QT Prolongation, Torsade de Pointes, Myocardial Ischemia From Coronary Vasospasm, and Headache Medications. Part 2: Review of Headache Medications, Drug–Drug Interactions, QTc Prolongation, and Other Arrhythmias

Mark J. Stillman, MD; Deborah E. Tepper, MD; Stewart J. Tepper, MD; Leslie Cho, MD

Serotonin (5-hydroxytryptamine)$_{1B/1D}$ agonists can vasoconstrict coronary and cerebral arteries. Chest, jaw, and arm discomfort, so-called "triptan sensations," are often felt to be noncardiac. In Part 1 of this review, the relationship of triptans, coronary artery narrowing, and spasm was discussed, along with a case of a 53-year-old woman without cardiac risk factors who developed polymorphic ventricular tachycardia and cardiac ischemia with acquired corrected QT (QTc) interval prolongation following oral sumatriptan.

In Part 2 of this review, headache medications, drug–drug interactions, QTc prolongation, and cardiac arrhythmias are appraised and discussed. Triptans, cardiac arrhythmias, and ischemia by prescribing information are summarized. The reader is provided tables on QTc prolongation by medication.

The problem of QTc prolongation with a variety of headache medications at conventional doses, including triptans, serotonin reuptake inhibitors (selective serotonin reuptake inhibitors and serotonin norepinephrine reuptake inhibitors), other antidepressants, antihistamines, and antinauseants should lead to proactively obtaining electrocardiograms and more vigilant surveillance of headache patients. This may be the place to start in protecting patients from these cardiac adverse events.

Key words: triptan, polymorphic ventricular tachycardia, Torsade de Pointes, corrected QT prolongation, Prinzmetal angina, vasospasm, migraine medication

In Part 1 of this review, triptans as serotonin (5-hydroxytryptamine [5-HT])$_{1B/1D}$ agonists and vasoconstrictors were reviewed, along with the documented co-occurrence of vasospasm, coronary events, Raynaud's, and cardiac arrhythmias, accompanied by an illustrative case. These cardiac risks are clearly increased and can be triggered pharmacologically with triptans. Many headache medications in common use lengthen corrected QT (QTc) and destabilize cardiac rhythms. Some medications are particularly prone to causing electrocardiogram (EKG) changes, such as verapamil and citalopram.

From the Headache Center, Neurological Institute, Cleveland Clinic, Cleveland, OH, USA (M.J. Stillman, D.E. Tepper, and S.J. Tepper); Department of Cardiology, Cleveland Clinic, Cleveland, OH, USA (L. Cho).

Address all correspondence to M.J. Stillman, MD, C21 Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195.

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Headache

Complicating these dangers is the specter of drug–drug interactions. Complex metabolic relationships can raise drug levels of 1 or more medications, with which a headache patient is treated, escalating arrhythmia and cardiac risks. There may be an added threat by virtue of the 5-HT receptor profile of so many headache medications.

HEADACHE MEDICATIONS, DRUG–DRUG INTERACTIONS, QTc PROLONGATION, AND OTHER CARDIAC ARRHYTHMIAS

As noted in Part 1, the QT interval represents the measured interval between the beginnings of the QRS complex to the end of the T wave. The interval is usually measured by automated EKG in V2 or V3 because they represent the longest QT.[1]

QT intervals need to be corrected by rate via the Bazett formula, which divides the measured QT by the square root of the RR interval. More recently, formulas have been used that adjust the QT as a linear or power function of the RR rate and are more accurate in completely removing the rate dependence when evaluating the QT interval. Gender as well as rate are now considered when evaluating the QT interval.[1] General rules of thumb are that a QTc interval longer than 440-470 milliseconds in a man is abnormal and a QTc longer than 470-480 milliseconds in a woman is abnormal, although as noted, there are varying opinions and numbers cited across the literature.[1,2]

Many medications used by headache patients target 5-HT receptors and are also known to widen the QTc interval. These

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include headache preventives as well as those used to treat frequently seen or comorbid conditions, such as depression, anxiety, and insomnia.

