The Effectiveness of Adenosine in Treating the Acute Attacks of Supra-ventricular Tachycardia

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Abstract:

Background: Adenosine is a natural adenine nucleoside available endogenously that decreases heart beat by blocking atrioventricular (AV) node transiently so that extend the duration of conduction in (AV) node when injected intravenously. It has a curative value in the conversion of majority of supraventricular tachycardia (SVT) to sinus rhythm. In order to evaluate the adenosine in the management of arrhythmias we conduct this study.

Objective: This study was conducted to evaluate the safety and efficacy of intravenous adenosine therapy for treatment of (SVT), to determine the optimal adenosine dose effective in (SVT), and to determine the underlying conditions affecting the effective dose. And to evaluate the effectiveness of vagal maneuvers in terminating of spontaneous SVT

patients and methods: A cross-sectional study conducts in a group consist of 69 patients ranged from 23-70 years old admitted to the Coronary care unit in Azadi Teaching Hospital ,in Kirkuk city, from July 2014 to June 2016. The diagnosis of (SVT) was made by present of tachycardia which is of narrow complex with a heart beat rate greater than 140 beats/ min by 12 leads chest electrocardiography (ECG).

In patients who are hemodynamically stable, vagal maneuvers were carried out initially in the form of carotid sinus massage, gag reflex and Valsalva maneuver, if this failed intravenous administration of adenosine as recommended doses were preformed. If three doses of adenosine boluses were unsuccessful to convert the arrhythmia, patients were managed with other available antiarrythmias or managed with direct electrical cardio version (DC). In unstable patients were managed with (DC).

Results: Of 69 included patients, diagnosed as (SVT), M: F ratio was 1:2.1. Their age ranged from 23 years to 70 years with mean age of 57 years. Vagal maneuvers (VM) resulted in restoration of sinus rhythm (SR) in 8patients (7.6%). Out of 57 episodes of (SVT), Adenosine was effective in reverting 51 episodes of SVT to sinus rhythm (89.5%). Of those converted, 18 required a single dose (6mg) (31.6%), fifteen required one additional (12mg) dose (26.3%), and another 18 required two additional doses (81mg) (31.6%).four patients were hemo-dynamically unstable (systolic blood pressure <90 mm Hg) which required (DC). Six patients (10.5%) not responding to full adenosine dose(81mg), started treatment with other medication, 1 with verapamil, 4 with amiodarone, and1 with digoxin. All of them were successfully treated.

Conclusions: Adenosine is an effective medicine in treating (SVT) in those patients in whom vagal maneuvers has unsuccessful. It demonstrates a high rate of success in terminating acute attack of SVT. A higher dose may be required in majority of patients specially

Keywords: Adenosine, Supra-ventricular tachycardia, Effective, Safety, Vagal manoeuvre.

Introduction:

Supraventricular tachycardia (SVT) is one of the common cardiac arrhythmia, which may be due to many cardiac electrophysiological disorders; the incidence of (SVT) is approximately 35 cases per 100,000 patients while the prevalence is around 2.25 cases per 1,000 in the community [1]. In general population the common presentation of (SVT) includes a fasting heart beat rate (>140 beats per minute) accompanied by palpitations, chest pain, shortness of breath and dizziness [2]. SVT may results from a many kind of electrophysiological disorders, including enhanced automaticity and increase re-entry circuits with the transmission of electrical impulses over an accessory pathway from the atrium of the heart to the ventricle (atrio-ventricular re-entry tachycardia (AVRT) or transmission within the a trio-ventricular node (AV node) (atrio-ventricular node re-entry tachycardia, (AVNRT) [3,4]. Patients with (SVT) with no associated cardiovascular disease (CVD) were labelled as having lone (SVT) [1].

In practice the clinical approach to a subject with suspected (SVT) includes a medical history taking and an accurate interpretation of the (ECG), in order to differentiate (SVT) from other narrow-complex tachycardia [5, 6].

