bilateral otorrhea. Otolaryngologic evaluation showed bilateral tympanic perforations, without a history of previous tympanic or ear problems.

**Discussion**

CPAP is an effective and simple method to increase arterial oxygenation in nonintubated patients. In this case, intubation was required for hypercapnia, although arterial oxygenation improved with CPAP and increased FIO₂.

There are many complications associated with CPAP, including subconjunctival emphysema, pulmonary venous and systemic gas embolism, and corneal abrasions. Pneumocephalus has been reported in association with CPAP in a patient with an unrecognized basilar skull fracture.

This case reports bilateral tympanic membrane rupture and otorrhea associated with CPAP. It is probable that the patient ruptured his tympanic membranes by coughing against the CPAP. Others have reported the need for low resistance expiratory circuits and have demonstrated that the Downs valve we used has low expiratory flow resistance. A transtympanic pressure of 724 to 2,320 cmH₂O is necessary for tympanic rupture with normal tympanic membranes. At no time was the CPAP this high unless a transient, high pressure impulse occurred that resulted in tympanic rupture but was not reflected on the manometer.

Bilateral tympanic membrane rupture and otorrhea can be added to the complications of CPAP in patients who are agitated and coughing. We recommend cautious use of CPAP in a coughing and agitated patient.

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**References**


**Rapid Suppression of Flecainide-Induced Incessant Ventricular Tachycardia with High-Dose Intravenous Amiodarone**

Alex Sagie, M.D., Boris Strasberg, M.D.; Jairo Kamliecz, M.D.; Samuel Sclarovsky, M.D.; Eldad Rechavia, M.D.; and Jacob Agmon, M.D.

A severe case of flecainide-induced incessant ventricular arrhythmias is presented. These arrhythmias were resistant to various intravenous antiarrhythmic drugs and to cardiac pacing. Intravenous amiodarone administered over a short period and in a high dose strikingly abolished all ventricular arrhythmias.

The proarrhythmic potential of flecainide acetate, a class IC antiarhythmic agent, has been well documented in the last few years. It is estimated to occur in 6.8 percent of the patients overall and was serious in 2.3 percent and lethal in 1 percent. We herein report the findings in a patient with flecainide-induced incessant symptomatic ventricular tachycardia, in whom we observed a striking and immediate response to high-dose intravenous amiodarone, with total abolition of ventricular tachycardia.

**Case Report**

A 62-year-old man with a history of anterior myocardial infarction and paroxysmal sustained ventricular tachycardia was admitted following the documentation of symptomatic (dizziness and presyncope) nonsustained ventricular tachycardia. He was receiving amiodarone (200 mg/day) and mexiletine (600 mg/day). Physical examination revealed mild signs of heart failure. The electrocardiogram revealed multiforn premature ventricular complexes. The PR interval and QTc duration were normal, as were the Q-T and QTc intervals (0.36 second and 0.34 second, respectively). A two-dimensional echocardiogram showed a dilated and poorly contracting left ventricle.

In view of the ineffectiveness of the drugs, all prior antiarrhythmic therapy was withdrawn (two weeks). Therapeutic trials with quinidine and propafenone were unsuccessful, with persistence of complex premature ventricular contractions and nonsustained ventricular tachycardia. Oral flecainide (100 mg twice daily) was administered without improvement. The dosage was then gradually increased every four days up to 200 mg twice daily. An increase in the number of complex premature ventricular contractions and nonsustained ventricular tachycardia was documented by Holter monitoring. There was no significant prolongation of the P-R, QRS and QTc intervals and no electrolyte disturbances were detected.

After 48 hours of therapy with flecainide (400 mg/day), the patient developed almost incessant self-sustained ventricular tachycardia with two distinct morphologies and rates (Fig I). These two morphologies of ventricular tachycardia were different from the previously observed paroxysmal sustained and nonsustained ventricular tachycardia and were considered to be nonclinical. During a period of eight hours, the patient suffered recurrent episodes of sustained ventricular tachycardia despite therapy with intravenous lidocaine (100-mg bolus), bretylium tosylate (bolus dose of 5 mg/kg), and procainamide hydrochloride (stopped after 200 mg because of hypotension). Pacing techniques failed to terminate the ventricular tachycardia. Because of hemodynamic deterioration, cardioversion became necessary.

