American Journal of Emergency Medicine (2008) **26**, 879–882

The American Journal of Emergency Medicine

www.elsevier.com/locate/ajem

Original Contribution

Adenosine in the treatment of supraventricular tachycardia: 5 years of experience (2002-2006)

Alessandro Riccardi MD[a,*], Eleonora Arboscello MD[b], Maria Ghinatti MD[a], Pierangela Minuto MD[a], Roberto Lerza MD[a]

[a]*Pronto Soccorso, Dipartimento di Emergenza, Ospedale San Paolo, 17100 Savona, Italy*
[b]*Pronto Soccorso, Dipartimento di Emergenza, Azienda Ospedaliera San Martino, Genova, Italy*

Received 30 October 2007; revised 22 November 2007; accepted 23 November 2007

Abstract We report a retrospective analysis of 5 years of adenosine use in our emergency department (2002-2006). We treated 454 patients with an intravenous bolus of adenosine. The cohort was made up of 40.7% men and 59.3% women, with mean age of 47.32 years, mean heart rate of 162.48 beats per minute. Among them, 73% responded immediately to the 6-mg dose, 15% responded after the second 12-mg dose, and 11% responded to a further 12-mg dose, whereas 11% were unresponsive. We observed minor side effects in a high percentage of patients (ie, chest tightness 83%, flushing 39.4%, sense of impending death 7%). Only 1 major adverse effect was recorded, that is, administering 12 mg of adenosine induced a marked acceleration in the ventricular rate of a patient with an undiagnosed atrial flutter, caused by induction of atrioventricular conduction (1:1). Our results confirm that when patients are appropriately selected, adenosine is probably the best available drug to treat paroxysmal supraventricular tachycardias, especially in emergency situations.

1. Introduction

Adenosine is an endogenous purine nucleoside that has been used in clinical practice in Italy for the last 10 years. It has received increasing attention in our emergency departments (ED) because of its ability to terminate a high number of paroxysmal supraventricular tachycardias (PSVT) and because it is relatively transient and does not lead to serious side effects [1,2].

Herein, we report a retrospective analysis of 5 years of adenosine use in our ED, with special focus on the percentage of arrhythmia reversions and on the most commonly reported side effects. This study is an opportunity to briefly review and discuss the improvements to be had by administering adenosine to manage supraventricular tachycardia in emergency medicine.

2. Methods

This retrospective study was performed by retrieving and reviewing all the ED files reporting the use of adenosine to treat supraventricular tachycardia between 2002 and 2006. A detailed analysis of the rhythm disorder was not carried out. We collected data concerning patients who were characterized by the sudden onset of regular tachycardia (<0.02-s variation in successive R-R interval) and whose ventricular rate was above 140 beats per minute (bpm).

* Corresponding author. Tel.: +39 0198404271, +39 3470441460 (Mobile); fax: +39 0108404359.
E-mail address: a.riccardi@asl2.liguria.it (A. Riccardi).

0735-6757/$ – see front matter © 2008 Elsevier Inc. All rights reserved.
doi:10.1016/j.ajem.2007.11.029

3. Results

Between 2002 and 2006, 454 patients affected by supraventricular tachycardia who were unresponsive to carotid sinus massage were treated with an intravenous bolus of adenosine in our ED. The patient group included 185 men (40.7%) and 269 women (59.3%). The mean age was 47.32 years (ranging from 17-72 years), and the mean heart rate was 162.48 bpm (140-240 bpm). Among them, 331 (73%) responded immediately to the 6-mg dose, whereas sinus rhythm was restored in 68 patients (15%) after administering the second 12-mg dose. Tachycardia stopped after a further 12-mg bolus of adenosine in another 5 patients (1%). The remaining 50 patients (11%) were unresponsive to adenosine; therefore, they underwent different treatment including other drugs (β-blockers, verapamil, amiodarone or class IC agents) or electrical cardioversion.

We observed minor side effects in a high percentage of patients (chest tightness in 377 patients [83%], flushing in 179 patients [39.4%], shortness of breath in 149 patients [32.2%], headache in 123 patients [27.1%], nausea in 69 patients [15.1%], and sense of impending death in 32 patients [7%]). Only one major adverse effect was recorded. Administering a second dose of adenosine (12 mg) induced a marked acceleration in the ventricular rate of a 57-year-old woman. The patient was affected by an undiagnosed atrial flutter (Fig. 1), and administering adenosine led to the evolution of the atrioventricular (AV) conduction from 2:1 to 1:1 (Fig. 2).