According to International resuscitation guidelines recommendation, the primary management for treating (SVT) during acute attack are two interventions: first is a vagal manoeuvre and the second is pharmacological agents, both therapies are usually considered as the first-line treatment of choice in patients with hemodynamically stable (SVT). While synchronized direct electrical cardio-version is confined and restricted for the management of collapsed patients or haemodynamically unstable patients with (SVT) [7-12]. The relative efficacy of each therapy in treatment of (SVT) has been evaluated in many different published studies [13–18]. Vagal manoeuvres are suitable non-invasive step of enhancing the refractoriness of (AV node) by exciting the baroreceptors which are sitting in the aortic sinus and in the carotid bodies, so that cut off the tachyarrhythmia [18].

The gag reflex and carotid sinus massage are the most ordinarily preceded vagal manoeuvres in the practice. While pharmacological medical therapy is suitable method in patients when the vagal manoeuvres unsuccessful, it supplies a similar raise in refractoriness by diminishing normal ion activity through the cell wall channels of the (AVnode) [19]. Some studies report an approximately (25%) success rate of vagal manoeuvres, although reported rates vary in the literature between (6%-54%). studies support placing the patient in a supine situation and trying to attempt the manoeuvre for 15-20 seconds [18, 19, 21].

The Valsalva manoeuvre has a predominant effect on SVT ending when compares to carotid sinus massage, in trying to attempt carotid sinus massage in old age patient, one should be in caution, as there is a potential risk of athero-embolism from the carotid vessel and establishing a stroke even when an audible bruit is absent on auscultation. Till now there is no guidelines currently present regarding the suitable number of trial before starting other therapies, although many studies advice a maximum trial of 2 attempts prior to initiation other kinds of treatment [20-25].

The main pharmacological therapy for ending SVT is intravenous (IV) adenosine (a natural form of purine nucleoside which acts by inhibiting sodium ion channels) or a verapamil (non dihydropyridine calcium channel blocker) [26, 27, 28]. Effectiveness of adenosine are perfectly appears within 15-30 seconds (half-life is 0.6 to 10 seconds) after (IV) bolus administration and it is then undergo an enzymatic metabolism with quickly cleared from blood by the cellular elements in blood and by the endothelial cells of the vascular beds .Side effects of adenosine are minimal, transient well tolerated and short-lasting due to its very short half life in plasma, include (flushing, chest pain, dyspnoea, headache, cough, sinus bradycardia, atrial fibrillation, ventricular arrhythmias, and various degrees of AV block). It is reported that the reversion effectiveness of both adenosine and verapamil in cut off (SVT) to sinus rhythm is similar (~92%) [22]. The American Heart Association recommends use of adenosine as the first-line successful medicine in the treatment of (SVT) [29].

In order to evaluate the role of adenosine in the management of arrhythmias we conducted this study, to investigate the safety and efficacy of intravenous adenosine therapy for treatment of (SVT).

Materials and Methods:

Study design and patients:

The study was conducted at the Azadi Teaching Hospital, Kirkuk, Iraq, from July 2014 to June 2016. All patients aged from 23 to 71 years presenting with SVT, diagnosed and documented on 12 lead ECG were enrolled in the study.

We collected data concerning patients who were presented to the emergency department and coronary care unit (CCU) with sudden onset of regular tachycardia (<0.02-s variation in successive R-R interval) and whose heart rate was above 140 beats per minute (bpm).

Prior to treatment vital signs were assessed, including measurement of blood pressure (BP). Pulse rate, and respiratory rate; a review of prior treatment. The vagal manoeuvre is used at the beginning for the treatment of all SVT patients; it is used initially in the stable patient, while (IV) access is being obtained.

Direct current (DC) as in guidelines had been used in a patient with a hemodynamically unstable (SVT).

All patients evaluated by physician in the (CCU) unit had been included in this study when having a narrow complex tachycardia (QRS width< 0.12 sec) with no distinguishable P waves on ECG and a ventricular rate of 140-300 beats/min .Farther criteria for inclusion included a palpable radial pulse and a patent (IV) line access.

