DIA

Therapeutic Innovation
& Regulatory Science
2018, Vol. 52(5) 529-530

DOI: 10.1177/2168479018797715
tirs.sagepub.com

Proposed Proarrhythmic Cardiac Safety Education in Medical, Pharmacy, and Nursing Schools: An Interprofessional Model

At the start of this Editorial, I'd like to congratulate all concerned on the success of our recent DIA Global Annual Meeting, held in Boston in June 2018. The meeting had its highest attendance in nearly a decade, and was graced with moderate temperatures (quite different from the forecast of 93°F for August 7, the day I'm writing this Editorial) that made sightseeing while in the city delightful.

The Science of Proarrhythmic Cardiac Safety

As Link and colleagues[1] observed, "One of the most feared complications in medicine is sudden death caused by drug-induced proarrhythmia. Accordingly, concerted efforts have been made to define a drug's proarrhythmic potential before regulatory approval." Proarrhythmic cardiac safety considerations are a central component of contemporary new drug development.[2] Concerted nonclinical and clinical investigations assess whether a drug has a proarrhythmic propensity (liability). Reports of these investigations are submitted with a marketing application. If a regulatory agency considers the drug to have an overall favorable benefit-risk balance at the public health level but also to have an identified proarrhythmic liability, appropriate language addressing risk management strategies for individual patients when the drug is employed in clinical practice will be included in the drug's Prescribing Information.

As an example of such information, consider vandetanib, a kinase inhibitor indicated for the treatment of symptomatic or progressive medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease. Part of the labeling information[3] reads as follows (*vandetanib* has been used to replace the trade name):

- Vandetanib can prolong the QT interval. *Torsades de pointes* and sudden death have occurred in patients receiving vandetanib.
- Do not use vandetanib in patients with hypocalcemia, hypokalemia, hypomagnesemia, or long QT syndrome.
- Correct hypocalcemia, hypokalemia and/or hypomagnesemia prior to vandetanib administration.
- Monitor electrolytes periodically.
- Avoid [prescribing other] drugs known to prolong the QT interval.

The pathway via which patients receive medicines involves contributions from multiple health care professions: physicians prescribe drugs, pharmacists dispense them, and (in inpatient hospital or residential care settings) nurses administer them. An important question that arises, therefore, is this: Do medical, pharmacy, and nursing schools typically teach their students the science of proarrhythmic cardiac safety such that they fully understand the origins and ramifications of this information? That is, do these schools teach students in an integrated manner about drug-induced QT interval prolongation as seen on the surface electrocardiogram (ECG), torsade de pointes (a rare polymorphic ventricular arrhythmia that typically occurs in self-limiting bursts that can lead to symptoms of dizziness, palpitations, syncope, and seizures, but which can occasionally progress to ventricular fibrillation and sudden cardiac death), and why monitoring and correcting electrolyte balances is important when a patient is receiving vandetanib? Based on an initial (admittedly very small and informal) assessment, the answer to this question is very likely to be no.

A second question is: How can we help practitioners of medicine, pharmacy, and nursing who did not receive education in proarrhythmic cardiac safety during their training to educate themselves in this field, including how they can protect patient well-being in the practice of their respective professional activities?

Proarrhythmic Cardiac Safety Education: An Interprofessional Model

At the invitation of Dr Fabio Badilini, I wrote a 2017 Editorial[4] entitled "Cardiac Safety Education: A Call to Action" for *AMPS-QT*, his organization's quarterly journal dedicated to all people and organizations involved in cardiac safety. I argued that embedding the discipline of proarrhythmic cardiac safety into mainstream medical education—where "medical" covers physicians, pharmacists, nurses, and allied health care professionals—is now essential. I realize that doing so is not likely to be an easy task since most schools regard their curricula as already full to overflowing.[5] Nonetheless, I believe it is incumbent on those of us in this field to work diligently in this regard. While still considering how best to address this challenge, one relatively simple initial strategy may be to create a small set of PowerPoint slides and lecture notes (ideally endorsed by

multiple academic societies and professional organizations) and sending these at no cost to all medical, pharmacy, and nursing schools in a given country in the appropriate language: the most appropriate professor(s) in each school could then deliver these lectures.[4]

Going one step further, at universities where there are more than one of these professional schools, perhaps such lectures could be given to students from all schools at the same time, and interprofessional discussions could take place about the roles each profession can play in ensuring the safest use of drugs with a proarrhythmic liability.

With regard to educating professionals already in clinical practice, Continuing Education initiatives are of considerable importance. As an example, one of the American College of Clinical Pharmacology's (ACCP's) journals, the *Journal of Clinical Pharmacology*, regularly publishes papers utilized for Continuing Education in Medicine and Pharmacy. A group of coauthors representing the Cardiac Safety Research Consortium recently published a paper titled "Drug-Induced Proarrhythmia and Torsade de Pointes: A Primer for Students and Practitioners of Medicine and Pharmacy" that will be used for this purpose.[6] My colleague Dr Ralph Klotzbaugh and I are currently discussing how best to implement something similar for the nursing profession.

Why the Descriptor "Interprofessional" Is So Important

Fortunately (if that is the right word), the occurrence of drug-induced torsade de pointes typically requires multiple factors to be present at the same time. Clinical risk factors such as age, female sex, structural heart disease, metabolic and electrolyte abnormalities, bradycardia and conduction disease, increased drug bioavailability, coprescription of loop diuretics, coprescription of other drugs with a proarrhythmic liability, and symptomless inheritance of certain abnormal genetic variants influencing cardiac electrical activity can act as effect amplifiers to make an otherwise relatively safe drug dangerous with regard to a risk for polymorphic ventricular tachycardia.[7-9]

First, consider the role of the physician. As Beach and colleagues[10] observed, "The most important risk-reducing intervention clinicians can make is undertaking a careful analysis of other QT risk factors" when prescribing medications with a known QT-prolongation liability. Second, consider the role of the pharmacist. Given their expert knowledge of clinical pharmacology, pharmacists are well placed to work closely with physicians as influential arbiters of sound prescribing decisions, and to alert physicians to injudicious prescribing decisions.[11] They are also well placed to counsel patients regarding signs and symptoms suggestive of torsade de pointes and to instruct them to seek immediate medical attention if these occur. They can also advise patients to inform their health care provider of any changes to, or new use of other, medications, including over-the-counter drugs and natural health products. Third, nurses in inpatient and residential care settings are well placed to conduct a final check before a prescribed and dispensed medicine is administered to a patient.

I will keep readers updated on the progress of this Initiative.

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Acknowledgments

Inaugural support from several individuals and professional organizations for the Interprofessional Cardiac Safety Educational Initiative discussed in this Editorial is gratefully acknowledged: Dr Fabio Badilini, AMPS; Dr. Byron May, Campbell University College of Pharmacy & Health Sciences; Dean Joseph Barone and Dr Michael Toscani, Ernest Mario School of Pharmacy, Rutgers University; Dr Emily Mantovani, Celgene Corp; Dr Ralph Klotzbaugh, University of New Mexico; and Dr Laura Hayman, University of Massachusetts Boston.

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