior and 4 week after cardioversion. A reason to defer cardioversion is the unavailability of TEE in an anticoagulated patient with AF of unclear duration or duration more than 48 hours.

Long-Term Management of Atrial Fibrillation.

Pharmacological Control:

Studies have demonstrated a significantly lower rate of rehospitalization with a rate-control strategy, but no significant differences in other major outcomes, such as all-cause mortality, strokes, bleeding events, worsening heart failure, or quality of life.[2]

The decision to pursue a rhythm-control strategy versus a rate-control strategy should be individualized with consideration of several factors. These include the nature, frequency, and severity of symptoms; the length of time that AF has been present continuously in patients with persistent AF; left atrial size; comorbidities; the response to prior cardioversions; age; the side effects and efficacy of the AADs already used to treat the patient; and the patient's preference.

When the AF is persistent, it is reasonable to restore sinus rhythm with AAD therapy or transthoracic cardioversion at least once in patients younger than 65 and in patients 65 or older who are symptomatic from the AF despite adequate heart rate control.

After cardioversion, the decision to maintain the patient on AAD therapy to delay the next episode of AF is based on the patient's preference, the perceived risk of an early recurrence of AF, and the duration of sinus rhythm between prior cardioversions. Treatment with a rhythm-control drug usually is appropriate when AF recurs within a few months of cardioversion. The most realistic goal of AAD therapy in patients with persistent AF is to delay the onset of the next episode by at least several months, not for several years.

Direct Current (DC) Cardioversion

Efficacy of cardioversion is 95 % approximately. Biphasic waveform shocks is more effective than Monophasic in AF and allows the use of lesser energy. The first shock strength used in biphasic is 150 J to 200 Joules, higher energy upto 360 Joules if required. If a 360-J biphasic shock is unsuccessful, ibutilide should be infused before another shock is delivered because it lowers the defibrillation energy requirement and improves the success rate of transthoracic cardioversion.[3]

Non-pharmacologic Management of AF:

The non-pharmacological options available for management of AF includes Pacing, Catheter ablation, Surgical removal or closure of LA appendage and Maze procedure.

MATERIAL AND METHODOLOGY

Prospective observational study consisting of 80 patients of AF in ICU of MIMS, Mandya during a period of June 2020 to May 2021 who had given consent and meet the inclusion criteria. In 80 patients ,40 patients were divided into Group A and other 40 patients are divided into Group B.Group A patients received Diltiazem and Group B patients received Metoprolol. Metoprolol was administered intravenously at a dose of 5 mg, if patient was not responding, up to three dose can be given at interval of 5 min. Diltiazem as a bolus dose of 0.25mg per kg of actual body weight over 2 min and if patient was not responding a repeat dose of 0.35 mg per kg after 15 min.In 40

patients who were receiving Metoprolol and in 40 patients who were receiving Diltiazem ECG was taken at 5 min, 10 min, 15 min, 20 min and results were compared.

Inclusion Criteria

All patients with AF admitted to ICCU Mandya Institute of Medical Science, Mandya

Exclusion Criteria

1. Atrial rate < 120 bpm or > 220 bpm
2. SBP < 90 mm Hg
3. 2nd or 3rd degree AV block
4. Temperature > 38 Degree Celsius
5. Acute STEMI Known NYHA Class IV heart failure
6. Chronic COPD
7. Pre-hospital administration of any AV nodal blocking agent
8. History of allergic reaction to Diltiazem or Metoprolol
9. History of sick sinus or pre-excitation syndrome
10. Pregnancy or breastfeeding Women
11. Any history of drug abuse within 72 hours

Data Analysis: Continuous data was represented in terms of means and standard deviations. And the categorical data was represented in the form of frequencies and proportions. Graphical representation of the data was done using Microsoft Excel and Microsoft Word.Statistical Software SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyse the data. Appropriate tests of significance was used based on the type of data. P-value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

RESULTS

In the study, majority of the participants i.e., about 55.0% were aged less than 50 years in the Group A, whereas the majority i.e., around 57.5% were above 50 years in the group B.The mean age was 56.53 years with a standard deviation of around 14.63 years in group A, which was comparatively lesser than that in the group B where the mean age was 57.35 years with a standard deviation of around 11.43 years.

Majority of the participants in the study were females as a whole. On analyzing with respect to each group, majority i.e., about 60.0% were females in group A, while males and females were equally present in group B.