Exclusion criteria in this study included patients with a history of hypersensitivity to adenosine, cardiorespiratory arrest, and traumatic cause of arrhythmia (acute trauma), asthmatic patients current medical treatment with theophylline, carbamazepine or dipyridamole drugs, presence of underlying heart blocks, bundle branch blocks(BBB),presence of acute pulmonary oedema, significant history of chronic left ventricular (LV) dysfunction confirmed by echocardiography, and wide QRS complex tachycardia (QRS width > 0.12 sec).

Cardiovascular diseases (CVD) was considered present if the patient has a documented diagnosis of systemic hypertension, coronary artery disease, heart failure, valvular heart disease, atrial fibrillation or flutter, history of sick sinus syndrome, congenital heart disease or presence of pericarditis.

Treatment Protocol:

The studied treatments were considered the standards of care for (SVT) management in our (CCU) during the study periods. An algorithm for uniform management of patient with (SVT) was submitted according to the treatment protocol.

Approval was discussed and acquired from ethics committee of our hospital before patient insertion in the study; vagal manoeuvres (Valsalva and carotid sinus massage) were attempted in all patients prior to administration of adenosine drug. By placing the patient in a supine position and attempting the vagal manoeuvre for 15-20 seconds [18, 19, 21]. We are trying a maximum of two attempts [20-24]. Caution was advised when considering to try the carotid massage in older aged patients, as there is a potential risk of thrombo-embolism from the carotid vessel and establishing a stroke even when an audible bruit is absent on auscultation. Antecubital venous access line was achieved by using a wide bore cannula in all patients who did not respond to vagal manoeuvres ,then administration of adenosine therapy followed after the case had been reviewed by the physician [30, 31].

Adenosine therapy was administered by rapid (IV) push, followed instantly by rapid (IV) normal saline flush push [27, 28, 30]. The initial first dose was 6 mg. followed by 2 more additional doses of 12 mg then 18 mg if there was no clinical response noted after 2 minutes of adenosine administration [28, 30]. For all patients the vital signs and repeat ECG rhythm strips were obtained after drug administration .For patients with continued SVT after the adenosine, further therapy by other drugs was specified at the free hand of the physician.

Measurements:

Clinical response was decided after proper attempt of vagal manoeuver and if unsuccessful after adenosine use. Then the patients grouped into 2 categories: no response and complete response to treatment.

The (ECG) strips was reviewed in actual time and the post therapy rhythms was registered. No response, was defined as continued existence of (SVT) or transient un-sustained transformation to sinus rhythm (<2 min), while complete response was defined as sustained reversion of (SVT) for at least 2 minutes after adenosine administration [32]. The presence of sinus rhythm was documented on ECG.

Echocardiography was done on all patients after achieving sinus rhythm to record any underlying structural heart defect or any cardiac illness.

The rhythm strips on (ECG) were checked retrospectively for treatment groups by specialist for confirmation of the rhythm diagnoses. Diagnosis of the rhythm and definition of the hemodynamic instability had been made based on certain criteria as guidelines used by (AHA ACLS) [33].

Patients medical records, including emergency department (ED), (CCU) and patient hospital discharge summaries, were reviewed for the following patients information: age,

sex, (ECG) rhythm at (ED) arrival, vital signs at (ED), additional (ED) treatment, any complications, presence of pre excitation patterns on the 12 (ECG) record, presence of pregnancy, and eventual final result (defined as either survival or death in the (ED) or (CCU) or during the hospital stay).

Statistical analysis:

Descriptive data were represented as tables; the data collected were analyzed by the Chi-squared test as appropriate between variables. A P-value if<0.05 was considered as statistically significant.

Results:

Sixty-nine patients were initially enrolled in the study. Four patients were hemodynamically unstable and were converted electrically to sinus rhythm on presentation. The patients included 47 females (69.7%) and 22 males (33.3%) with M:F ratio of 1:2.1. The mean age of cases was 57.86 years (minimum 23, maximum 71). The mean systolic blood pressure was 120.7 (minimum: 80-maximum: 217 mmHg) and the mean diastolic blood pressure was 74.45 minimum: 50-maximum: 144 mmHg). Mean heart rate was 174.29 (minimum: 140- maximum: 210 bpm) table (1).

