

Quinidine, A Life-Saving Medication for Brugada Syndrome, Is Inaccessible in Many Countries

Sami Viskin, MD,* Arthur A. M. Wilde, MD,† Milton E. Guevara-Valdivia, MD,‡
Amin Daoulah, MD,§ Andrew D. Krahn, MD,|| Douglas P. Zipes, MD,¶ Amir Halkin, MD,*
Kalyanam Shivkumar, MD, PhD,# Noel G. Boyle, MD, PhD,# Arnon Adler, MD,*
Bernard Belhassen, MD,* Edgardo Schapachnik, MD,** Farhan Asrar, MD, MSc, MPH,††
Raphael Rosso, MD*

Tel Aviv, Israel; Amsterdam, the Netherlands; Mexico City, Mexico; Jeddah, Kingdom of Saudi Arabia; Vancouver, British Columbia, and Hamilton, Ontario, Canada; Indianapolis, Indiana; Los Angeles, California; and Buenos Aires, Argentina

Objectives	The aim of this study was to determine the availability of quinidine throughout the world.
Background	Quinidine is the only oral medication that is effective for preventing life-threatening ventricular arrhythmias due to Brugada syndrome and idiopathic ventricular fibrillation. However, because of its low price and restricted indication, this medication is not marketed in many countries.
Methods	We conducted a survey of the availability of quinidine by contacting professional medical societies and arrhythmia specialists worldwide. Physicians were e-mailed questionnaires requesting information concerning the quinidine preparation available at their hospital. We also requested information concerning cases of adverse arrhythmic events resulting from unavailability of quinidine.
Results	A total of 273 physicians from 131 countries provided information regarding the availability of quinidine. Quinidine was readily available in 19 countries (14%), not accessible in 99 countries (76%), and available only through specific regulatory processes that require 4 to 90 days for completion in 13 countries (10%). We were able to gather information concerning 22 patients who had serious arrhythmias probably related (10 cases) or possibility related (12 cases) to the absence of quinidine, including 2 fatalities possibly attributable to the unavailability of quinidine.
Conclusions	The lack of accessibility of quinidine is a serious medical hazard at the global level. (J Am Coll Cardiol 2013;61:2383-7) © 2013 by the American College of Cardiology Foundation

E-mail received on June 8, 2012 (no editing was done):

*Hi, I hope this finds you well!
I am sorry to trouble you, but I have no one else to ask! I have a patient who had an out-of-hospital cardiac arrest a couple of years ago, and had a defibrillator implanted. He returned last week with*

*multiple shocks for VF, and a suspicious ECG for Brugada syndrome. He did not respond to beta-blocker therapy and I wanted to start quinidine for him - I recall having a few patients at Sunnybrook as a resident who were taking quinidine, and we ordered it without a problem. I tried to get quinidine for this patient via SAP with Health Canada, and it was declined - they stated they did not provide it for NEW patients, only patients already on the therapy. How are you managing your Brugada patients with multiple shocks or recurrent arrhythmias? This seems completely ridiculous!
With kind regards,
Signed by a Cardiology Fellow in Canada
(personal communication, 2012)*

From the *Tel-Aviv Sourasky Medical Center, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel; †Academic Medical Centre, Amsterdam, the Netherlands; ‡UMAE Hospital de Especialidades Dr. Antonio Fraga Mouret, CMN La Raza IMSS, Mexico City, Mexico; §King Faisal Specialist Hospital and Research Center, Jeddah, Kingdom of Saudi Arabia; ||University of British Columbia, Vancouver, British Columbia, Canada; ¶Kranert Institute of Cardiology, Indiana University School of Medicine, Indianapolis, Indiana; #UCLA Cardiac Arrhythmia Center, Los Angeles, California; and the **Asociación Carlos Chagas, Buenos Aires, Argentina; and ††McMaster University, Hamilton, Ontario, Canada. The authors have reported that they have no relationships relevant to the content of this paper to disclose.

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Limited patient access to curative or life-prolonging medications is a major problem worldwide. It is well acknowledged that this problem commonly results from the inability

Abbreviations and Acronyms

ICD = implantable
cardioverter-defibrillator

VF = ventricular fibrillation

of healthcare resources to meet the high costs of patented drugs or even that of generic substitutes (e.g., antiretroviral medications in Africa or heart failure therapy for the uninsured in the United

States) (1,2). Less well recognized is the opposite situation, in which the unavailability or inaccessibility of a life-saving medication is governed by its low price and restricted indication for a low-prevalence disease, rendering unfavorable pharmaceutical market forces from the perspective of the industry. The latter setting is exemplified by the case of quinidine (3-5).