**References**

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necessary five times, and in one episode the ventricular tachycardia degenerated into ventricular fibrillation. The blood level of flecainide was not determined. Intravenous amiodarone (600 mg) was then infused over 20 minutes. There was a striking and total disappearance of ventricular tachycardia and premature ventricular contractions at the end of the infusion. During the next 24 hours the patient was given 2 g of amiodarone intravenously, and an oral loading dosage of 2 g/24 hours was started concomitantly. Except for one episode of ventricular tachycardia which occurred ten hours following the initiation of intravenous amiodarone and which we believed was due to a reduction in the dose of intravenous amiodarone, the patient remained free of arrhythmias. The dosage of amiodarone was gradually reduced every four days. Holter monitoring performed 3 and 14 days later documented less than ten premature ventricular contractions per hour and no episode of couplets or ventricular tachycardia.

**Discussion**

Almost all antiarrhythmic drugs have also been shown to have proarrhythmic effects, and flecainide is no exception. Morganroth et al. reviewed the proarrhythmic potential of flecainide in 1,330 patients derived from various studies. Proarrhythmic events occurred in 6.8 percent of the patients overall and were serious in 2.3 percent and lethal in 1 percent. The incidence of such events varies according to the types of patients treated. It was significantly higher in patients with a history of sustained ventricular tachycardia (6.6 percent) than in patients with nonsustained ventricular tachycardia (0.9 percent) or premature ventricular contractions only (zero). Higher rates were also observed in patients with severe compromised left ventricular function and patients who were receiving a higher dosage. Our patient had a history of ventricular tachycardia and severe left ventricular dysfunction and was therefore prone to develop proarrhythmic events.

Although there have been many publications on flecainide-induced ventricular tachycardia, there is still no definite therapy for this condition. In the few detailed reported cases with incessant ventricular tachycardia, recurrent cardioversions with discontinuation of flecainide was the only effective therapy. Horowitz et al. described a patient in whom vasopressor drugs were required during seven hours of flecainide-induced ventricular tachycardia, after which the patient underwent successful cardioversion. Spivack et al. described a patient with incessant ventricular tachycardia in whom repeated cardioversion and overdrive suppression trials were unsuccessful, and the patient died. In our patient, we observed a striking and immediate effect of intravenous amiodarone following a period of eight hours of recurrent symptomatic ventricular tachycardia which was refractory to various antiarrhythmic agents. Since amiodarone has a long half-life and since the patient received this drug orally (stopped four weeks before intravenous administration), it is possible that some amiodarone was still present in the body, therefore potentiating the effect of intravenous amiodarone.

It is of note that lidocaine, bretylum, and procainamide were given only during the first two hours and in simple boluses and with no maintenance infusion. It is therefore highly unlikely that these drugs may have contributed to the favorable response obtained with the intravenous amiodarone. It is also probable that the blood level of flecainide had decreased significantly at the time of intravenous administration of amiodarone; however, the striking disappearance of "all" arrhythmias within 20 minutes of intravenous infusion of amiodarone supports the assumption that the beneficial antiarrhythmic effect was due to the drug and not to the discontinuation of flecainide.

**Rapid suppression of complex ventricular arrhythmias with high-dose intravenous amiodarone** has recently been reported. Mostow et al. reported 85 percent reduction of ventricular tachycardia in seven patients within 48 hours (total dose, 1,948 to 4,637 mg). The same group used high-dose oral amiodarone (between 800 and 2,000 mg two to three times daily) and demonstrated significant reduction in ventricular tachycardia beginning the second day. In all of these high-dose protocols, there were no significant hemodynamic alterations except for two patients with severe left ventricular dysfunction. In our patient, we used a similar rapid intravenous and oral loading protocol and observed no hemodynamic deterioration, despite the severe left ventricular dysfunction. Such rapid abolition of flecainide-induced incessant ventricular tachycardia has not been previously described, and therefore we believe that a similar protocol of amiodarone should be tested in future cases of this severe arrhythmia.

**References**

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IN PNEUMONIA

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IN PNEUMONIA...

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

INDICATIONS AND USAGE: TIMENTIN is indicated in the treatment of infections caused by susceptible strains of the designated organisms in the conditions listed below:

- Bacterial Septicemia, including bacteemia, caused by β-lactamase producing strains of Staphylococcus aureus and Pseudomonas aeruginosa and other Pseudomonas species.
- Lower Respiratory Infections, caused by β-lactamase producing strains of Staphylococcus aureus, Methicillin-resistant Staphylococcus aureus (MRSA), and Staphylococcus epidermidis. When TIMENTIN is indicated only for the conditions listed above, infections caused by β-lactamase susceptible organisms are also amenable to TIMENTIN treatment due to its ticarcillin content. Therefore, mixed infections caused by ticarcillin susceptible organisms and β-lactamase producing organisms can be treated with TIMENTIN if the ticarcillin component of TIMENTIN is not required for the treatment of β-lactamase producing organisms.
- Urinary tract infections, caused by β-lactamase producing strains of Staphylococcus aureus, Klebsiella spp. and E. coli. Ticarcillin is contraindicated in patients receiving ticarcillin.