Out of the sixty-nine patients with (SVT), 59 (85.5%) of the patients presented with palpitation and it was statistically significant (p<0.05), 5 (7.2%) patients presented with resting dyspnoea, chest discomfort was the clinical presentation in 3 (4.3%), and the faintness was the clinical presentation in 2(2.9%) patients.

Cardiovascular diseases (CVD) was present in 43(62.3%), while 26 (37.7%) of patients with (SVT) had no CVD and were labelled as having lone (SVT). Sixteen subjects were under chronic anti-arrhythmic therapy (7 of which were consuming verapamil, 5 amiodarone, two sotalol and two diltiazem). Diabetes Mellitus was found to be the most common disease in past medical histories in 11 patients, table (2).

Eighteen episodes of SVT occurred in 20-40 age groups (28.2%), 29 in 40-50 age group (42.7%) and 22 in 60-70age group (29.1%) table (3).

Fifty–seven patients affected by SVT who were unresponsive to vagal manoeuver were treated with an IV adenosine and second line treatment in resistant cases in our coronary care unit, table (4).

Adenosine was effective in reverting to sinus rhythm in 51 episodes (89.5%) while 6 patients had to be treated with second line antiarrhythmic. A dose of 6mg adenosine was only effective in 18 episodes of SVT (31.6%); 12 mg was effective in 15 episodes (26.3%) of those not responding to the 6mg dose. A dose of 18 mg was effective in further 18 patients (31.6%) who not responding to lower doses. Adenosine was not effective in reverting to sinus rhythm in 6 out of 57 episodes (10.5%), (table 4).

A vagal manoeuvre was attempted in sixty -five patients initially prior to administration of drug. The percentage of (SVT) reverting to sinus rhythm with a vagal manoeuvre was 8 (12.3%) consistently lower in comparison with the adenosine drug (P <0:00032), table (4).

There was significant difference in effective dose of adenosine between first episodes of SVT (N = 22) and recurrences (N =29, P = 0.03), table (5, 6).

In adenosine responsive patients, mean effective dose was (11.68 mg) with median effective dose of 12 mg. Mean

effective dose of adenosine in 20-40 age group was (14mg) (median 12mg), while 13mg (median 12mg) in 40-50 and (15mg))(median 12mg) in 50-70. There was no significant difference in mean effective adenosine dose in various age groups (p = 0.21), table (6, 7).

Out of 57 patients the effective dose was lower in patients with lone SVT (n=22) (9mg, median 6mg) than cardiovascular disease (n=35) (13.7mg median 12mg), p = 0.19. There was no significant difference in mean effective dose of adenosine between patient with lone (SVT) (n = 22) or patient with diabetes mellitus (n = 11), (11mg, median 12mg vs. 13mg, median 12mg, p = 0.26), table (7).

Six patients (10.5%) not responding to adenosine started treatment with other medication, 1 with verapamil, 4 with amiodarone, and 1 with digoxin. All of them were successfully treated.

Complications:

There were no significant complications registered after an intravenous bolus of adenosine in our subjects while comparatively mild and transient side effects were common. A transient headache and disturbance of respiration and flushing were common but not distressing. One patient complained of nausea and headache. One patient, experienced a sinus bradycardia of 45 beats per minute after termination, but the heart rate returned to normal within 1 minute.

Table (1): General characteristics of SVT patients.

Variable	Frequency
Mean Age (years	57.86
Sex (M/F)	22/47
Mean systolic blood pressure (mmHg)	120.7
Mean diastolic blood pressure (mmHg)	74.4
Mean Heart Rate (bpm)	174.29

Table (2): Chief complaints and associated cardiovascular disease in patients with SVT.

Variable	Numbers of the patients	Percentage %
Palpitation	59	(85.5%)
Resting Dyspnea	5	(7.2%)
Chest Discomfort And Pain	3	(4.3%)
Faintness	2	(2.9%)
Associated CV disease*	43	(62.3)
Lone SVT	26	(37.7)

*Associated CV disease (hypertension .coronary artery disease, congestive heart failure, mitral regurgitation mitral valve prolapse, aortic regurgitation, ventricular septal defect).

