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RESEARCH ARTICLE
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PAROXYSMAL SUPRA-VENTRICULAR TACHYCARDIA: FACTORS DETERMINING ADENOSINE SENSITIVE VS ADENOSINE RESISTANCE

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ABSTRACT

Objective

To analyze the demographic features, medical history and clinical features which may or may not be responsible for adenosine resistance among patients of supra-ventricular tachycardia presenting to the cardiac emergency department.

Methodology

A single centered, prospective, cross-sectional, comparative study conducted from May 14 to August 15, 2022 on 100 patients with supra-ventricular tachycardia presenting to emergency department of Sheikh Zayed Medical College/Hospital were included in the study after fulfilling inclusion criteria.

Results

Mean age was 41.32 years with 38% patients being males and 62% being females. Total 71% patients reported to be adenosine sensitive and 29% patients were adenosine resistant. 71% presented with palpitations, 17% with palpitations and shortness of breath both and 10% with palpations and chest pain, 2% with shortness of breath alone. No significant co-relation was observed between demographic characteristics (age, gender, BMI, clinical presentation) and adenosine resistance. Moreover, in adenosine resistant group of 29 patients, 10 had history of SVT, 17 had diabetes mellitus, 23 had hypertension, 11 had history of IHD/HF, 5 had history of anti-psychotic medications, 18 had history of asthma/COPD, 2 had history of thyroid disorder, 19 had history of smoking, 15 had history of caffeine intake, 3 had history of alcohol intake, 7 had history of cola intake.

Conclusion

It is concluded that adenosine resistance in patients of paroxysmal supra-ventricular tachycardia is independent of demographic characteristics but, some factors including hypertension, Asthma/COPD,

smoking and caffeine/alcohol/cola intake do play some role in the adenosine resistance, as effect modifiers.

Key Words: Paroxysmal supra-ventricular tachycardia, Adenosine Sensitive, Adenosine Resistance

INTRODUCTION

Supra-ventricular tachycardia (SVT) is characterized as dysrhythmia that originates at or above the atrio-ventricular (AV) node and is defined as tachycardia with regular rhythm and narrow QRS complexes. [1]

The overall prevalence of supra-ventricular tachycardia (SVT) is around 2.25 per 1000 persons with a female to male predominance of 2:1; among all age groups. [2,3] While, some studies have shown that older individuals have 5 times higher risk of developing supra-ventricular tachycardia as compared to younger persons. [4]

In context to the management of supra-ventricular tachycardia, electrophysiological (EP) study followed by catheter ablation therapy is its definite treatment. However, in acute settings where advanced treatment options are not readily available, vagal maneuvers play a key role in restoration of normal sinus rhythm by increasing the vagal tone among hemodynamically stable patients. After that, adenosine and calcium channel blockers (Verapamil preferably) are the first line drugs as pharmacological options. Both drugs are proven to be effective in termination of supra-ventricular tachycardia in majority of the cases. [5]

In general, both adenosine or verapamil administration works by slowing down the electrical conduction pathway and also interrupts the re-entry circuits through the atrio-ventricular (AV) node; thus, restoring the normal sinus rhythm of patients presenting with supra-ventricular tachycardia. [6]

In the majority of the cases, adenosine terminates the arrhythmia but when adenosine does not successfully terminate the supra-ventricular tachycardia, it is termed as "adenosine failure". This can be attributed to either very short half-life of adenosine or its improper delivery or resistance to adenosine or transient termination of supra-ventricular tachycardia. [7,8]

In patients susceptible to SVT, medications (anti-psychotics & used in Asthma), caffeine, alcohol, physical or emotional stress, or cigarette smoking have been found triggering SVT. [9][10]

But, at present, there is not much information/data available to describe the risk factors/causes associated with adenosine resistance in SVT patients; that also needs to be figured out in order to provide better and timely effective management to these patients as well as to control the modifiable risk factors in such patients thus, preventing adenosine resistance among SVT patients. That is the main focus of this study.

METHODOLOGY

- Study Design: Cross-sectional / Comparative Study
- Study Setting: Emergency Chest Pain Unit of Cardiology Department, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan.
- Study Duration: This study was conducted from May 14 to August 15, 2022; after getting ethical approval from the Institutional Review Board of Sheikh Zayed Medical College/Hospital, Rahim Yar Khan.
- Sample Size: The sample size was calculated to be 100 by taking 95% confidence interval with 5% margin of error and 80% power of test.
- Sampling Technique: Non-probability Consecutive Sampling
- Inclusion Criteria: All patients (regardless of age and gender) presenting with narrow complex tachycardia (SVT) to the Chest-Pain-Unit in Emergency Department of Sheikh Zayed Medical College/Hospital, Rahim Yar Khan were included in the study.
- Exclusion Criteria : Any patient with bundle branch block tachycardia or multifocal atrial tachycardia or atrial fibrillation or broad complex tachycardia or electrolyte imbalance (potassium more than 6 mEq/L) or having any pre-existing chronic liver/kidney disease (assessed by history and medical record) was excluded from the study.

