A PROSPECTIVE OBSERVATIONAL STUDY ON HEMODYNAMIC, ELECTROPHYSIOLOGICAL CHANGES AND ADVERSE EFFECTS WITH INTRAVENOUS AMIODARONE

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ABSTRACT:

Background: Among available antiarrhythmics, amiodarone was more effective than beta-blockers or other Drugs in reducing re-occurrences of symptomatic atrial fibrillation and ventricular tachycardia or fibrillation. The goal of this study is to demonstrate the efficacy and adverse effects of intravenous amiodarone in arrhythmic patients.

Methodology:

A total of 50 patients were considered. Informed consent was obtained from all the patients. This study data is collected from the patients who were admitted to the ICU and HDU. This study appraises electrophysiological, hemodynamic changes, and efficacy of intravenous amiodarone along with adverse effects.

Result: The study, shows post Amiodarone effects are; a decrease in the diastolic blood pressure, ECG parameters were normal in a majority of the patients but when we examined individually 8(16%) during the treatment they showed QT prolongation, 6(12%) with atrial fibrillation, 1(2%) with atrial flutter and 1(2%) with ventricular tachycardia. 6 (12%) patients suffered from thrombophlebitis among them 3(6%) patients showed grade I and 3 (6%) patients showed grade III. Also, atrial fibrillation was reported in 5 COVID-19 patients where 2(4%) had post covid arrhythmia and 3(6%) had arrhythmia during covid treatment.

Conclusion: Intravenous Amiodarone has shown many beneficial effects in patients with arrhythmias. Care should be taken for adverse effects like QT prolongation, thrombophlebitis, and hyponatremia.

KEYWORDS:

Amiodarone, Arrhythmia, Anti-arrhythmic, Hemodynamic, Electrophysiology, Thrombophlebitis, QT prolongation, Atrial fibrillation.

INTRODUCTION:

Arrhythmias occur when the electrical signals that coordinate heartbeats are not working correctly. An irregular heartbeat may feel like a rising heart or fluttering (1). Cardiac arrhythmias that cause the heart to beat too slowly are known as bradycardia (below 60 bpm), or Bradyarrhythmia. In contrast, arrhythmias that cause the heart to beat too fast are referred to as tachycardia (more than 100bpm), or tachyarrhythmia (2) Amiodarone is a class III antiarrhythmic agent. It is both an antiarrhythmic and a potent vasodilator. It is considered a 'broad spectrum' antiarrhythmic with multiple and complex electrophysiologic effects. In general, the efficacy of amiodarone equals or exceeds that of all other antiarrhythmic Drugs (AADs) and may be in the range of 60% to 80% for most supraventricular tachyarrhythmias and 40% to 60% for ventricular tachyarrhythmias(1). Used to treat ventricular and atrial arrhythmias, refractory atrioventricular nodal, and atrioventricular re-entrant tachycardia (3) (4). It blocks potassium currents that cause repolarization of the heart muscle during phase-3 of a cardiac action potential. As a result, it increases the duration of the action potential as well as the effective refractory period for cardiac cells. Therefore cardiac muscle cell excitability is reduced preventing and treating abnormal heart rhythm (5). Intravenous Amiodarone induces arteriolar vasodilation and atrioventricular nodal suppression, prolongs the atrioventricular nodal refractory period, and slows atrioventricular nodal conduction (6). It is particularly useful in haemodynamically unstable patients and patients with congestive heart failure with reduced left ventricular ejection fraction. Adverse effects of intravenous Amiodarone include hypotension, bradycardia, thrombophlebitis, QT prolongation. Amiodarone is contraindicated in patients with severe sinus-node dysfunction, marked sinus bradycardia, second- or third-degree atrioventricular block (7).

