Pharmacologic Therapy of Ventricular Tachyarrhythmias

Kelley P. Anderson, MD, Susan Brode, MD, Venkateshwar Gottipaty, MD, PHD, Alaa Shalaby, MD, Vladimir Shusterman, MD, PHD, and Raul Weiss, MD

CONTENTS

INTRODUCTION
GENERAL PRINCIPLES OF ANTI-ARRHYTHMIC THERAPY
IMMEDIATE MANAGEMENT OF VENTRICULAR TACHYARRHYTHMIAS
LONG-TERM MANAGEMENT OF VTA
THE FUTURE OF PHARMACOLOGICAL THERAPY
REFERENCES

Half of what we know in medicine today is wrong.
The trouble is we don’t know which half.

INTRODUCTION

Quinidine in the form of cinchona bark has been used to treat palpitations since at least 1749 (1). Its first use for ventricular tachyarrhythmias (VTA) is uncertain because the clinical distinction between supraventricular tachycardia (SVT) and ventricular tachycardia (VT) was probably not appreciated before it was hypothesized by MacKenzie on the basis of venous pulsation in 1908 (2). VT was first demonstrated electrocardiographically by Lewis in 1909 in the first issue of Lancet (3). The first case of control of VT by quinidine was reported in 1921 (4). Fifty years ago, in the first issue of Circulation, a series of cases of “paroxysmal ventricular tachycardia” collected between 1915 and 1948 at the Peter Bent Brigham Hospital in Boston, was reported by Armbrust and Levine (5). They examined the efficacy of various medications, including quinidine,
procainamide, magnesium sulfate, potassium salts, atropine, and morphine. Quinidine was the most effective, demonstrating benefit in 46 of 57 treated episodes with oral administration. Additional cases were controlled using rectal and intravenous (iv) administration. However, of 31 patients treated with iv quinidine, six died, two in incessant VT and four of “quinidine toxicity.” Single oral doses of quinidine ranged between 200 and 2,500 mg and single iv doses ranged between 200 and 1,500 mg. In retrospect, the ability to make diagnostic and treatment conclusions based on such a varied collection of VT origins and mechanisms demonstrates not only insight and clinical acumen, but some naiveté as well. The administration of such high doses of quinidine seems cavalier in view of the caution we now believe is essential to the safe use of antiarrhythmic drugs. Before the availability of electrical defibrillators, however, the risk of iv quinidine seemed appropriate, given the high likelihood of death associated with “paroxysmal ventricular tachycardia.” We now recognize the existence of benign forms of VT that would be refractory to the medications available 50 years ago, and could be rapidly converted into a malignant form if high doses of antiarrhythmic drugs were administered. On the other hand, our early colleagues would likely be both amazed and dubious about the value and ethics of an implanted device that delivers powerful and painful shocks automatically to unanesthetized patients. It is sobering to consider that before the first publication of the Cardiac Arrhythmia Suppression Trial (CAST) (6) in 1989, it was standard practice to prescribe the most potent antiarrhythmic drugs to suppress ventricular ectopic activity regardless of the presentation. The spirits of our predecessors and the specers of their errors should remind us that much of what we think accurate today may be proven wrong tomorrow. We must be skeptical of our knowledge, and be ready to change when we are satisfied that the evidence from well-conducted studies provides a better guide than the untrustworthy anecdotes of our own experience and intuition.

GENERAL PRINCIPLES OF ANTI-ARRHYTHMIC THERAPY

Steps in the Selection of Antiarrhythmic Therapy

Thorough evaluation of the individual patient and the clinical context is the essential first step in the selection of the optimal treatment strategy. This includes a determination of the underlying cardiac disorder and its severity, comorbid conditions, response to previous therapy, and other factors that affect prognosis and the response to various treatment alternatives. The second step includes risk assessment for each mode of death: arrhythmic, nonarrhythmic cardiovascular, and noncardiac. The third step is to determine possible treatment strategies. The fourth step is a risk-to-benefit analysis of each of the possible treatment alternatives. This is based on an estimate of impact of therapy on the risk of death and on quality of life. It must be acknowledged that it is rarely possible to comprehensively address any one of the “essential steps,” much less all four. Nevertheless, a methodological approach is needed to select the therapy that will achieve the ultimate goal: prolongation of life and enhancement of quality of life. In the midst of the drama of a cardiac arrest and the urgency associated with VT, it is sometimes forgotten that the arrhythmia itself may be a secondary issue and may or may not be the only important target of therapy. The risk of another episode of VTA may be lower than other modes of death. The priorities of care should always be set after the physician defines 1) the ultimate goal (i.e., prolongation of life vs improving