Taking the study subjects, a twelve leads ECG monitoring was performed to document SVT and data of each patient regarding his/her identity, socio-demographic profile, risk factors i.e. history of SVT, diabetes mellitus, hypertension, ischemic heart disease/heart failure, anti-psychotic drugs, chest diseases (Asthma/COPD), thyroid disorder, smoking and intake of caffeine or alcohol or cola drink within last one hour was recorded on the study performa.

Upon treatment of these patients, the pool of patients who get their SVT terminated by Adenosine were labeled as Adenosine-Sensitive Group (AS-Group) and those who do not respond to 6mg-12mg-12mg doses of Adenosine were labeled as Adenosine-Resistant Group (AR-Group). Then, their data was digitalized and analyzed with the help of SPSS version 21. Quantitative variables like age were presented in terms of mean ± SD (Standard Deviation) while, frequency & percentages are calculated for qualitative variables like gender, history of SVT, diabetes mellitus, hypertension, ischemic heart disease/heart failure, anti-psychotic drugs, chest diseases (Asthma/COPD), thyroid disorder, smoking and intake of caffeine or alcohol or cola drink. Effect modifiers were controlled through stratification. Post-stratification chi-square test was applied and p-value of <0.05 was considered significant.

RESULTS:

A total of 100 patients were included in the study. Mean age of study subjects came out to be 43.32±14.78 years. Demographic characteristics of study subjects are mentioned below in table 1; having majority of patients 57% falling in the age group of 41-60 years and majority patients were females (62%).

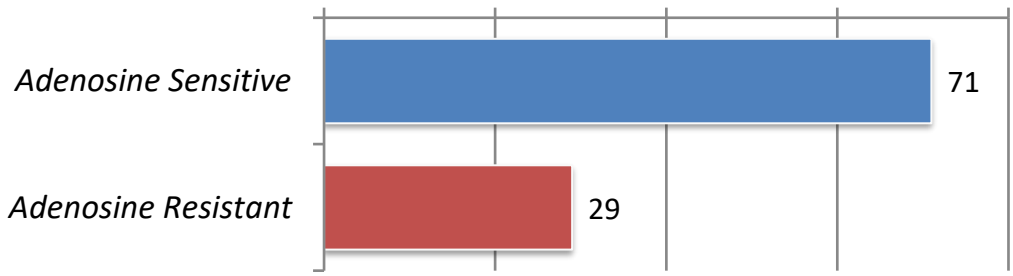
Table 1

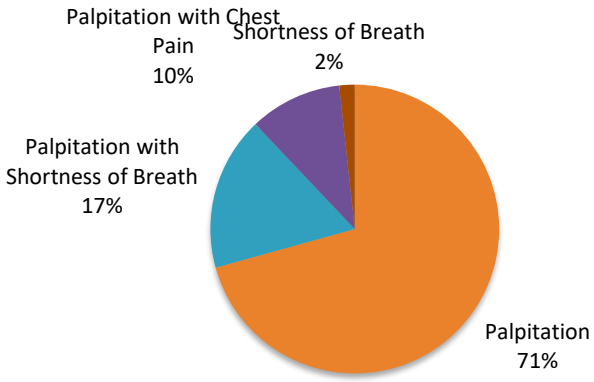
Demographic Parameters		Frequencies (%)
Age Groups	less than 20 years	5
	21-40 years	25
	41-60 years	57
	61-80 years	13
Gender	Female	62
	Male	38
BMI	Under weight	19
	Normal weight	45
	Over weight	28
	Obese	8

Upon grouping them according to symptoms at presentation, we got:

In our study sample (n=100), 71% patients were adenosine sensitive (labelled as AS-Group); while remaining 29% patients were were adenosine resistant (labelled as AR-Group) i.e. given in figure 1.