Quinidine is the only oral medication that has consistently shown efficacy in preventing arrhythmias and terminating arrhythmic storms due to recurrent ventricular fibrillation (VF) in patients with Brugada syndrome (6-14), idiopathic VF (15-20), and early repolarization syndrome (21-23). Without appropriate drug therapy, such events can prove lethal even in patients with an implantable cardioverter-defibrillator (ICD), who may receive numerous ICD shocks per day, eventually leading to cardiogenic shock. Quinidine is also the only antiarrhythmic drug that normalizes the QT interval in patients with the congenital short QT syndrome (24,25). However, ever since the unexpected cessation of quinidine production by its main manufacturer (26), prescribing this valuable medication has become increasingly difficult in many countries. In fact, on several occasions during recent years, the first author had to mail emergency supplies of quinidine overseas to physicians treating patients in urgent need of this medication because of arrhythmic storms. In view of this emerging problem, we conducted a worldwide survey designed to estimate the magnitude of the shortage of quinidine and its clinical implications.

Methods

We conducted a survey of the availability of quinidine by contacting professional societies of cardiology, national working groups on arrhythmia and electrophysiology, arrhythmia specialists, and cardiologists worldwide through e-mail. We also took advantage of dedicated e-mail networks (Foro Iberoamericano de Arritmias en Internet, with >700 subscribers) and a Chinese forum. Additional e-mail addresses were obtained via a literature search for articles published on Brugada syndrome, idiopathic VF, and early repolarization syndromes. All recipients were e-mailed a questionnaire requesting information concerning the quinidine preparation available at their hospital (including commercial name and manufacturer). We also requested information pertaining to the actual time required for quinidine to be supplied for use as well as the regulatory processes involved. In addition, we specifically requested information about the number of patients at each center treated with quinidine for Brugada syndrome, idiopathic

VF, or early repolarization syndromes. Corroborating evidence was sought from at least one other physician or pharmacist and all searchable public and regulatory bodies to validate physician reports. Finally, we requested information concerning cases of serious adverse arrhythmic events (defined as recurrent life-threatening ventricular arrhythmias or ICD shocks) resulting from unavailability of quinidine. All contacted physicians were also requested to forward the study questionnaire to contacts of their own. Therefore, although the number of responders is known, the number of physicians who declined to respond is not. The entire e-mail survey was conducted from June to September 2012.

Arrhythmic events were defined as related to unavailability of quinidine when the following criteria were met: 1) occurrence of arrhythmias known to respond to quinidine (i.e., polymorphic ventricular tachycardia or VF) in an appropriate clinical setting (i.e., a definite diagnosis of Brugada syndrome or idiopathic VF with or without early repolarization); 2) inability to administer quinidine at the time of its prescription; and 3) further ventricular tachyarrhythmias requiring defibrillation occurring from the time of quinidine prescription to the time of its actual administration. Events associated with unavailability of quinidine were further classified as “probably resulting” from the absence of the medication in cases in which resolution of arrhythmia was ultimately achieved by administration of quinidine. All cases in which quinidine was never administered were classified as “possibly resulting” from unavailability of quinidine. The definitions in the preceding text take into account that the efficacy of quinidine for these specific arrhythmic syndromes is well established (6,18-20, 22,27,28).

Results

We received information concerning the availability of quinidine in 131 countries (Fig. 1). Missing data are almost exclusively from African countries. There was discordant information from only 5 countries (Argentina, China, Czech Republic, Norway, and Sweden) and was mostly attributable to discrepancies in classification of the availability of quinidine as either “not available” or “available with restrictions.”

Quinidine is readily and immediately available in only 19 countries (14%). In contrast, this medication is unavailable in 99 countries (76%) and is available but only through restrictive regulatory processes that require 4 to 90 days to complete in 13 countries (10%) (Fig. 1). Of the 273 physicians responding to our survey, 71 (26%) had at least one patient in need of quinidine therapy because of idiopathic VF or Brugada syndrome. Importantly, 28 physicians (representing 10% of all survey responders and 39% of physicians who treated patients with Brugada syndrome or idiopathic VF) reported having one or more patients who developed arrhythmic events related to inaccessibility to quinidine when prescribed. Within 4 months (June to September 2012),

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