4. Discussion

Adenosine has a half-life of less than 1 minute. It inhibits cAMP-mediated calcium influx and enhances potassium conduction. This mechanism leads to the inhibition of AV nodal conduction and to an increase in the AV nodal refractory period, thus slowing the sinus heart rate and depressing the impulse conduction through the AV node. [2] Thanks to its mechanism of action, adenosine is highly effective in terminating supraventricular tachycardias involving the AV node as part of the reentry circuit [3-6]. Sixty to eighty percent of patients respond to a single, 6-mg dose of adenosine, and the overall success of the drug is above 90% when 12 mg is administered [6]. Time to tachycardia reversion ranges from seconds to a few minutes [2] after the adenosine bolus. A number of side effects have been reported but are short-lived and are usually not severe. Despite the brief duration of the symptoms, which mainly consist in chest pain or discomfort, flushing, dyspnea, nausea, and headache, the perception that patients have is very unpleasant, and a sense of impending death is sometimes reported.

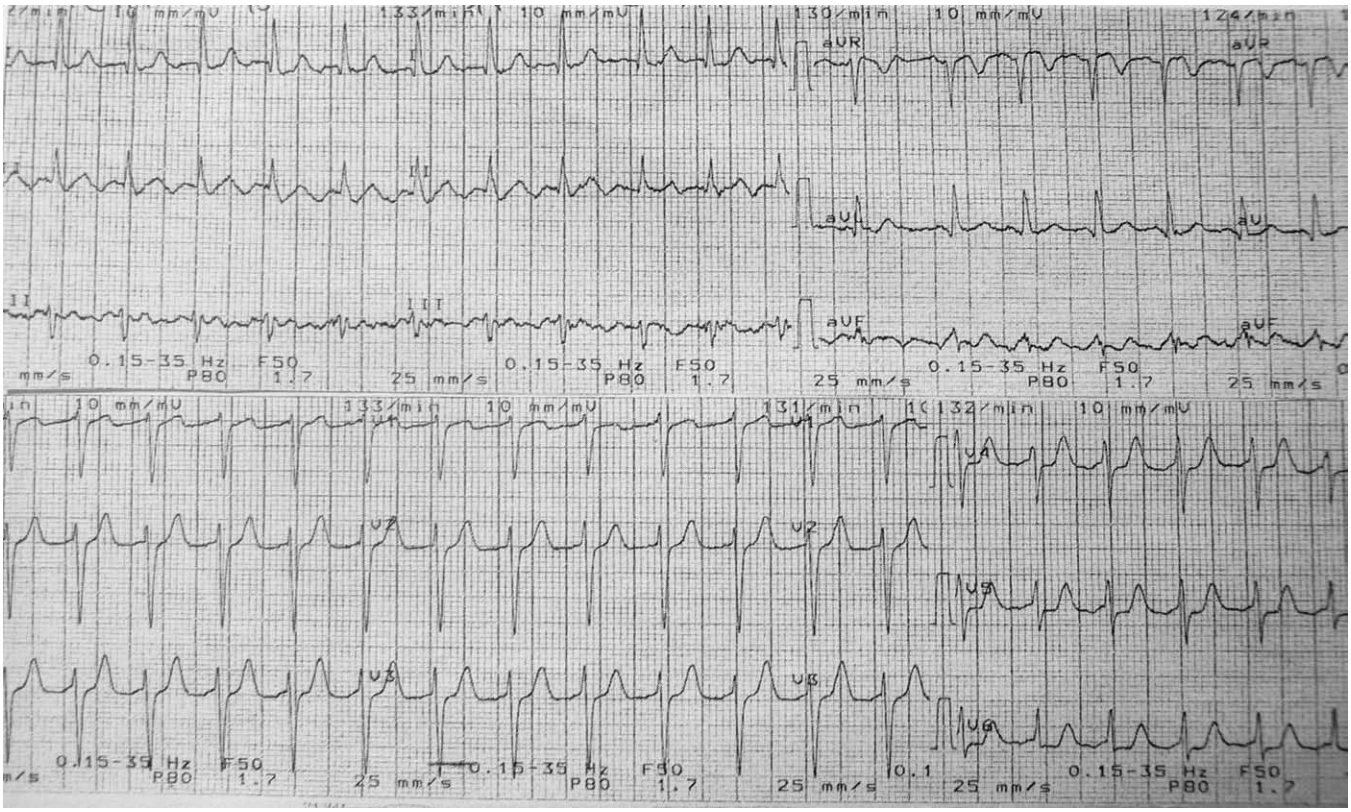

Fig. 1 12-leads ECG in a 57-year-old woman with an undiagnosed atrial flutter at presentation.