Table (3): Age group.

Age	Patients No. (%)	Percentage %	P. value
20-30	8	(11.6)	NS
30-40	10	(14.5)	NS
40-50	29	(42.7)	<0.05
50-60	14	(20.3)	NS
60-70	8	(11.6)	NS

Table (4): Conversion rate in 69 patients by using, direct current, vagal manoeuver, adenosine and resistant cases.

Drugs	converted patient to sinus rhythm	
	N	%
Adenosine group	51	(89.5%)
Adenosine (6mg)	18	(31.6%)
Adenosine (12mg)	15	(26.3%)
Adenosine (total dose)*	18	(31.6%)
Resistant cases**	6	(10.5%)
Vagal manoeuvre	8	(12.3%)
Direct current	4	(8.6%)

*Adenosine total dose; 6mg+12mg+12mg
** Resistant cases; resistant to adenosine and vagal manoeuvre.
N: Number

Table (5): Responce to different type of treatment in the study population.

Demographic characteristics	No. of patients Converted to sinus rhythm by adenosine	Percentage %	No. of patients Converted to sinus rhythm by vagal manoeuvers	Percentage %	P. value
Total No. of the patients	51	89.5	8	11.6	<0.002
Lone SVT	22	38.6	3	37.5	NS
Associated CV disease*	35	61.4	5	62.5	NS
History of recurrent	29	50.9	4	50.0	NS
Chronic antiarrhythmic therapy	14	24.5	2	25	NS

*Associated CV disease (hypertension .coronary artery disease, congestive heart failure, mitral regurgitation mitral valve prolapse, aortic regurgitation, ventricular septal defect).
NO. (Number).
NS. (Not significant).

Table (6): Conversion response to different doses of adenosine in 57 patients. demographic characteristics.

demographic characteristics	Successful conversion by adenosine in (51 patents)			Resistant to adenosine in 6 patients	P. value
	6mg	12mg	18mg		
Female/M	45/24	47/25	49/23		N.S
Mean age(years)	56.3	57.7	55.6		N.S
Mean Systolic BP (mmHg)	120.2	118.4	121.3		N.S
Mean diastolic BP (mmHg)	70.4	71	72.2		N.S
Lone (SVT)	14	6	2		<0.05
Associated CV disease*	7	11	17		<0.05
First episode (SVT)	14	5	3		<0.05
Recurrent episode(SVT)	4	10	15		<0.05
chronic anti-arrhythmic therapy	6	5	6		N.S
Mean heart beat(bpm)	174.3	172.3	173.4		N.S

*Associated CV disease (hypertension .coronary artery disease, congestive heart failure, mitral regurgitation mitral valve prolapse, aortic regurgitation, ventricular septal defect).

Table (7): Mean effective dose of adenosine and different demographic characters and types of SVT.

Demographic characters		Mean effective dose	P. Value
Lone (SVT)		8.7	<0.05
Associated CV disease*		13.7	
First episode (SVT)		9	<0.05
Recurrent episode(SVT)		14.3	
Pre-excitation		15	0.005
Normal ECG		9.4mg	
Age group(years	20-40	14	NS
	40-50	13	
	50-70	15	

Discussion:

The essential therapies for treating acute attacks of (SVT) are two: vagal manoeuvres and pharmacological interventions, both therapies are generally believed as the first-line treatment of choice in stable patients (hemodynamically) [7-12]. The relative efficacy of each therapy in treatment of (SVT) has been evaluated in many different studies [13–18].