An examination of 37 cases of QTc interval prolongation in individuals taking antipsychotic or antidepressant medication was culled from 20 years of literature and presented in an analysis by Vieweg and colleagues in 2009.[3] Included were individuals taking commonly used antidepressants for headache prevention, such as doxepin, amitriptyline, nortriptyline, trazodone, and venlafaxine, as well as fluoxetine. All individuals had significant QTc prolongation, with complications ranging from syncope to cardiac arrest. In most cases, the doses and types of these medications were not unusual. Within those 37 cases was 1 case of a patient on chlorpromazine and nortriptyline who was switched to amitriptyline, 2 cases of amitriptyline alone, 1 case of trazodone on 150 mg, 1 case on fluoxetine 20 mg who 3 weeks prior had stopped amitriptyline, 1 case on venlafaxine 150 mg, and 1 case on doxepin 40 mg. All individuals in this case review were age 60 or above.

A progressive increase of QTc length occurs with age.[3-6] Nighttime hours, female sex when testosterone levels are low, cardiovascular disease, hypokalemia, and hypomagnesaemia all predispose or induce an individual to have long QTc. The QTc stretches out by about 20 millisecond at night, believed to be secondary to autonomic tone.[6]

About 70% of Torsade de Pointes (TdP) cases are female, making gender a risk.[7] Other risk factors cited include thyroid disease, bradycardia, and diseases that predispose an individual to electrolyte imbalance because of the medicines used to treat them, such as diabetes, congestive heart failure, renal impairment, and hypertension.[8] These individuals can further increase their risk through intake of QTc-prolonging medications.

Lithium, which is used to treat cluster headache as mood disorders, lengthens the QTc. Cluster patients will often use triptans daily or even twice daily until their attacks are controlled.

Medications used to treat adult attention deficit disorder such as amphetamines and methylphenidate are also QTc-prolonging drugs and are frequently coupled with antidepressants in migraineurs.

Antihistamines such as diphenhydramine and hydroxyzine are frequently used for intravenous (IV) rescue of migraines or for sleep, and will also prolong the QTc interval. Again, these antihistamines are often used in the context of co-pharmacy for headache prevention and treatment. Because diphenhydramine is available over the counter and used for sleep, allergies, and upper respiratory conditions, a patient may not think to mention its use to the clinician treating their headache.

The Food and Drug Administration (FDA) has been following issues stemming from QTc prolongation associated with the use of selective serotonin reuptake inhibitors (SSRIs), particularly citalopram, available in generic form in the USA, and commonly used as an antidepressant and anxiolytic. On March 28, 2012, an alert was issued from the agency recommending that citalopram not be used in doses exceeding 40 mg because of the QTc interval changes associated with it, potentially leading to TdP.[9,10]

DRUG–DRUG INTERACTIONS

Certain potential drug–drug interactions have attracted attention to headache pharmacotherapy. The serotonin syndrome, in particular, has been the subject of recent articles and is a frequent cause for concern among dispensing pharmacists.[11] This concern relates to the potential for serotonin syndrome with the concomitant use of SSRIs, serotonin norepinephrine reuptake inhibitors (SNRIs), and triptans. However, triptans do not bind to 5-HT_{2A} receptors, and the receptor felt to activate serotonin syndrome, so the concern for coadministration seems largely unjustified as far as serotonin syndrome is concerned.[11] In contrast, a more significant issue might arise in susceptible individuals if triptans widen the QTc interval at the same time the patient is taking another QTc-prolonging medication.

The potential for widening of the QTc can take place with concurrent use of citalopram and cytochrome P4502C19 (CYP2C19) inhibitors, such as omeprazole, esomeprazole, or oxcarbazepine, which increase plasma levels of this SSRI.[12] Concurrent use of trazodone for sleep can further widen the QTc interval, setting the patient up for increased vulnerability to arrhythmia. The FDA has recommended that EKGs be considered more frequently in certain individuals on citalopram who have bradyarrhythmias or hypomagnesemia, or who are taking other medications that prolong the QTc interval.[7] Because the SSRI and tricyclic classes as a whole all widen the QTc in varying degrees, one may extrapolate from this recommendation that EKGs be considered for the broader group of patients taking any of these medicines either in higher doses or in combination with another QTc-expanding medications. Clarifying whether this includes the use of triptans will be an important issue to address.