TIMENTIN is particularly useful for the treatment of mixed infections and for prophylactic use prior to the identification of the causative organisms.

TIMENTIN has been shown to be effective as single drug therapy in the treatment of some serious infections where normally combination antibiotic therapy might be employed. Therapy with TIMENTIN may be initiated before results of such tests are known when there is reason to believe the infection may involve any of the ticarcillin producing organisms listed above; however, once these results become available, appropriate therapy should be continued.

ON ADMISSION

Based on in vitro synergism between TIMENTIN and aminoglycosides against certain strains of Pseudomonas aeruginosa, combined therapy has been successful especially in patients with impaired host defenses. Both drugs should be used in full therapeutic doses as soon as results of culture and susceptibility tests become available. Antimicrobial therapy should be adjusted as indicated.

CONTRAINDICATIONS: TIMENTIN is contraindicated in patients with a history of hypersensitivity reactions to any of the penicillins.

WARNINGS: SERIOUS AND OCCASIONALLY FATAL HYPERSENSITIVITY (ANAPHYLACTOID) REACTIONS HAVE BEEN REPORTED IN PATIENTS ON PENICILLIN THERAPY. THESE REACTIONS ARE MORE LIKELY TO OCCUR IN INDIVIDUALS WITH A HISTORY OF PENICILLIN HYPERSENSITIVITY AND/OR A HISTORY OF SENSITIVITY TO MULTIPLE ALLERGENS. THERE HAVE BEEN REPORTS OF INDIVIDUALS WITH A HISTORY OF PENICILLIN HYPERSENSITIVITY WHO HAVE EXPERIENCED SEVERE REACTIONS WHEN TREATED WITH CEPHALOSPORINS AND/or β-LACTAMASE PRODUCING ORGANISMS. BEFORE INITIATING THERAPY WITH TIMENTIN, CARFUL INQUIRY SHOULD BE MADE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO PENICILLIN, CEPHALOSPORINS, OR OTHER DRUGS. IF AN ALLERGIC HISTORY IS MADE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO ANY OF THE PENICILLINS, TIMENTIN SHOULD NOT BE ADMINISTERED TO THESE PATIENTS. TIMENTIN SHOULD BE DISCONTINUED AND Appropriate therapy instituted.

PREGNANCY: Category B. Reproduction studies have been performed in rats given doses up to 1000 mg/kg/day and have revealed no evidence of impaired fertility or harm to the fetus due to TIMENTIN. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Dosage and Administration: TIMENTIN should be administered by intravenous infusion (30 min.). Usual recommended dose for systemic and urinary tract infections is an average of 900 mg/day in 3.1 grams of TIMENTIN (3.1 gms containing 3 gms ticarcillin and 100 mg clavulanate potassium given every 6 to 8 hours in single tract infections, 6 grams of TIMENTIN (3.7 gms containing 3 gms ticarcillin and 300 mg clavulanate potassium given every 12 hours) in acute glomerulonephritis. Please see official package insert for details on dosage for other patients including those with renal insufficiency.

SUPPLIED: 3.1 g and 3.7 g Standard Vials, 3.1 g and 3.7 g Piggyback Bottles, 31 gm Bulk Pharmacy Package. 31 gm Add-Maintenance Antibiotic Vial.

1 Data on file, Medical Department, Beecham Laboratories. 1974B EBS 2 In retrospective reviews of 11221 pneumonia patients enrolled in comparative studies and 12181 patients with lower respiratory tract infections enrolled in multicenter TIMENTIN clinical trial protocols, who would appear to be candidates for DRG 79 (respiratory infection + inflammation, age 65 and 65 C.)

Due to susceptible organisms, in vivo activity does not necessarily imply in vitro efficacies.

Clinical response defined as cured or improved. Clinical cure defined as complete resolution of all present signs and symptoms by the end of therapy. Improvement defined as substantial diminution in the severity of present signs and symptoms. Bacteriologic response defined as elimination of initial pathogen during therapy and for the duration of follow-up or unavailability of culture material.

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