Figure 1





Cross tabulation done to determine the relationship between our study variables for Adenosine Sensitive and Adenosine Resistance Groups is as under as table 2 & 3:

Table 2

Characteristics		Adenosine Status		*p*-value
		Adenosine resistance	Adenosine sensitive	
Age Groups	less than 20 years	1	4	0.417
	21-40 years	7	18	
	41-60 years	19	38	
	61-80 years	2	11	
Gender	Female	9	53	0.572
	Male	20	18	
BMI	Under weight	5	14	0.231
	Normal weight	13	32	
	Over weight	8	20	
	Obese	3	5	
Presenting Symptoms	Palpitation	17	56	0.224
	Palpitation with Shortness of Breath	7	10	
	Palpitation with Chest Pain	4	6	
	Shortness of Breath	1	1	

Hx of SVT	No	19	23	0.183
	Yes	10	48	
Hx of Diabetes Mellitus	No	12	41	0.268
	Yes	17	30	

Table 3

Characteristics		Adenosine Status		*p*-value
		Adenosine resistance	Adenosine sensitive	
Hx of Hypertension	No	6	32	0.146
	Yes	23	39	
Hx of Ischemic Heart Disease/Heart Failure	No	18	47	0.179
	Yes	11	24	
Hx of Anti-Psychotic Medications	No	24	64	0.403
	Yes	5	7	
Hx of Asthma/COPD	No	11	56	0.139
	Yes	18	15	
Hx of Thyroid Disorder	No	27	66	0.173
	Yes	2	5	
Hx of Smoking	No	10	30	0.109
	Yes	19	41	
Hx of Caffeine Intake	No	14	42	0.164
	Yes	15	29	
Hx of Alcohol Intake	No	26	67	0.382
	Yes	3	4	
Hx of Cola Intake	No	22	52	0.194
	Yes	7	19	

A graphical comparison of study variables between the two study groups can be simplified as Figure 2 in a graphical representation:

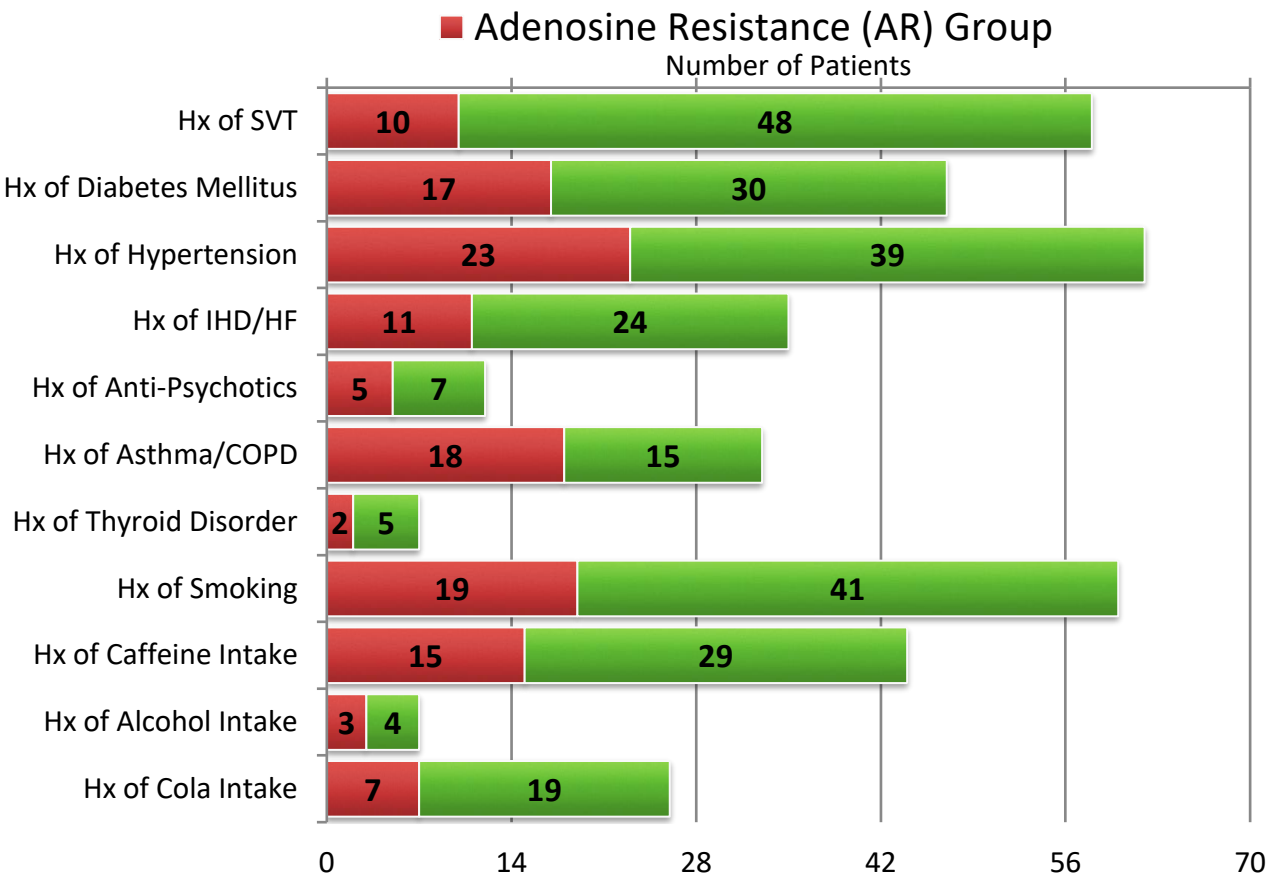


Figure 2

DISCUSSION

Manifestations of supra-ventricular tachycardia are quite variable as patients may present with palpitations or with more severe symptoms including chest discomfort or sometimes, even without any symptoms. Electrophysiological study analyses have helped demonstrating the pathophysiology of supra-ventricular tachycardia to be some abnormalities in impulse formation or in the electrical conduction circuits. Whereas re-entrant tachycardia is the most commonly involved mechanism in supra-ventricular tachycardia.i.e. AVRT and AVNRT. [11]

In our study the mean age of study subjects, presenting to emergency department, was 43.32 ±14.78 years and the most age group presented is between 41-60 years comprising 57% of total studied population. 58% of patients had past history of supra-ventricular tachycardia. It was also noted that female gender had more disease prevalence (62% vs 38%); which comes in line with other international studies and literature. [12]

A case report showed SVT in a patient of uncontrolled diabetes that was resistant to adenosine which comes out to be in accordance with our study results having 17% diabetics in adenosine resistance group that did not respond to adenosine therapy for successful termination of SVT. [13]

Our study showed that 18% of the total study subjects had history of medications for Asthma/COPD, 11% having history of IHD/HF, 23% having significant history of hypertension and 3% had history of alcohol abuse; within the adenosine resistance group. This finding corresponds to a case report presented by Seyeda Maryam Hosseini quoting adenosine resistance against SVT in a patient with history of hypertension, heart failure, alcohol abuse and chronic theophylline intake for COPD. [14]

Thyroid disorder (thyroid storm to be more specific) has been shown to be a precipitating factor for SVT by Christopher P Austin in a case report; that approves our finding of 7% thyroid disorder patients having SVT including 2% adenosine resistant patients; whereas the patient quoted in this case report was DC cardioverted for SVT being in shock. [15]

A randomized control trial, conducted on heart failure patients, demonstrated continued cigarette smoking to be associated with significantly increased incidence rates of life-threatening SVT and VT;

which were being reverted with ICD shocks. Our study found 60% of the SVT patients having smoking history; including 19% from adenosine resistant group and 41% from adenosine sensitive group, respectively. [16]

Caffeine intake (1-4 hours before presentation with SVT) was found in 44% of our study subjects. Out of these 44% patients, 15% showed resistance to adenosine therapy. This finding coincides with the results of a multi-centre case-control study concluding that ingestion of caffeine less than 4 hours before a 6mg adenosine bolus significantly reduces its effectiveness in the treatment of SVT. [17]

Our study concluded the adenosine sensitivity/resistance to be independent of demographic variables which is as same as found by Althunayyan et al in their study. [12]

However, there are multiple other factors affecting the sensitivity/resistance to adenosine e.g diabetes mellitus, hypertension, ischemic heart disease/heart failure, anti-psychotic drugs, chest diseases (Asthma/COPD), thyroid disorder, smoking and intake of caffeine or alcohol or cola drink; that further need to be studied separately.

CONCLUSION

It is concluded that adenosine resistance in patients of paroxysmal supra-ventricular tachycardia is independent of demographic characteristics but, some factors including hypertension, Asthma/COPD, smoking and caffeine/alcohol/cola intake do play some role in the adenosine resistance; as effect modifiers.

LIMITATIONS

Study is conducted on a limited data and study design does not include any electrophysiological studies. That's why further studies on this subject with large number of patients in multi center environments are needed for a clearer picture about effect modifiers causing adenosine resistance in SVT patients.