Inadvertent increases in plasma levels of drugs such as venlafaxine can be brought about by coadministration with diphenhydramine and bupropion. The addition of bupropion 150 mg to venlafaxine can raise the plasma concentration of venlafaxine by 2.5 times.[13] Diphenhydramine at 50 mg twice a day, combined with venlafaxine at 18.75 mg twice a day, doubles the plasma concentration of the venlafaxine.[14] Venlafaxine metabolism is further complicated by fast and slow metabolizers, with slow metabolizers presumably having higher blood levels and greater risk for adverse events, including cardiac.[12]

The implication from the many drug interactions seen even with these newer antidepressants is that apparent doses from a medication list may not reflect actual plasma levels in a patient taking multiple, seemingly benign combinations such as an antidepressant, a proton pump inhibitor, and an antihistamine. In the susceptible individual, it is possible that the addition of certain triptans could push the QTc interval into vulnerable

territory for an arrhythmia, without high doses of any 1 drug on the medication list and with only modest doses of a single drug with QTc interval warnings.

AN ILLUSTRATIVE CASE

A 45-year-old woman with a history of depression and seizures came to a headache clinic for evaluation of her worsening migraines. She was being treated at a different institution and was seeking advice on getting her migraines under better control. For her seizures, she was taking levatiracetam, and for both depression and migraine prevention, she was taking nortriptyline 75 mg.

On that first evaluation, she was evaluated for her migraine without aura, and no EKG was done. Specific recommendations were made to avoid medication overuse and treat promptly with a triptan at the onset of the migraine.

Five months later, she returned for further evaluation and treatment. At this visit, an EKG was done, and a prolonged QTc of 486 was noted. This is prolonged regardless of what upper limit of normal for women is used. She was therefore taken off the nortriptyline, and her QTc normalized to 432.

This case illustrates the importance of obtaining a baseline EKG in patients taking medications known to prolong the QT interval even in instances where the medications are being prescribed by another physician. Although there were no consequences in this case, there was the clear potential for arrhythmia on her current nortriptyline, and the addition of an antinauseant, antibiotic, or antihistamine could have tipped the balance.

TABLES ON MEDICATIONS CAUSING QT PROLONGATION

The Arizona Center for Education and Research on Therapeutics at http://www.QTdrugs.org published tables on risk for QT prolongation that are extremely useful for the clinician to keep at hand.[4] These are adapted in Tables 1-3 for reader use.

THE VERAPAMIL PROBLEM

In the 2012 American Headache Society/American Academy of Neurology Guidelines for episodic migraine prevention, verapamil is listed as level U, inadequate or conflicting data to support or refute use in prophylaxis.[15] Despite this poor level of evidence for efficacy in migraine, it is used frequently, especially in patients with migrainous aura and in cluster patients.[16-18]

The American Academy of Neurology Guidelines on treatment of cluster headache states that verapamil at 360 mg daily may be considered for prevention of cluster headache with level C evidence possibly effective.[16] Verapamil is the foundation for cluster prevention clinically.[18]

However, verapamil carries with it the potential for significant cardiac risk. Cohen and colleagues studied 128 cluster patients on verapamil with EKGs. "Twenty-one of 108 patients (19%) had arrhythmias. Thirteen (12%) had first-degree heart block (PR >0.2 sec), at 240 to 960 mg/day, with one requiring a permanent pacemaker. Four patients had junctional rhythm, and one had second-degree heart block. Four patients had right bundle branch block. There was bradycardia (HR <60) in 39 patients (36%), but verapamil was stopped in only 4 patients," presumably because of the severity of cluster headache and the fact that the patients were for the most part asymptomatic. "In eight patients the PR interval was lengthened, but not to >0.2 sec. The incidence of arrhythmias on verapamil in this patient group is 19%, and bradycardia 36%." Thus, EKGs are extremely important for patients on verapamil, even at doses as low as 240 mg daily.[18]

TRIPTANS, CARDIAC ARRHYTHMIAS, AND ISCHEMIA BY PRESCRIBING INFORMATION

All triptan prescribing information in the USA lists the risk of myocardial infarction and vasospasm. The sumatriptan package insert is the most extensive, and because experience with sumatriptan is the largest, it is worth reviewing. It reads, "Among approximately 4000 patients with migraine who participated in premarketing controlled and uncontrolled clinical trials of sumatriptan nasal spray, one patient experienced an asymptomatic subendocardial infarction possibly subsequent to a coronary vasospastic event. . . . Cardiac events that have been observed to have onset within 1 hour of sumatriptan administration include: coronary artery vasospasm, transient ischemia, myocardial infarction, ventricular tachycardia and ventricular fibrillation, cardiac arrest, and death. . . ."

