SHORT REPORTS

CARDIAC DYSRHYTHMIA WITH THE USE OF CLONIDINE IN EXPLOSIVE DISORDER

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ABSTRACT: Clonidine has been used in the management of hypertension in adults with few cases of cardiac dysrhythmia reported. These appear to occur most frequently in association with preexisting cardiac disease or toxic concentrations of the drug. We observed a case of clonidine-induced bradycardia and irregular firing of the sinoatrial node in a child who does not have cardiac disease given low doses of the drug in the treatment of intermittent explosive disorder.

DICP 1989;*23*:465-6.

CLONIDINE IS APPROVED only for the treatment of hypertension in adults. Reports have suggested, however, that clonidine may have value in the treatment of a variety of neuropsychiatric conditions including anxiety,[1] panic attacks,[2] mania,[3-5] schizophrenia,[6] and attention-deficit hyperactivity disorder (ADHD).[7,8] These effects are presumed to occur by stimulation of alpha$_2$ inhibitory neurons resulting in a decrease in noradrenergic transmission in the central nervous system. In higher doses, clonidine also affects postsynaptic receptors, resulting in increases in norepinephrine concentrations.

The use of clonidine in behavior problems of childhood has been limited to ADHD. Clonidine appears to offer some advantage over stimulants in its adverse-effect profile and in situations where ADHD is associated with explosive behavior. In a controlled study of clonidine in childhood ADHD,[7] the drug was shown significantly to improve compliance, task orientation, and frustration tolerance. In addition, oppositional behavior decreased. These results led to a trial of clonidine in the patient described here.

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CASE REPORT

A ten-year-old boy had been hospitalized for nine months with a diagnosis of intermittent explosive disorder, manifested by sudden outbursts of rage. Desipramine and carbamazepine had not reduced his irritability and rage reactions. He had no history or physical signs of heart disease. He weighed 28 kg and his heart rate averaged 76 beats/min. He was begun on increasing doses of propranolol nine weeks before the episode reported here. While on propranolol 100 mg tid, he had a normal electrocardiogram (ECG) with sinus bradycardia (54 beats/min). Propranolol did not improve his behavior so it was gradually discontinued: he received 50 mg bid eight and seven days before the dysrhythmia, 50 mg qhs six through three days before, 20 mg qhs two days before, and none the day before. The night before the dysrhythmia and the next morning, he was given clonidine 0.05 mg (total of two doses). Thus it was 36 hours from the last dose of propranolol until the dysrhythmia was observed. His pulse was noted to be slow and irregular. He felt somewhat tired but experienced no dizziness and participated in all of his usual activities. Blood pressure was normal and unchanged from previous readings. Physical examination was normal except for his pulse. An ECG showed marked sinus dysrhythmia, bradycardia (rate 46 beats/min), first-degree heart block, and several nonconducted P waves (Figure 1.) Clonidine was discontinued, and another ECG performed the following day was normal, with a rate of 64 beats/min. Rechallenge was not attempted because the dysrhythmia appeared too severe.

Clonidine has no direct effects on the myocardium, but reductions in cardiac output are produced in some

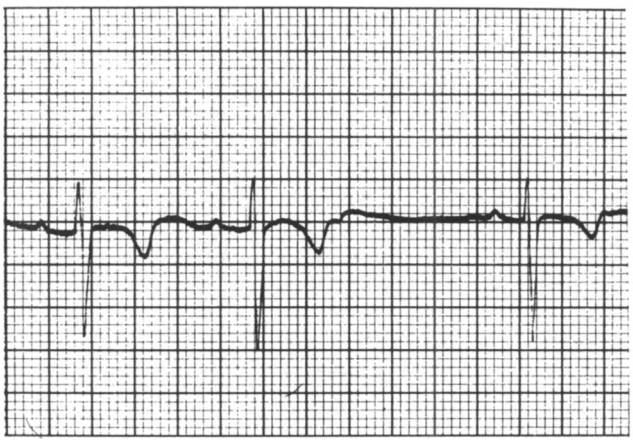

Figure 1. Lead V_3 rhythm strip of the ECG shows sinus dysrhythmia, bradycardia, and first-degree heart block.

patients by decreases in both heart rate and stroke volume. Peripheral vascular resistance is also reduced after long-term use. The reduction in heart rate is usually very small and is mediated through the central nervous system. Because clonidine reduces peripheral sympathetic activity, decreases automaticity of the bundle of His, and increases vagal activity,[9] cardiac dysrhythmias other than sinus bradycardia may be expected. Transient Wenckebach phenomenon has been reported with therapeutic doses of the drug,[10] and high-grade atrioventricular block has been reported in a limited number of patients.[11,12] These appear to occur only in patients with preexisting cardiac disease, particularly those receiving digoxin, and in patients receiving extremely high doses of clonidine. In addition, rare cases of sinoatrial-node dysfunction have been reported, usually in patients with preexisting disease of the sinus node.[13,14]

Because of the coincidence of the dysrhythmia with the start of clonidine, we suspect that clonidine was the cause. It is also possible that an interaction occurred between the propranolol that had just been discontinued and the clonidine that had been begun. This explanation seems less likely to us because the propranolol was discontinued 36 hours before the dysrhythmia was observed and the propranolol should have been metabolized by then.

Although not approved for behavioral indications, clonidine has been shown to be useful as an alternative therapy for several neuropsychiatric conditions. As it is used more frequently for behavioral indications, it appears that ECG monitoring before and during its use may be a wise precaution. ≏

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STABILITY OF CAFFEINE INJECTION IN INTRAVENOUS ADMIXTURES AND PARENTERAL NUTRITION SOLUTIONS

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ABSTRACT: Our objective was to determine the stability of caffeine base in intravenous admixtures and parenteral nutrition solutions at room temperature for 24 hours. Caffeine 10 mg/mL was used in this study. The admixtures included D5W; D5W with NaCl 0.2% injection; D5W with NaCl 0.2% and 20 mEq/L of potassium chloride injection; D10W injection; and D10W with NaCl 0.2% and 5 mEq/L of KCl injection. The parenteral nutrition solutions included 1.1% amino acids with electrolytes; 2.2% amino acids with electrolytes; and 4.25% amino acids with electrolytes. These parenteral nutrition solutions were prepared in D10W. Ten milliliters of caffeine were added to glass test tubes containing 10 mL of various solutions to yield a final concentration of 5 mg/mL. One milliliter aliquots were removed at 0, 2, 4, 8, and 24 hours and caffeine was measured by a stability-indicating HPLC method. The largest change in the concentrations of caffeine was 4.1 percent during the study period. Thus, caffeine injection is stable in various admixtures and parenteral nutrition solutions at room temperature for 24 hours.

DICP 1989;*23*:466-7.

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APNEA OCCURS FREQUENTLY in premature infants. Although theophylline is used widely in these patients, recent experience suggests that caffeine may be equally effective.[1] Further, the use of caffeine may offer some advantages over theophylline. Caffeine has a wider therapeutic index so it may not be necessary to monitor