Co-morbidities	Group of Drug				p value
	Group A		Group B		
	Count	%	Count	%	
HTN	24	60.00%	27	67.50%	0.485

DM	19	47.50%	21	52.50%	0.655
IHD	20	50.00%	21	52.50%	0.823
RHD	10	25.00%	8	20.00%	0.592
CKD	5	12.50%	4	10.00%	0.723
Hyperthyroidism	6	15.00%	3	7.50%	0.288
Smoker	11	27.50%	13	32.50%	0.626
Alcohol	8	20.00%	6	15.00%	0.556

Table 1: Co-morbidities Distribution between two groups

The co-morbidities present among the participants in the study were recorded, and majority were suffering from hypertension, followed by ischemic heart disease, and diabetes mellitus. Few participants even gave history of rheumatic heart disease, chronic kidney disease, and hyperthyroidisim. More than one fourth of the participants were smokers, and few were alcoholics in the study. Further, on analyzing for any association with respect to co-morbidities between the groups, the study did not find any statistically significant relation.

Figure 1: Bar Diagram Showing Comorbidities Distribution between two groups
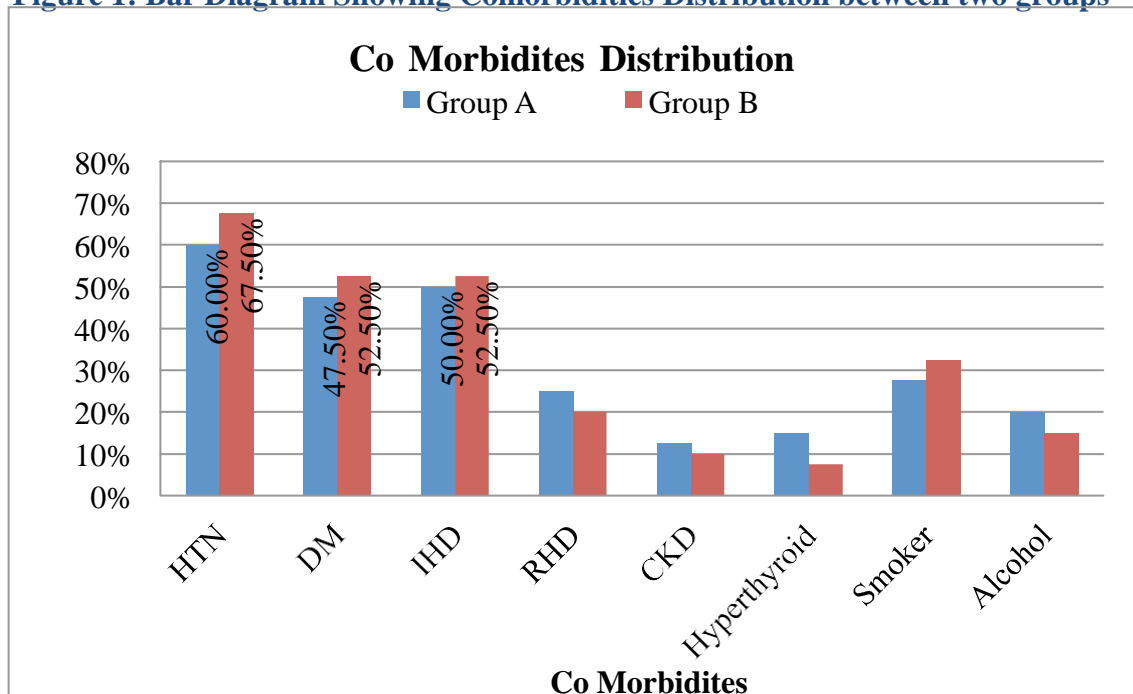
ECG changes		Group of Drug				p value
		Group A		Group B		
		Frequency	Percentage	Frequency	Percentage	
At 0 mins	HR ≤100bpm	40	100.0	40	100.0	
	HR >100bpm	0	0.0	0	0.0	
At 5 mins	HR ≤100bpm	22	55.0	12	30.0	0.024
	HR >100bpm	18	45.0	28	70.0	
At 10 mins	HR ≤100bpm	27	67.5	17	42.5	0.025
	HR >100bpm	13	32.5	23	57.5	
At 15 mins	HR ≤100bpm	34	85.0	22	55.0	0.003
	HR >100bpm	6	15.0	18	45.0	
At 20 mins	HR ≤100bpm	33	82.5	25	62.5	0.045
	HR >100bpm	7	17.5	15	37.5	

Table 2: Association with respect to changes in ECG between two groups at different intervals of time