"Frequent adverse events are defined as those occurring in at least 1/100 patients, infrequent adverse events are those occurring in 1/100 to 1/1000 patients, and rare adverse events are those occurring in fewer than 1/1000 patients. . . . Frequent were palpitations, syncope, decreased blood pressure, and increased blood pressure. Infrequent were arrhythmia, changes in EKG, hypertension, hypotension, pallor, pulsating sensations, and tachycardia. Rare were angina, atherosclerosis, bradycardia, cerebral ischemia, cerebrovascular lesion, heart block, peripheral cyanosis, thrombosis, transient myocardial ischemia, and vasodilation. . . ."

"The following adverse events occurred in clinical trials with [sumatriptan] injection and . . . nasal spray from open and uncontrolled studies: . . . abnormal pulse, flushing, Raynaud's syndrome, and various transient EKG changes (nonspecific ST or T wave changes, prolongation of PR or QTc intervals, sinus arrhythmia, nonsustained ventricular premature beats, isolated junctional ectopic beats, atrial ectopic beats), and delayed activation of the right ventricle."[19]

Other triptan prescribing information lists the risk for vasospastic angina in the absence of coronary artery disease. For example, zolmitriptan is cited as causing coronary vasospasm in

Table 1.—Drugs That Prolong QT Intervals

Agent	Brand name(s)	Comment
Anti-arrhythmic agents		
Amiodarone	Cordarone, Pacerone	—
Disopyramide	Norpace	—
Dofetilide	Tikosyn	—
Flecainide	Tambocor	—
Ibutilide	Corvert	—
Procainamide	Pronestyl, Procan	—
Quinidine	Quiniglute, Cardioquin	—
Sotalol	Betapace	—
Anti-infectives		
Azithromycin	Zithromax	—
Clarithromycin	Biaxin	—
Erythromycin	EES, Erythrocin	—
Halofantrine	Halfan	Antimalarial
Moxifloxacin	Avelox	—
Pentamidine	Pentam, Nebupent	—
Sparfloxacin	Zagam	—
Chloroquine	Aralen	Antimalarial
Anticancer agents		
Arsenic trioxide	Trisenox	—
Vandetanib	Caprelsa	—
Psychotropic agents		
Chlorpromazine	Thorazine	Antinausea and antipsychotic
Citalopram	Celexa	—
Haloperidol	Haldol	Increased risk IV
Mesoridazine	Serentil	—
Pimozide	Orap	—
Thioridazine	Mellaril	—
Antinausea/gastrointestinal stimulant		
Domperidone	Motilium	Available in Canada
Droperidol	Inapsine	—
Cisapride	Propulsid	Off US market
Antihistamines		
Astemizole	Hismanal	Off US market
Terfenadine	Seldane	Off US market
Analgesic agents		
Bepridil	Vascor	Anti-angina
Methadone	Dolphine, Methadose	—
Levomethadyl	Orlaam	Not available in USA, methadone derivative
Bepridil	Vascor	Anti-anginal agent

Adapted from Arizona Center for Education and Research on Therapeutics (http://www.QTdrugs.org).[4]
EES = erythromycin ethylsuccinate; IV = intravenous; — = no specific comments.

at least 1 patient with no cardiac disease history and with documented absence of coronary artery disease.

Zolmitriptan also has a specific warning on exacerbation of Wolf–Parkinson–White (WPW). Zolmitriptan is explicitly contraindicated in WPW and cardiac accessory conduction pathway disorders.[20] Whether other triptans trigger WPW is unknown and unreported.

Prescribing information yields variable information on triptans and QTc prolongation. The US prescribing information for sumatriptan, zolmitriptan, and naratriptan explicitly lists QTc prolongation under adverse events. For sumatriptan, the QTc prolongation is listed in open-label studies done subsequently on injection and nasal spray users. For zolmitriptan, QTc prolongation is described as rare, that is, occurring <1/1000.