METHODOLOGY:

1. STUDY SITE: The study will be conducted at AIG Hospitals, Gachibowli, Hyderabad.

2. STUDY DESIGN: This study is a prospective observational study.

3. STUDY DURATION: 6 months from the day of approval

4. STUDY POPULATION: 50 Subjects

5. STUDY CRITERIA:

INCLUSION CRITERIA:

1. Patients who are conscious, cooperative, can communicate verbally and are willing to give informed consent.
2. Patients who are taking intravenous Amiodarone
3. Includes patients of both genders.
4. Age 18-85yrs.
5. Patients with tachycardia more than 120 bpm, QRS more than 120ms haemodynamically well tolerated defined as systolic blood pressure more than 90 mmHg

EXCLUSION CRITERIA:

1. Patients who are not willing to give consent.
2. QRS tachycardia is less than 120ms.

3. Pregnant or lactating mothers.
4. Chronic hepatic failure.

6. SOURCES OF DATA COLLECTION:

All the relevant and necessary data will be collected from;

- Case notes, Laboratory reports.
- Interviewing nurse or physician about the patient.
- Any other significant source.

7. **DESIGN:** A suitable data collection form was designed to collect, document, and analyze data. Data collection form includes provision for collection of information related to:

- Patient demographic profile
- Chief complaints
- Past medical history
- Past medication history
- Physical examination
- Other co-morbidities
- ECG & other lab investigations
- Duration of Amiodarone and other related information

8. METHODOLOGY:

A total of 50 patients diagnosed with cardiac arrhythmias attending the in-patient department of cardiology will be enrolled in the study. Clearance from the institutional ethics committee will be taken before the start of the study and written informed consent for the study purpose will be obtained from all the enrolled participants will be asked about the details enlisted in pre-tested Pro-forma involving demographic data such as age, gender, weight, height, BMI, Drug allergies, previous intake of amiodarone, co-morbidities along with clinical investigation and follow up the patient till discharge. Phlebitis grading scale (measuring the grade and severity of thrombophlebitis), Tisdale risk score (predicts the risk of corrected QT interval prolongation).

RESULTS: In this prospective observational study, a total of 50 patients were considered, where we saw the following

1. **BASED ON GENDER:** Out of 50 patients 64% were found to be male and 36% were found to be female (n=50). Figure 1
2. **BASED ON AGE:** The total population was divided into 'different age groups according to WHO guideline i.e., early adulthood (6%), adulthood (12%), late adulthood (34%), young-old (18%), middle old (24%), old-old (6%). Most of the patients using this drug were found to be in late adulthood. . Average age of all 50 patients was found to be 63 ± 15. Figure 2
3. **BASED ON BMI:** Based on BMI, patients with healthy weight were found to be more in number i.e., (60%). The average BMI of all the 50 patients was found to be 23±3.63. Figure 3
4. **BASED ON CO-MORBIDITY:** Out of 50 patients observed, the majority of the patients with co-morbidities The 'comorbidities' taken into consideration was diabetes mellitus, hypertension, hypothyroidism, and hyperthyroidism of which diabetes mellitus (74%), hypertension (76%), and hypothyroidism (14%) were the most commonly occurring comorbidities. The medical history of 50

patients shows that 58% had chronic kidney disease. Figure 4

5. **BASED ON DIAGNOSIS:** Out of 50 patient's majority of the patients Diagnosed with The patients were found to be diagnosed with atrial fibrillation (76%), Atrial flutter (2%), Atrial tachycardia (4%), Ventricular tachycardia (18%). Figure 5

6. **BASED ON THROMBOPHLEBITIS:** Out of the 50 patients, 6% of patients were found to be Grade-I and 6% patients were found to be Grade-III thrombophlebitis. Figure 6.

The grading of thrombophlebitis is shown in table1

1. **BASED ON QT PROLONGATION:** Among 50 patients, 6% males & 2% females were found to be at moderate risk and 8% of females were found to be at low risk for QT prolongation.

Tisdale risk score is shown in table 2

We observed hemodynamic changes, ECG changes, adverse Drug reactions, and efficacy of the Drug IV amiodarone in patients who were diagnosed with arrhythmia. The effect of amiodarone is shown in table 3

The study done is based on parameters that include hemodynamics (Temperature, HR, RR, BP), electrophysiology (ECG) and thrombophlebitis (phlebitis grading scale), QT prolongation (Tisdale risk score), and other adverse drug reactions along with survival rate, mortality, type of arrhythmias, site of the cannula, type of administration (bolus/infusion) and iv preparation (dextrose/NS).