Out of fifty –seven patients affected by (SVT) enrolled in this study, vagal manoeuver was effective in reverting 8 episodes of SVT to sinus rhythm (12.3%) its efficacy appears to be actually lower in comparison with the adenosine drug ,but the manoeuvres possess some advantage of being comparatively simple, easy and non-invasive. The efficacy of the manoeuver in terminating SVT had been documented in many studies similar to our result with percentages of (SVT) termination ranging from (6%) to (22%) [18, 19, 21, 22, 34, 35]. The two groups (vagal manoeuver and adenosine group) were identical regarding mean age, gender, arterial systolic and diastolic blood pressures, and presence of CV disease, recurrence, and heart rate, table (5). In this study adenosine proved to be highly effective in reverting SVT to sinus rhythm in 51 episodes, table (5) with rapid termination rate of (89.5%), the efficacy of adenosine in reverting (SVT) as the present results were documented and in parallel with other studies results which show that (87–100%) response rate at different progressive increasing doses [12-14, 22, 36, 37].

A dose of 6mg adenosine was appear to be effective in 18 episodes of SVT (table 4) with rapid termination rate of (31.6%), this result is far away than the optimal results proved for reverting episodes of (SVT) to sinus rhythm as in compares with result demonstrated by DiMarco JP et.al. [27] which noticed that with a 6 mg dose of adenosine, (60%) of SVT return to sinus rhythm, while with the following next conduction of a 12 mg dose of bolus adenosine, the rate had been rose to (90%) [38], which is parallel with the finding of this study which show that with total dose of adenosine the efficacy in reverting (SVT) to sinus rhythm proved in 51 episodes table (5) with rapid termination rate of (89.5%).

No significant difference found in mean effective dose of adenosine in different age groups table (7) this result is parallel with the result demonstrated by Dixon J et.al [39] which show no difference in mean effective adenosine dose in different age groups. The effective dose was lower in patients with lone (SVT)

than patients with cardiovascular disease table (7), but no such significant difference in mean effective dose of adenosine between patients with lone (SVT) and those with cardiovascular disease had been documented in previous equivalent studies [40].

Out of 57 patients responding to adenosine, 22 patients (38.6%) were first episode of (SVT) while 29 (50.9%) were recurrent episodes there was significant difference in effective dose of adenosine between first episodes and recurrences (table 7) but there was no such significant difference in effective dose of adenosine had been found between first episodes and recurrent episodes of (SVT) in other previous equivalent studies [42].

A higher starting dose of 12mg may be used as first bolus followed by another 12mg for optimum response in patient with CVD or having history of recurrent episodes of SVT for these specific special groups of patients with CVD or having recurrent episodes of SVT a larger case control studies might be needed to find the optimum dose response.

The most common clinical presentation of (SVT) patients in this study were palpitation 59 cases (85.5%) while 5(7.2%) patients presented with resting dyspnoea, (table 2),this finding is in parallel with other studies which demonstrate that palpitation is the most common presentation of patient with SVT [41].

Adenosine was not effective in reverting to sinus rhythm in 6 out of 57 episodes (10.5%) table (6).

In spite of that, the Side effects with adenosine were noticed during treatment but they were quite acceptable because these side effects were transient and un sustained and no need further drugs intervention. A transient headache and disturbance of respiration and flushing were quite common but not disturbing. No one of the patients in this study developed any kind of sustained tachyarrhythmia in spite of repeated administration of relatively higher doses of adenosine, this result was in parallel and similar to reported side effects in previous equivalent studies [42].

Conclusion:

Adenosine is an effective medicine in treating (SVT) in those patients in whom vagal manoeuvres has unsuccessful. It demonstrates a high rate of success in terminating acute attack of SVT. A higher starting dose may be required in majority of patients especially in those with cardiovascular disease or those with history of recurrent episodes of (SVT). The safety profile of adenosine suggests that it should be the drug of first choice for termination of (SVT).

Recommendation:

Because a higher doses of adenosine were needed for optimum response in patient with CVD or patients having history of recurrent episodes of SVT. For these specific special groups of patients a larger case control studies might be needed to find the optimum dose responses.

Limitations of this study:

The primary limitation of this study is that in the design we did not involve the electrophysiological study of the patients, so that the effectiveness of various electrical fashions in influencing the success of the vagal manoeuver and drugs have not been well evaluated. Because it is known widely that, the response of various subtypes of (SVT) to anti-arrhythmics medication is unequable.

Also this study did not test the possibility of the effect of duration of the SVT on the effectiveness of the management.

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