The naratriptan prescribing information lists QTc prolongation as infrequent, that is, occurring from 1/100 patients to 1/1000. Other cardiac adverse events for naratriptan listed as "infrequent (1/100 to 1/1000) were palpitations, increased blood

Table 2.—Drugs Causing QT Prolongation Without Evidence of Inducing Torsade de Pointes When Used Alone

Agent	Brand name(s)	Comment
Anti-arrhythmic agents/cardiac active drugs		
Alfluzosin	Uroxatral	Alpha blocker used for prostatism
Dronedarone	Multaq	—
Isradipine	Dynacirc	—
Moexipril/HCTZ	Uniretc	—
Nicardipine	Cardene	—
Ranolazine	Ranexa	Anti-angina
Anti-emetics		
Dolasetron	Anzemet	—
Famotidine	Pepcid	—
Granisetron	Kytril	—
Ondansetron	Zofran	—
Anticancer agents/transplantation medications		
Eribulin	Halaven	—
Lapatinib	Tykerb, Tyverb	—
Nilotinib	Tasigna	—
Sunitinib	Sutent	—
Tacrolimus	Prograf	—
Tamoxifen	Nolvadex	—
Psychotropic agents		
Amantadine	Symmetrel	—
Chloral hydrate	Noctec	—
Clozapine	Clozaril	—
Escitalopram	Lexapro, Cipralex	—
Felbamate	Felbatrol	—
Fingolimod	Gilenya	—
Fosphenytoin	Cerebryx	—
Iloperidone	Fanapt	—
Lithium	Eskalith, Lithobid	—
Paliperidone	Invega	—
Quetiapine	Seroquel	—
Risperidone	Risperdal	—
Sertindole	Serlect	—
Venlafaxine	Effexor	—
Ziprasidone	Geodon	—
Anti-infectives		
Atazanavir	Reyataz	—
Foscarnet	Foscavir	—
Gatifloxacin	Tequin	—
Gemifloxacin	Factive	—
Levofloxacin	Levoquin	—
Ofloxacin	Floxin	—
Roxithromycin	Rulide	—
Telithromycin	Ketek	—
Voraconizole	Vfend	—
Miscellaneous		
Octreotide	Sandostatin	Endocrine agent
Oxytocin	Pitocin	Oxytocic
Perflutren lipid microspheres	Definity	Imaging contrast agent
Ranolazine	Ranexa	Anti-anginal
Tizanidine	Zanaflex	Muscle relaxant
Vardenafil	Levitra	Phosphodiesterase inhibitor, vasodilator

Adapted from Arizona Center for Education and Research on Therapeutics (http://www.QTdrugs.org).[4]
HCTZ = hydrochlorothiazide; — = no specific comments.

Table 3.—Drugs That Prolong QT Interval and Can Cause Torsade de Pointes in Certain Circumstances

Agent	Brand name(s)	Comment
Miscellaneous		
Galantamine	Reminyl	Cholinesterase inhibitor for Alzheimer's disease
Solifenacin	Vesicare	Bladder overactivity treatment, muscarinic receptor antagonist
Anti-infectives		
Ciprofloxacin	Cipro	Drug–drug interaction, drug metabolism inhibitor
Fluconazole	Diflucon	Drug–drug interaction, drug metabolism inhibitor; increased QT at doses >800 mg/day
Itraconazole	Sporanox	Drug–drug interaction, drug metabolism inhibitor
Ketoconazole	Nizoral	Drug–drug interaction, drug metabolism inhibitor
Ritonavir	Norvir	Protease inhibitor HIV
Trimethoprim-sulfasoxazole	Septra; Bactrim	—
Antihistamine agents		
Dephenhydramine	Benadryl	Risk with overdosage
Psychotropic agents		
Amisulpride	Solian	Tricyclinc antidepressant (TCAD), risk with overdosage
Amitriptyline	Elavil	TCAD
Clomipramine	Anafranil	TCAD
Desipramine	Pertofrane	TCAD
Doxepin	Sinequan	TCAD
Fluoxetine	Prozac, Serafem	—
Imipramine	Norfranil	TCAD
Nortriptyline	Pamelor	TCAD
Paroxetine	Paxil	—
Protriptyline	Vivactil	TCAD
Sertraline	Zoloft	—
Trazodone	Desyrel	—
Trimepramine	Surmontil	TCAD

Adapted from Arizona Center for Education and Research on Therapeutics (http://www.QTdrugs.org).[4]
Antidepressants found to be associated with symptomatic QT prolongation include: amitriptyline, nortriptyline, doxepin, trazodone, venlafaxine, and fluoxetine. Lithium is associated with prolongation of QT interval. Concurrent administration of bupropion and venalfaxine can increase the latter's serum concentration by greater than 2-fold. The Food and Drug Administration has warned not to use citalopram in doses exceeding 40 mg a day because of QT interval changes associate with it. CYP2C19 inhibitors (omeprazole, esomeprazole, and oxcarbazepine) may raise the serum levels of citalopram when used in conjunction. Diphenhydramine may double venlafaxine concentrations when the 2 are used in conjunction.
— = no specific comments.