Figure 3; shows the total population was distributed based on 'BMI' into different groups i.e., underweight (4%), healthy (60%), overweight (26%), obese (10%).

In table 4 distribution of patients based on 'site of cannula' among these group majority of the patients received IV amiodarone through peripheral line i.e; 62% and 38% received through a central line.

The majority of the patients received IV amiodarone by bolus i.e.; 28%, followed by 18% received by infusion, and 54% by both infusion and bolus. As shown in table 4.

In table 4 among 50 patients only 10% has a history of 'the previous intake of amiodarone', and 60% has dosage conversion of IV to oral.

DISCUSSION:

We observed thrombophlebitis occurred in patients who received amiodarone through the peripheral line and none of the patients suffered from thrombophlebitis who received amiodarone through the central line which is similar to the study conducted by **Carol Ann Oragano.** (4)

Distribution of patients based on 'IV preparation' Majority of the patients received IV amiodarone in dextrose (74%) and a few patients in NS (26%). This is similar to the study design of **Gerald V. Naccarelli et al.**(9)

Distribution of patients based on 'thrombophlebitis' was calculated as shown in figure 6 and pictures showing out of 50 patients 6(12%) patients with thrombophlebitis during hospitalization of which grade I was seen in 3(6%) and grade III was seen in 3(6%). This is similar to a study conducted by **Carol Ann Oragano et al.**

Patients were further divided Based on 'QT prolongation' we observed 16% of patients had QT prolongation after administration of IV amiodarone, according to Tisdale risk score we found 6% males & 2% females were found to be at moderate risk and 8% females were found to be at low risk as shown in figure 7. The results were in accordance with the study conducted by **Anna P. Kotsia et al.**(10)

Based on 'hemodynamic' results table 3 shows pre-administration of IV amiodarone in which 8% had pyrexia and 12% with hypothermia, post administration of IV amiodarone shows 12% had pyrexia and 10% with hypothermia. Pre administration shows 34% had high SBP and 58% with low SBP, post-administration shows 40% had high SBP and 82% had low SBP. Pre administration shows 22% had high DBP and 74% with low DBP and post-administration shows 10% had high DBP and 82% had low DBP. Drug-induced hypotension due to negative inotropic effects of the vehicle

(polysorbate 80). Pre administration shows 44% had tachycardia and 2% had bradycardia and post-administration shows 42% had tachycardia and 2% had bradycardia. Pre administration shows 52% had tachypnoea and no patient had bradypnea and post-administration shows 48% had tachypnoea and no patient had bradypnea. This is similar to the study conducted by **Jeffrey R. Balser et al.**(6)

Distribution of patients Based on 'ECG' results table 3 shows before administration of IV amiodarone, the majority of the patients shows low P wave (96%) followed by low QRS (92%), T wave (88%), PR (12%). In post Drug administration we saw a majority of patients had a low P wave (92%) followed by low QRS (88%), T wave (74%), PR (10%). In pre, Drug administration the majority of patients showed a high QTc range (90%) followed by QRSD (34%), QT (16%), PR (12%), T wave (10%), and (4%) of the P wave and QRS range. Whereas in post Drug administration majority of patients showed a high QTc range (68%), followed by QRSD and T wave (26%), QT (14%), PR (10%), P wave (6%), and QRS with 4%. The results are in contour with the study conducted by **John N. Nanas et al.**(11)

Based on 'Renal function test' results table 3 of pre-administration of IV amiodarone shows (58%) had high levels of blood urea nitrogen and (42%) with low levels of blood urea nitrogen, post administration of IV amiodarone shows (56%) had high levels of BUN and (2%) with low levels of BUN. Pre administration shows (60%) had high serum creatinine levels and (0%) with low serum creatinine levels, post-administration shows (50%) had high serum creatinine levels and (0%) had low serum creatinine levels. Pre administration shows (50%) had hypernatremia and (2%) had hyponatremia and post-administration shows (6%) had hypernatremia and (42%) had hyponatremia, which is due to synDrome of inappropriate anti-diuretic hormone secretion (SIADH) which is a rare phenomenon and is similar to the study conducted by **Linh phan et al.**

Pre administration shows (18%) had hyperkalemia and (6%) hypokalaemia and post-administration show (6%) had hyperkalemia and (14%) hypokalaemia and remaining had normal levels.

