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CARDIAC ARRHYTHMIAS CAUSED BY HYDROXYZINE USE

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ABSTRACT

Hydroxyzine, an H1 receptor antagonist, is a drug commonly used to treat anxiety, pruritus, urticaria or used during premedication before surgery. It was introduced to the market as early as the 1950s, but it was not until 2015 that a warning was issued regarding its potential to cause arrhythmias. This action is due to its effect on the transport of potassium ions through ion channels in myocardial cells, leading to a prolongation of the QT segment, which can contribute to torsade de pointes-type arrhythmias.

Numerous clinical cases of cardiac arrhythmias and QT prolongation following hydroxyzine use have been reported in the literature. This is most likely to occur in patients with comorbidities, genetic factors that prolong the QT segment, or those taking other drugs that can cause arrhythmias.

Meta-analyses of safety reports published by manufacturers of drugs containing hydroxyzine and non-clinical studies also provide information on the potential for cardiac torsade de pointes arrhythmias while taking hydroxyzine.

Therefore, it is extremely important to take a thorough patient history before initiating hydroxyzine treatment, to rule out risk factors for cardiac arrhythmias, and to assess the benefits and risks of the drug. This is particularly important in elderly patients and those suffering from multiple chronic diseases.

Extreme caution should also be exercised when administering hydroxyzine to patients in emergency conditions in a hospital emergency department setting or by emergency medical teams, when it may not be possible to establish an accurate history. Despite the high efficacy of hydroxyzine in both reducing symptoms of anxiety, pruritus and premedication preoperatively, the potential risk of cardiac arrhythmias in certain groups of patients should always be considered and the benefit/risk ratio assessed when including treatment.

KEYWORDS

Hydroxyzine, QT Segment, Torsade De Pointes, Arrhythmia

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Introduction

Hydroxyzine is one of the most widely used sedative drugs in clinical practice. The mechanism of action of hydroxyzine is probably related to the inhibition of the activity of centers in the subcortical layer of the central nervous system, but it does not inhibit the activity of the cerebral cortex. It reduces internal tension, anxiety, anxiety tension and muscle tension. In addition, it exhibits antihistaminic, cholinolytic, analgesic and antiemetic properties, so it is also used to treat pruritus or relieve symptoms of allergic reactions. In therapeutic doses, it does not increase secretion or lower the pH of gastric acid, and in most cases shows mild antisecretory effects.

Hydroxyzine is most often administered orally, in syrup or tablet form, but intramuscular administration is also acceptable in situations where oral administration is difficult. After oral administration, hydroxyzine begins to take effect after just 5-10 minutes in syrup form and 30-40 minutes for tablets. The effect lasts from 6 to 8 hours, the drug is metabolized in the liver (with the participation of alcohol dehydrogenase) and excreted from the body in the form of metabolites via the kidneys. Therefore, special care should be taken when using hydroxyzine in patients with renal and hepatic insufficiency.

The most common side effects of hydroxyzine include drowsiness, headache, dry mouth, confusion, nausea, dizziness or paradoxical agitation. One of the most significant side effects, the incidence of which has not yet been established, is ventricular arrhythmias (e.g., *torsade de pointes*) and QT interval prolongation.

In 2015, a safety communication for hydroxyzine was issued in all European Union countries, stating that its administration is contraindicated in patients with prolonged QT, both congenital and acquired, and who have risk factors for QT prolongation. Therefore, the communication makes it clear that hydroxyzine should not be combined with other drugs that cause QT prolongation, and an ECG should be performed before each

administration and a list of medications taken should be discussed with the patient. This causes problems mainly when hydroxyzine is administered in emergency situations, in the ED setting or by emergency medical teams.

Drug-induced QT interval prolongation is a significant risk factor for ventricular *arrhythmias*, including *torsade de pointes* tachycardia and sudden cardiac death. Due to the difficulty in unequivocally confirming the causal relationship between the use of a particular drug and the occurrence of arrhythmias, the length of the QT interval is often used as a proxy for arrhythmogenic risk

The mechanism of action of most QT-prolonging substances is based on influencing the flow of potassium ions through cell membrane channels or interfering with the transport and function of structural proteins of these channels. Improved knowledge of the structure and function of ion channels has led to a better understanding of the phenomena underlying drug-induced QT prolongation and related cardiac arrhythmias

Pharmacotherapy-induced arrhythmias are relatively rare clinical phenomena and usually require the presence of several comorbid risk factors. Among them are the simultaneous use of two or more drugs affecting the same electrophysiological pathway, electrolyte disturbances - especially hypokalemia - and genetic predisposition

The most important factors favoring the occurrence of drug-induced arrhythmias include female gender, the use of polypharmacotherapy including drugs that prolong the QT interval, adverse drug interactions resulting in impaired repolarization, electrolyte disturbances (hypokalemia, hypomagnesemia), bradycardia, organic heart disease and heart failure

Therefore, a thorough history should be taken before administering hydroxyzine, paying particular attention to medications used chronically and those the patient is taking on an ad hoc basis. Drugs that increase the risk of *torsade de pointes* in combination with hydroxyzine include digoxin, moxifloxacin, propafenone and flecainide. Concomitant use of hydroxyzine and clarithromycin, quetiapine, theophylline, papaverine or phenothiazide neuroleptics increases the risk of ventricular arrhythmias, and combination with amiodarone or haloperidol results in an increased risk of sudden cardiac death. On the other hand, when escitalopram or citalopram is used concomitantly with hydroxyzine, the side effects of both drugs have been shown to add up.