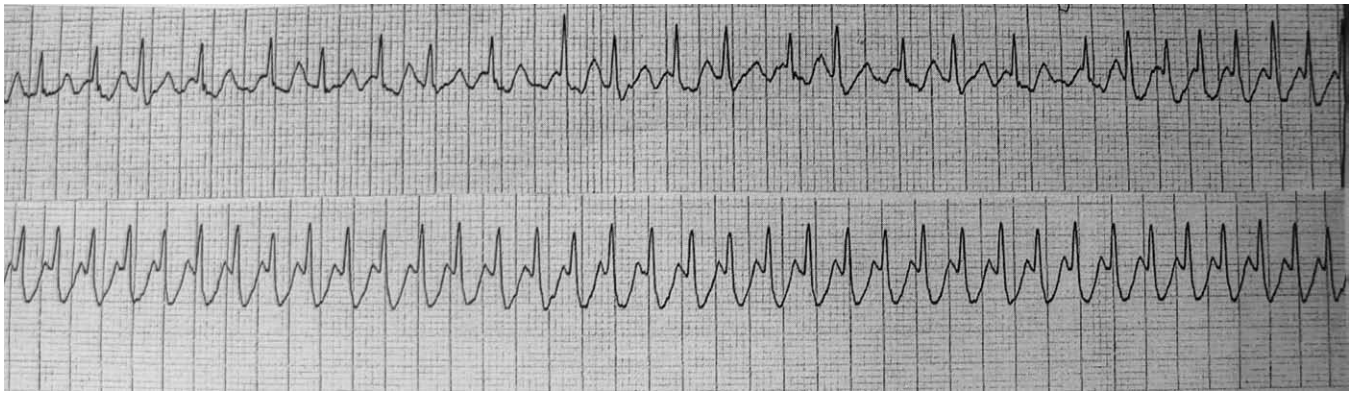

Fig. 2 Administering adenosine led to the 1:1 AV conclusion in a patient with undiagnosed atrial flutter.

Our results are consistent with those reported in the literature [2,6] and confirm that adenosine is probably an effective agent for the management of supraventricular tachycardia, showing a high rate of cardioversion and a low rate of serious adverse effect. As a matter of fact, we observed only minor side effects in most patients, although before administering the drug, we usually warned them about the possibility that unpleasant side effects might have occurred. This may have led to a bias to these data. Most of the adverse effects were transient and reflected the changes in the electrocardiogram that were detected at the time of successful arrhythmia reversion (Fig. 3). No major side effects, such as bronchospasm, occurred among our patients. We only observed 1 major, although transient, side effect (0.2%), that is, administering 12 mg of adenosine to a patient with an undiagnosed atrial flutter with 2:1 AV conduction led to a 1:1 AV conduction and a ventricular rate of 280 bpm, which, however, recovered spontaneously after 30 seconds. This experience emphasizes what was reported in the Cochrane review [2], that is, that adenosine lacks any serious side effects when patients are selected appropriately and that the life-threatening alterations in heart rate that have been reported after the use of this drug [7-9] are extremely rare and generally due to improper use. These latter events were previously reported as being a proarrhythmic effect of adenosine, especially when it was used for diagnostic purposes [10-12].

Adenosine has proved to be of diagnostic value in both narrow and broad complex tachycardias [13-18] for understanding the mechanism of tachycardia itself [3,19]. Moreover, adenosine can help clarify the underlying atrial tachyarrhythmia in atrial flutter and atrial tachycardia by transiently slowing ventricular response [7,8,20,21].

The rare but possible occurrence of a marked acceleration or depression in heart rate as a consequence of adenosine therapy suggests that caution should be taken when the drug is administered for diagnostic purposes in patients with atrial flutter and that resuscitation equipment should be readily available [20]. Figs. 1 and 2 are examples of what is reported above. They show the acceleration of ventricular response to atrial flutter with a 2:1 AV block in a patient we observed in our ED. A possible explanation for ventricular rate acceleration after adenosine administration is the presence of preexcitation, or an increase in the sympathetic tone and serum catecholamine levels [4]. The transient discomfort that patients experience after adenosine injection, as well as the vasodilating effect of the drug, may be a further factor in the increase in heart rate [7,8]. Moreover, the dose, the speed of administration, and the serum concentration of the drug might play an additional role in this phenomenon [3,19]. Currently, adenosine is not recommended in patients with broad QRS complex tachycardia unless a diagnosis of aberrant conduction is certain [1,6]. This should prevent the