pressure, tachyarrhythmias, and abnormal ECG (PR prolongation, QTc prolongation [as noted], ST/T wave abnormalities, premature ventricular contractions, atrial flutter, or atrial fibrillation), and syncope. Rare were bradycardia, hypotension, and heart murmurs."[21]

The remaining triptans, rizatriptan, almotriptan, eletriptan, and frovatriptan do not list QTc prolongation in their prescribing information.[22-25] This may be due to differences in triptans or due to the rarity of the event. It is wise to remember the adage that absence of evidence is not evidence of absence.

As stated earlier, use of any of the triptans includes the potential for myocardial infarction and vasospastic vascular and cardiovascular events, including the last 4. Eletriptan has additional information in the prescribing information reading, "In a clinical pharmacology study, in subjects undergoing diagnostic coronary angiography, a subject with a history of angina, hypertension and hypercholesterolemia, receiving IV eletriptan (maximal serum concentration of 127 ng/mL equivalent to 60 mg oral eletriptan), reported chest tightness and experienced angiographically documented coronary vasospasm with no EKG changes of ischemia. There was also one report of atrial fibrillation in a patient with a past history of atrial fibrillation. Rare adverse events described with eletriptan were angina pectoris, arrhythmia, atrial fibrillation, AV block, bradycardia, hypotension, syncope, vasospasm and ventricular arrhythmia."[24]

The almotriptan prescribing information notes during the clinical trials, "one patient was hospitalized for observation after a scheduled EKG was found to be abnormal (negative T-waves on the left leads) 48 hours after taking a single 6.25 mg dose of almotriptan. The patient, a 48-year-old female, had previously taken 3 other doses for earlier migraine attacks. Myocardial enzymes at the time of the abnormal EKG were normal. The patient was diagnosed as having had myocardial ischemia, and she had a family history of coronary disease. An EKG performed

2 days later was normal, as was a follow-up coronary angiography. The patient recovered without incident.[23] Frovatriptan also lists abnormal EKG as an adverse event."[25]

In the patient who has the sensations of chest or neck tightness or palpations with triptan use, yet has no significant cardiac risk factors, the entire medication list needs to be taken into account and the possibility of triptan-induced vasospasm or arrhythmia considered. A potential intervention would be to perform an EKG or other minimally invasive test after triptan ingestion, or where available, use an ergonovine challenge. In cases of borderline cardiac risk, where formal functional testing is not warranted, an EKG performed prior to triptan use would provide baseline readings on the usual medications, including length of QTc, as well as provide some information on occult cardiac disease.

In general, resting EKGs have not been found to be cost-effective in asymptomatic individuals who lack cardiovascular risk factors. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines lists such screening as a class IIb recommendation and EKG screening in patients with hypertension or diabetes as a class IIA recommendation, both with class C level of evidence.[26] However, in light of the evidence that many of the medications used to treat headaches and commonly accompanying conditions increase the risk of EKG abnormalities, an EKG would seemingly be prudent in the presence of medications known to be associated with QTc prolongation, multiple medications, and/or risk factors.

CONCLUSIONS

Serotonergic medications and many headache medications prolong QTc and can interact to result in increased cardiac risks. Doxepin, amitriptyline, nortriptyline, trazodone, venlafaxine, lithium, amphetamines, traditional antihistamines, certain antinauseants, and fluoxetine are all associated with QTc prolongation.

Age and female gender increase the risk of TdP. Certain drug–drug interactions add to the risk, such as bupropion and venlafaxine, or bupropion and diphenhydramine.

Citalopram at doses of 40 mg and above appears to be particularly dangerous. Concurrent use of citalopram and CYP2C19 inhibitors such as omeprazole, esomeprazole, or oxcarbazepine, as well as the combination of citalopram and trazodone, all combine to increase QTc prolongation.

Verapamil, at doses of 240 mg and above, is associated with cardiac arrhythmias, heart block, and bradycardia.

In the patient with triptan sensations and no significant cardiac risk factors, the entire medication list needs to be taken into account and the possibility of triptan-induced vasospasm or arrhythmia considered. A potential intervention would be to perform an EKG or other minimally invasive test after triptan ingestion, or where available, use an ergonovine challenge.

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