REFERENCES

1. Patti L, Ashurst JV. Supraventricular Tachycardia. [Updated 2023 Aug 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441972/
2. Brugada J, Katritsis DG, Arbelo E, et al. 2019 ESC guidelines for the management of patients with supraventricular tachycardia. The Task Force for the management of patients with supraventricular tachycardia of the European Society of Cardiology (ESC). Eur Heart J 2019: ehz467. [PubMed] [Google Scholar]
3. Lee KW, Badhwar N, Scheinman MM. Supraventricular tachycardia – part I. Curr Probl Cardiol 2008;33:467–546. [PubMed] [Google Scholar]
4. Khurshid S, Choi SH, Weng LC, Wang EY, Trinquart L, Benjamin EJ, Ellinor PT, Lubitz SA. Frequency of Cardiac Rhythm Abnormalities in a Half Million Adults. Circ Arrhythm Electrophysiol. 2018 Jul;11(7): e006273. [PMC free article] [PubMed]
5. Irum D Kotadia, Steven E Williams, Mark O'Neill; Supraventricular tachycardia: An overview of diagnosis and management. Clinical Medicine Jan 2020, 20 (1) 43-47; DOI: 10.7861/clinmed.cme.20.1.3
6. https://www.buzzrx.com/blog/adenosine-for-svt-supraventricular-tachycardia-side-effects-warnings. Written by Juhi Modi; Medically reviewed by HaVy Ngo-Hamilton, Pharm.D. | Updated Nov 24, 2023
7. Shortland J, Saravu Vijayashankar S, Sanatani S. When Adenosine Does Not Work: Apparent and Real Adenosine-Resistant Tachycardia. Pediatr Emerg Care. 2022 May 1;38(5):235-240. doi: 10.1097/PEC.0000000000002701. PMID: 35482497.
8. Weberding NT, Saladino RA, Minnigh MB, Oberly PJ, Tudorascu DL, Poloyac SM, Manole MD. Adenosine Administration With a Stopcock Technique Delivers Lower-Than-Intended Drug Doses. Ann Emerg Med. 2018 Feb;71(2):220-224. doi: 10.1016/j.annemergmed.2017.09.002. Epub 2017 Oct 28. PMID: 29089171.

9. Massari F, Scicchitano P, Potenza A, Sassara M, Sanasi M, Liccese M, Ciccone MM, Caldarola P. Supraventricular tachycardia, pregnancy, and water: A new insight in lifesaving treatment of rhythm disorders. Ann Noninvasive Electrocardiol. 2018 May;23(3):e12490. [PMC free article] [PubMed]
10. Corwin DJ, Scarfone RJ. Supraventricular Tachycardia Associated With Severe Anemia. Pediatr Emerg Care. 2018 Apr;34(4):e75-e78. [PubMed]
11. https://emedicine.medscape.com/article/156670-overview?form=fpf
12. Althunayyan SM, Khan AA, Samarkandi OA. Emergency department visits for paroxysmal supraventricular tachycardia in Saudi Arabia. Saudi J Anaesth. 2018 Oct-Dec;12(4):521-528. doi: 10.4103/sja.SJA_35_18. PMID: 30429731; PMCID: PMC6180673.
13. Finn BP, Fraser B, O'Connell SM. Supraventricular tachycardia as a complication of severe diabetic ketoacidosis in an adolescent with new-onset type 1 diabetes. BMJ Case Rep. 2018 Mar 15;2018: bcr2017222861. doi: 10.1136/bcr-2017-222861. PMID: 29545427; PMCID: PMC5878340.
14. Seyedeh Maryam Hosseini, Muhammad Ajmal, Ranjith Shetty, "Symptomatic Supraventricular Tachycardia Resistant to Adenosine Therapy in a Patient with Chronic Theophylline Use", Case Reports in Cardiology, vol. 2021, Article ID 2806193, 4 pages, 2021. https://doi.org/10.1155/2021/2806193
15. Austin CP, Odak M, Douedi S, Patel SV. Supraventricular Tachycardia: An Atypical Presentation of Thyroid Storm. Cureus. 2022 May 29;14(5):e25449. doi: 10.7759/cureus.25449. PMID: 35774700; PMCID: PMC9239283.
16. Goldenberg I, Moss AJ, McNitt S, Zareba W, Daubert JP, Hall WJ, Andrews ML; Multicenter Automatic Defibrillator Implantation Trial-II Investigators. Cigarette smoking and the risk of supraventricular and ventricular tachyarrhythmias in high-risk cardiac patients with implantable cardioverter defibrillators. J Cardiovasc Electrophysiol. 2006 Sep;17(9):931-6. doi: 10.1111/j.1540-8167.2006.00526. x. Epub 2006 Jun 6. PMID: 16759297.
17. Cabalag MS, Taylor DM, Knott JC, Buntine P, Smit D, Meyer A. Recent caffeine ingestion reduces adenosine efficacy in the treatment of paroxysmal supraventricular tachycardia. Acad Emerg Med. 2010 Jan;17(1):44-9. doi: 10.1111/j.1553-2712.2009.00616. x. Epub 2009 Dec 9. PMID: 20003123.