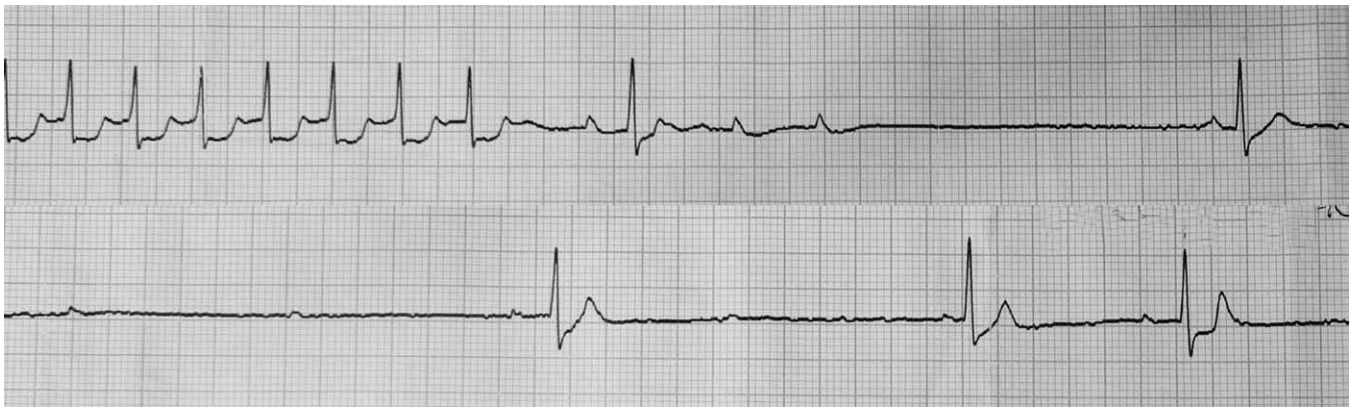

Fig. 3 Changes in the ECG detected at the time of arrhythmia reversion.

life-threatening arrhythmias that may be triggered by using it in patients with an accessory pathway. Good patient selection, as well as limiting the use of adenosine to narrow QRS complex tachycardia, should help the physician avoid the risk of major side effects. As a matter of fact, adenosine is considered a safe drug with few or no serious side effects, but a careful analysis of the electrocardiographic pattern is mandatory [2,6]. The use of adenosine in patients with a prolonged QT interval can trigger sustained torsades de pointes, as documented in the literature [20]. Furthermore, life threatening arrhythmias may be triggered by pauses or by ventricular ectopy induced by adenosine in patients who are predisposed to ventricular tachyarrhythmias. Patients with pre-excited atrial fibrillation may develop ventricular fibrillation after adenosine administration. The diagnostic use of adenosine in broad complex tachycardia has been discouraged after inducing ventricular fibrillation in patients with misdiagnosed stable ventricular tachycardia. Some caution should be taken in case of atrial flutter, as described above: secondary enhancement of AV nodal conduction following initial AV block seems to be related to sympathetic activation, after which it is perpetuated by the onset of 1:1 conduction. In addition, adenosine causes a reflex increase in circulating catecholamine levels and sympathetic nerve traffic by sympathetic stimulation in the carotid body chemoreceptors [20-22].

Together with verapamil, a calcium-channel blocker, adenosine is the most commonly used drug for paroxysmal supraventricular tachycardia [2]. Verapamil is cheaper than adenosine, and thus, it would be more cost-effective to use. Some authors report that the two drugs appear to have different probabilities of reversing tachycardia, thus suggesting that adenosine is more effective in high rate tachycardia (>170 bpm), whereas lower rates seem to be more responsive to verapamil [23,24]. Any drug to be used in the ED to treat PSVT should be characterized by prompt efficacy, a very low incidence of major side effects, a low number of contraindications, and obviously a high success rate. Adenosine fulfils these criteria, whereas verapamil takes a longer time to reversion, and it is clearly contraindicated in a number of clinical situations, such as hypotension, administration of β-blockers, acute heart failure, or poor left ventricular function, all of which are often observed in an ED [6]. On the basis of the aforementioned considerations, as well as on our experience over the recent years, we believe that adenosine is currently the best therapeutic option for treating supraventricular tachycardia in emergency situations.

References

[1] Bolton E. Disturbances of cardiac rhythm and conduction. In: Tintinalli JE, Kelen GD, Stapczcynski JS, editors. Emergency Medicine – a comprehensive study guide. 5th ed. New York: McGraw-Hill; 2000. p. 169-78.

[2] Holdgate A, Foo A. Adenosine versus intravenous calcium channel antagonists for the treatment of supraventricular tachycardia in adults. Cochrane Database Syst Rev 2006;18(4).