In the study, the changes in ECG was assessed by comparing the heart rate over the period of time. Accordingly, at the beginning, the heart rate of all the participants had crossed more than 100 bpm irrespective of the intervention groups. Later, the variation in heart rate was observed on 4 more occasions which includes 5, 10, 15 and 20 minutes duration. The proportion of the individuals whose heart rate was controlled below 100 bpm was estimated and the study found statistically significant association in each occasion. This is because, the proportion of the individuals with heart rate below 100 bpm was comparatively higher in the diltiazem group, thereby suggesting that diltiazem was more effective than metoprolol in controlling the atrial fibrillation.
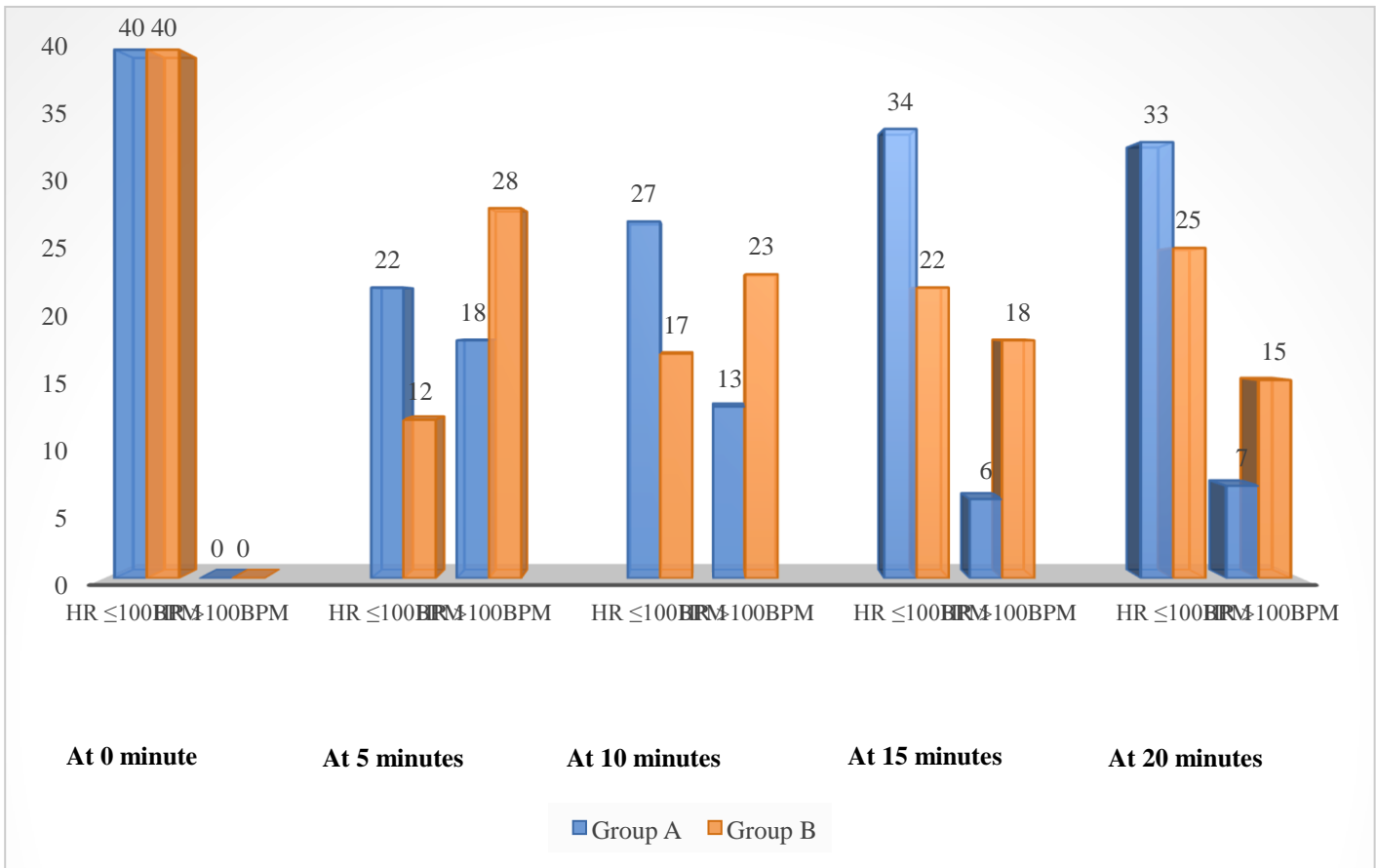
Figure 2: Diagram showing association with respect to changes in ECG between two groups at different intervals of time

		Group of Drug			
		Group A		Group B	
		Count	%	Count	%
No of doses	1	26	65.00%	16	40.00%
	2	14	35.00%	6	15.00%
	3	0	0.00%	18	45.00%

Table 3: Number of doses Distribution between two groups

In the study, the number of doses required in both the intervention groups were observed. Accordingly, majority of the participants i.e., about 65.0% required just a single dose in the Group A, whereas the majority i.e., around 45.0% required 3 doses in the group B. On further analysis, the study found statistically significant association with respect to number of doses between two groups, thereby suggesting that just a single dose was enough in case of diltiazem, while 3 doses were required in case of metoprolol.