Table 3 shows pre and post 'LFT' changes of IV amiodarone, we saw majority of patients in pre lft shows a high range of direct bilirubin 56%, followed by 50% with indirect bilirubin, 38% with total bilirubin, 34% SGOT, 32% SGPT and very few patients show high ALP 24% and 20% with globulin. In post LFT 50% of the patients shows high direct bilirubin and indirect bilirubin, followed by 40% with total bilirubin, 36% SGPT, 32% SGOT, 18% globulin, and 10% with ALP. In pre Drug administration few patients show low albumin 44% followed by 32% with total proteins and very few shows low levels of total bilirubin 4%, and 2% with globulin. In the post, Drug administration shows low albumin 52% followed by 50% with total protein, and very few showed low levels of globulin 6%. This showed similar results conducted by **Enrico P. Veltri MD et al.**(12)

Among 50 patients 10% of patients were diagnosed with covid at a certain point of the study of which 4% had post covid arrhythmia and 6% had arrhythmia during covid treatment as shown in figure 8. The results obtained were similar to the study conducted by **Monika Gawałko. et al.**(11)

CONCLUSION:

Through this study, we found males and late adulthood groups (51years-65years) of patients were affected more with arrhythmias. Of the 50 patients observed, the most common co-morbidities were diabetes mellitus, hypertension, and hypothyroidism. After the administration of IV amiodarone, we observed QT prolongation and thrombophlebitis as the common ADR. Few patients showed, increase in the Total Bilirubin levels, ALT (Alanine aminotransferase) or SGPT (Serum glutamic- pyruvic transaminase) were noticed, and a decrease in the total proteins (Albumin & Globulin) were observed, the renal function tests showed that decrease in the blood urea levels, Sodium and Potassium levels in some patients, hemodynamics parameters revealed that there is a decrease in the diastolic blood pressure. In Post Drug ECG majority showed stabilization of ECG waves, indicating the efficacy of the Drug.

TABLES

Table-I: THROMBOPHLEBITIS GRADING SCALE.

Grade	Site Observation	Stage
0	IV site appears healthy	No signs of Phlebitis/ Observe cannula
1	Slight pain near IV site/Slight redness near IV site	Possibly first signs of Phlebitis/Observe cannula
2	Pain at IV site and redness	Early stage of phlebitis/ Resite cannula
3	Pain along the path of cannula, Redness around site and swelling	Medium stage Phlebitis/Resite cannula, consider treatment
4	Pain along path of cannula, redness around site, swelling and palpable venous cord	Advance stage of Phlebitis/Resite cannula, consider treatment
5	Pain along path of cannula, redness around site, swelling and palpable venous cord and pyrexia	Advance stage of Phlebitis/Initiate treatment, Resite cannula

Table-II: TISDALE RISK SCORE: USED FOR THE ASSESSMENT OF QT PROLONGATION. (LOW RISK: 0-6, MODERATE RISK: 7-10, HIGH RISK: 11-21)

Risk factor	Points
Age ≥ 68 years	1
Females	1
Loop diuretics	1
Serum K+: ≤3.5mEq/L	2
Presenting QTc interval ≥450ms	2
Acute Myocardial infarction	2
Heart failure with reduced Ejection fraction	3
1 QTc interval prolonging medication	3
≥2 QTc interval prolonging medications	3
Sepsis	3
MAXIMUM SCORE	21