[3] Curtis AB, Belardinelli L, Woodard DA, et al. Induction of atrioventricular node reentrant tachycardia with adenosine: differential effect of adenosine on fast and slow atrioventricular node pathways. J Am Coll Cardiol 1997;30(7):1778-84.

[4] DiMarco JP, Sellers TD, Berne RM, et al. Adenosine: electrophysiologic effects and therapeutic use for terminating paroxysmal supraventricular tachycardia. Circulation 1983;68(6):1254-63.

[5] Slade AK, Garratt CJ. Proarrhythmic effect of adenosine in a patient with atrial flutter. Br Heart J 1993;70(1):91-2.

[6] Delacretaz E. Clinical practice. Supraventricular tachycardia. N Engl J Med 2006;354(10):1039-51.

[7] Brodsky MA, Hwang C, Hunter D, et al. Life-threatening alterations in heart rate after the use of adenosine in atrial flutter. Am Heart J 1995; 130(3 Pt 1):564-71.

[8] Rankin AC, Rae AP, Houston A. Acceleration of ventricular response to atrial flutter after intravenous adenosine. Br Heart J 1993;69(3): 263-5.

[9] Arboscello E, Botta M, Minuto P, et al. Effetto paradosso dell'adenosina in due casi di aritmia ipercinetica sopraventricolare. Genova 19-22 Maggio: Atti del IV congresso S.I.M.E.U. Nazionale; 2004.

[10] Belhassen B, Pelleg A, Shoshani D, et al. Atrial fibrillation induced by adenosine triphosphate. Am J Cardiol 1984;53(9):1405-6.

[11] Wesley Jr RC, Turnquest P. Torsades de pointe after intravenous adenosine in the presence of prolonged QT syndrome. Am Heart J 1992;123(3):794-6.

[12] Dougherty AH, Gilman JK, Wiggins S, et al. Provocation of atrioventricular reentry tachycardia: a paradoxical effect of adenosine. Pacing Clin Electrophysiol 1993;16(1 Pt 1):8-12.

[13] DiMarco JP, Sellers TD, Lerman BB, et al. Diagnostic and therapeutic use of adenosine in patients with supraventricular tachyarrhythmias. J Am Coll Cardiol 1985;6(2):417-25.

[14] Rankin AC, Oldroyd KG, Chong E, et al. Value and limitations of adenosine in the diagnosis and treatment of narrow and broad complex tachycardias. Br Heart J 1989;62(3):195-203.

[15] Till J, Shinebourne EA, Rigby ML, et al. Efficacy and safety of adenosine in the treatment of supraventricular tachycardia in infants and children. Br Heart J 1989;62(3):204-11.

[16] DiMarco JP, Miles W, Akhtar M, et al. Adenosine for paroxysmal supraventricular tachycardia: dose ranging and comparison with verapamil. Assessment in placebo-controlled, multicenter trials. The Adenosine for PSVT Study Group. Ann Intern Med 1990;113 (2):104-10 Erratum in: Ann Intern Med 1990 113 (12) 996 1.

[17] Moser GH, Schrader J, Deussen A. Turnover of adenosine in plasma of human and dog blood. Am J Physiol 1989;256(4 Pt 1):C799-806.

[18] Griffith MJ, Linker NJ, Ward DE, et al. Adenosine in the diagnosis of broad complex tachycardia. Lancet 1988;1(8587):672-5.

[19] Dora SK, Namboodiri N, Valaparambil AK, et al. Induction of atrioventricular nodal reentry tachycardia with intravenous adenosine. Singapore Med J 2007;48(5):e130-2.

[20] Mallet ML. Proarrhythmic effects of adenosine: a review of the literature. Emerg Med J 2004;21:408-10.

[21] Biaggioni I, Killian TJ, Mosqueda-Garcia R, et al. Adenosine increases sympathetic nerve traffic in humans. Circulation 1991;83(5):1668-75.

[22] Cairns CB, Niemann JT. Intravenous adenosine in the emergency department management of paroxysmal supraventricular tachycardia. Ann Emerg Med 1991;20(7):717-21.

[23] Steinbeck G, Reithmann C. Paroxysmal supraventricular tachycardia: preferential use of either adenosine or verapamil is dependent on the rate of tachycardia. Eur Heart J 2004;25(15):1277-8.

[24] Ballo P, Bernabo D, Faraguti SA. Heart rate is a predictor of success in the treatment of adults with symptomatic paroxysmal supraventricular tachycardia. Eur Heart J 2004;25(15):1310-7.