Number of Doses Distribution

176

15.00%

0.00%

Figure 3: Bar Diagram Showing Number of Doses Distribution between two groups

DISCUSSION

Various studies have been conducted all over the world in the recent years with the similar objectives. In Chicago, Hirschy R et al[4], examined the effects of metoprolol versus diltiazem in the acute management of atrial fibrillation (AF) with rapid ventricular response (RVR) in about 48 patients with heart failure with reduced ejection fraction. Hines MC et al[3] from Baltimore, conducted a retrospective cohort study to evaluate the influence of demographics, prior medication use, hemodynamic and clinical characteristics, and other variables on selection of first-line therapy for AF, meanwhile the patients received either diltiazem or metoprolol.

In the present study, majority of the participants i.e., about 55.0% were aged less than 50 years in the Group A, whereas the majority i.e., around 57.5% were above 50 years in the group B. Further, the mean ages in both the intervention groups were estimated, and the numbers were almost closer. Accordingly, the mean age was 56.53 years with a standard deviation of around 14.63 years in group A, which was comparatively lesser than that in the group B where the mean age was 57.35 years with a standard deviation of around 11.43 years.

Majority of the participants in the present study were females as a whole. On analyzing with respect to each group, majority i.e., about 60.0% were females in group A, while males and females were equally present in group B. This is similar to the study by McGrath P et al[5], where female predominance was evident. On the contrary, studies such as Hirschy R et al[4], where males were predominant comparatively. Thus, it suggests that atrial fibrillation can be prevalent irrespective of gender.

The co-morbidities present among the participants in the present study were recorded,

and majority were suffering from hypertension, followed by ischemic heart disease, and diabetes mellitus. This is almost similar to the findings from the study by Xiao SQ et al[6], where hypertension was present in majority, followed by heart failure, and diabetes mellitus. In the study by Fromm C et al[7], diabetes mellitus was present in nearly one fourth of the population.

More than one fourth of the participants in the present study were smokers, and few were alcoholics in the study. This is completely contrast to the study by Medeiros T et al[8], more than three fourth of the participants were smokers and alcoholics. This sort of difference was evident as a result of demographic variation with respect to 2 different regions.

The mean heart rate in both the intervention groups was estimated in the present study, and the numbers were almost closer. Accordingly, the mean HR was 161.0 bpm in group A, which was comparatively lesser than that in the group B where the mean HR was 166.0 bpm. This is lot more compared to most of the previous studies such as Hirschy R et al[4], McGrath P et al[5], Medeiros et al[8], and Fromm C et al[7], where the mean heart rate was 134.0 bpm, 135.0 bpm, 136.0 bpm, and 140.0 bpm respectively.

The changes in ECG was assessed in the present study by comparing the heart rate over the period of time. Accordingly, at the beginning, the heart rate of all the participants had crossed more than 100 bpm irrespective of the intervention groups, and it is quite obvious that all the participants in the study were presented with atrial fibrillation. Later, the variation in heart rate was observed on 4 more occasions which includes 5, 10, 15 and 20 minutes duration. The proportion of the individuals whose heart rate was controlled below 100 bpm was estimated and the study found statistically significant association in each occasion. This is because, the proportion of the individuals with heart rate below 100 bpm was comparatively higher in the diltiazem group, thereby suggesting that diltiazem was more effective than metoprolol in controlling the atrial fibrillation. This mimics the findings from the study by Fromm C et al[7], where the mean HR gradually decreased over the period of 30 minutes, and diltiazem was more successful in controlling the heart rate comparatively. Even this is justified by most of the other studies such as Medeiros T et al[8], Hirschy R et al[4], and McGrath P et al[5], thereby confirming that diltiazem is superior to metoprolol in controlling atrial fibrillation.

In the present study, the number of doses required in both the intervention groups were observed. Accordingly, majority of the participants i.e., about 65.0% required just a single dose in the Group A, whereas the majority i.e., around 45.0% required 3 doses in the group B. On further analysis, the study found statistically significant association with respect to number of doses between two groups, thereby suggesting that just a single dose was enough in case of diltiazem, while 3 doses were required in case of metoprolol. This resembles the study by Xiao SQ et al[6], single dose was more commonly required in diltiazem, while more than one dose in the metoprolol group.

CONCLUSION

Atrial fibrillation was more prevalent in elderly population, comparatively more among females. Both diltiazem and metoprolol reduced the heart rate of the participants below 100 bpm over the period of time, however diltiazem was more successful comparatively. Although, both diltiazem and metoprolol were effective in

controlling atrial fibrillation, diltiazem had statistically proven to be quite superior to metoprolol.

LIMITATIONS OF THE STUDY

Although simple randomization was done while allotting the participants within the group, the participants were selected to specific group based on the need of the patient and choice of the treating physician.The duration of the study could have been made even longer, however the time period taken for the study is quite acceptable.

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