Table-III: EFFECT OF AMIODARONE BEFORE AND AFTER

	PARAMETERS	PRE-AMIODARONE			POST AMIODARONE		
		HIGH	NORMAL	LOW	HIGH	NORMAL	LOW
1.ECG	PR	12%	76%	12%	10%	80%	10%
	QRSD	34%	66%	0%	26%	74%	0%
	QT	16%	84%	0%	14%	86%	0%
	QTc	90%	10%	0%	68%	32%	0%
	P	4%	0%	96%	6%	2%	92%
	QRS	4%	4%	92%	4%	8%	88%
	T	10%	2%	88%	26%	0%	74%
2. RFT	Blood ure	58%	42%	0%	56%	42%	2%
	Serum cre	60%	40%	0%	50%	50%	0%
	Sodium	50%	48%	2%	6%	52%	42%
	Potassium	18%	76%	6%	6%	80%	14%
3.HEMOD	Temperat	8%	80%	12%	12%	78%	10%
	SBP	34%	8%	58%	40%	56%	4%
	DBP	22%	4%	74%	10%	8%	82%
	PR	44%	54%	2%	42%	56%	2%
	RR	52%	48%	0%	48%	52%	0%
4.LFT	TB	38%	58%	4%	40%	60%	0%
	DB	56%	44%	0%	50%	50%	0%
	IDB	50%	50%	0%	50%	50%	0%
	SGPT	32%	68%	0%	36%	64%	0%
	SGOT	34%	66%	0%	32%	68%	0%
	ALP	24%	76%	0%	10%	90%	0%
	TP	0%	68%	32%	0%	50%	50%
	Albumin	0%	56%	44%	0%	48%	52%
	Globulin	20%	78%	2%	18%	76%	6%

SBP- systolic blood pressure, DBP- diastolic blood pressure, PR- pulse rate, RR- respiratory rate, TB-total bilirubin, DB-direct bilirubin, IDB-indirect bilirubin, TP-total proteins, ALP-alkaline phosphate, SGOT-serum glutamic-oxaloacetic transaminase, SGPT- serum glutamate pyruvic transaminase

Table-IV: AMIODARONE CHARACTERISTICS

		NUMBER OF PATIENTS	PERCENTAGE OF PATIENTS
1.Site of cannula	Central line	19	38%
	Peripheral line	31	62%
2.Type of administration	Infusion	9	18%
	Bolus	14	28%
	Both infusion &bolus	27	54%
3.Previous intake of amiodarone	YES	5	10%
	NO	45	90%
4.Dosage conversion	YES	30	60%
	NO	20	40%
5.chronic kidney disease	YES	29	58%
	NO	21	42%
6.Type of IV preparation	Dextrose	37	74%
	Normal saline	13	26%

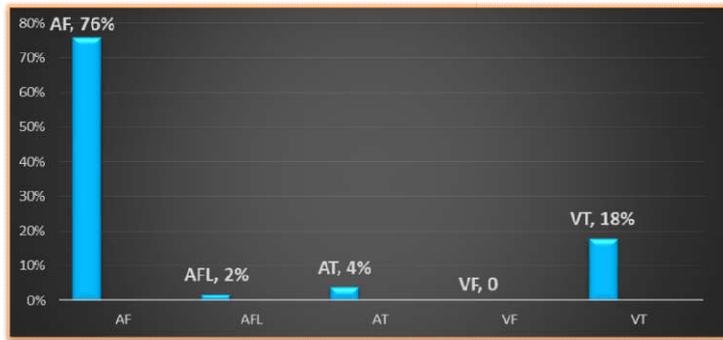**Figure-II: BASED ON AGE**
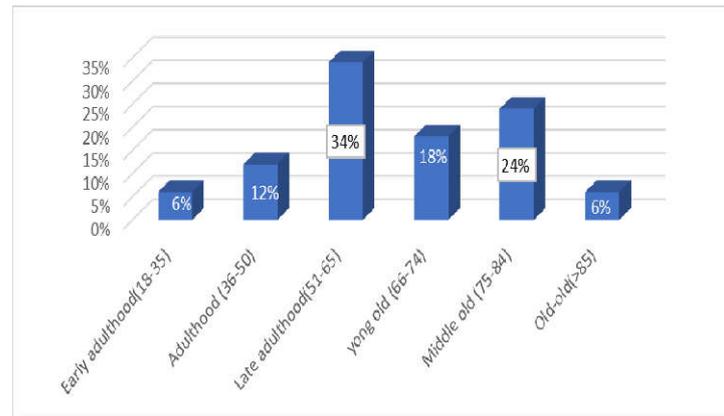
Figure-III: DISTRIBUTION OF BMI

Figure-IV: CO-MORBIDITIES

GRAPHS:

Figure-I: DISTRIBUTION OF MALE AND FEMALE
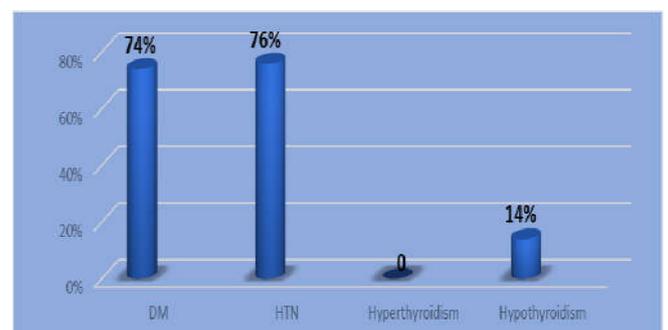
Figure-V: DISTRIBUTION BASED ON DIAGNOSIS

Figure-VI: % OF PATIENTS BASED ON THROMBOPHLEBITIS GRADE
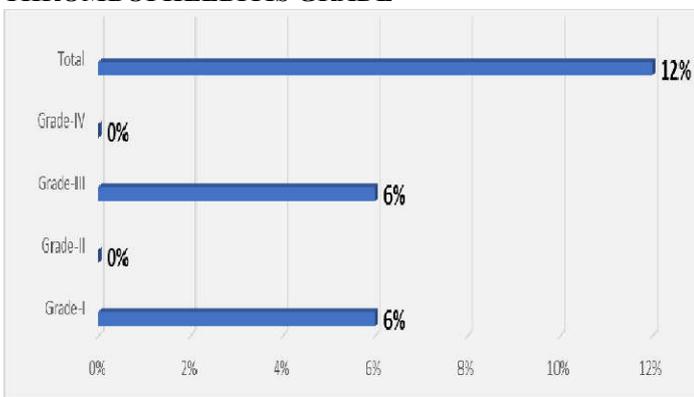

Figure-VII: BASED ON QT PROLONGATION

Figure VIII: DISTRIBUTION BASED ON ARRHYTHMIA VS COVID-19
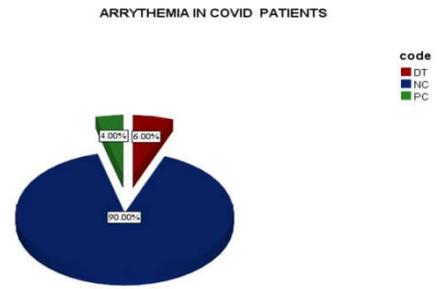
NC-NON COVID BUT ARRYTHEMIC, PC- POST COVID, DT- DURING COVID TREATMENT
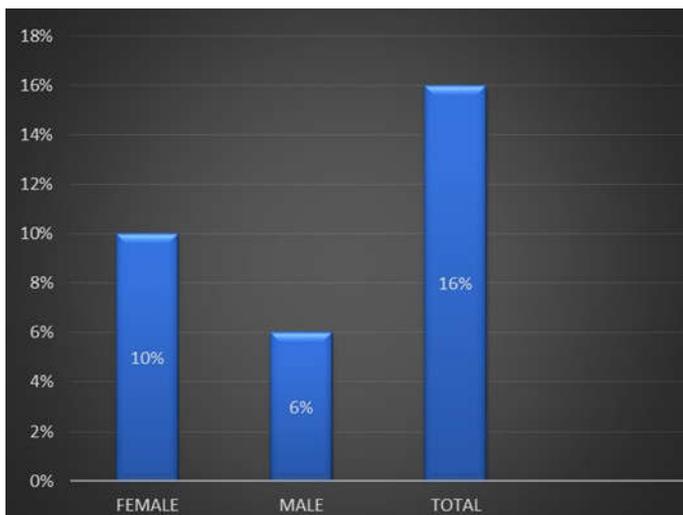
PICTURES:

Picture-I: GRADE-I THROMBOPHLEBITIS

Picture-II: GRADE-I THROMBOPHLEBITIS

Picture-III: GRADE-I THROMBOPHLEBITIS

Picture-IV: GRADE-III THROMBOPHLEBITIS

Picture-V: **GRADE-III**

THROMBOPHLEBITIS

Picture-VI: GRADE-III THROMBOPHLEBITIS

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