A number of clinical cases are also known in which the use of hydroxyzine has led to *torsade de pointes* arrhythmias and even sudden cardiac arrest.

Meta-analyses of safety reports provided by manufacturers of drugs containing hydroxyzine and non-clinical studies also provide information on the potential for cardiac *torsade de pointes* arrhythmias while taking hydroxyzine - the preparation affects the transport of potassium ions in the ion channels of the heart muscle, in effect prolonging the QT segment, resulting in an increased risk of arrhythmias.

Therefore, it is crucial to take a detailed patient history before starting hydroxyzine treatment. The presence of risk factors for cardiac arrhythmias should be ruled out, and a careful assessment of the benefit-to-potential risk ratio of the drug should be made. Particular attention should be paid to elderly patients and those with multiple comorbidities.

Increased caution is also recommended in emergency situations, especially in the hospital emergency department setting and in pre-hospital care, where taking a thorough history is sometimes impossible.

Despite the documented efficacy of hydroxyzine in the treatment of anxiety symptoms, pruritus and in preoperative premedication, in selected groups of patients it is always necessary to consider the risk of arrhythmia and make an informed therapeutic decision based on the analysis of benefits and risks.

The purpose of the above article is to provide an overview of the issues related to the effects of hydroxyzine on the risk of cardiac arrhythmias, particularly those of a *torsade de pointes* nature, as well as complications in the form of sudden cardiac death.

As a result, the work aims to make the audience aware of the potential risks of administering hydroxyzine, and to draw their attention to the importance of taking a proper history and making sure that there are no interactions of the drugs the patient is taking.

Methodology

An exhaustive review of the literature, meta-analyses on the topic described, and clinical case reports was conducted.

A review of scientific articles published and indexed in PubMed, an analysis of the specialized literature on the subject and clinical cases published in professional journals was conducted.

The published cases are from multiple countries and cover the adult population. Analyses of safety reports published by manufacturers of drugs containing hydroxyzine are also cited.

Discussion

A case of *torsade de pointes* after hydroxyzine administration in an 82-year-old female patient with atrioventricular block was described in 2021. The patient was admitted to the hospital because of dyspnea and bradycardia after exertion. The ECG performed showed complete atrioventricular block. During pacemaker implantation, the patient was given 12.5 mg of hydroxyzine intramuscularly for sedation. After administration of the drug, the patient developed *torsade de pointes* arrhythmia.

After the administration of hydroxyzine, a prolongation of the QT segment to 636 ms was observed, and the arrhythmia occurred after the R-on-T phenomenon (the occurrence of the R-wave near the T-wave in the ECG, which can lead to severe arrhythmias) was observed. This demonstrates the direct effect of hydroxyzine administration on the occurrence of arrhythmias. After the arrhythmia episode was controlled, the patient was discharged home and showed no symptoms in the following days.

The described case proves that special care should be taken when administering hydroxyzine during surgery, especially in patients who have bradycardia.

A similar case was reported in 2023. A 58-year-old man with a complex medical history was brought to the ED for shortness of breath and chest pain. The patient had a history of substance abuse and intoxication, including heroin, and suffered from multiple comorbidities: hypertension, heart failure with preserved ejection fraction, QT segment prolongation, and a history of *torsade de pointes* arrhythmia (status post implantation of a cardioverter-defibrillator). It was determined that the man was found by his family in a smoke-filled room.

The anesthesiology team assessed the patient's blood carbon monoxide concentration, with a result of 30%. Assessment of critical parameters showed an arterial pressure of 245/137 mm Hg, a pulse rate of 110 beats per minute, a respiratory rate of 23 per minute, a temperature of 36.6 degrees Celsius and a saturation of 100% with oxygen therapy using a reservoir mask. Analysis of laboratory results showed a COHb level of 4.1% in venous blood, a carbon monoxide level of 7.1%, a BNP of 489 pg/ml, an increase in troponin levels from 24 pg/ml to 114 pg/ml, a magnesium level of 1.7 mg/dL and a WBC of 12.4 thousand/ml.

A chest X-ray showed an implantable cardioverter-defibrillator (ICD) on the left side and increased bronchoscopy. An electrocardiogram (ECG) performed on admission showed sinus tachycardia, a prolonged QT segment of 484 ms, right atrial enlargement, left ventricular hypertrophy and q-wave changes in leads II, III and aVF, suggesting a history of myocardial infarction.

The patient was admitted to the cardiology department to stabilize his blood pressure. An intravenous infusion of nitroglycerin was administered to lower the pressure, after which the patient began to present symptoms of opioid withdrawal - sweating, nausea and anxiety. Symptoms were assessed by the clinical opioid withdrawal symptoms (COWS) scale and 8mg of buprenorphine was administered as prescribed. In addition, the patient was given clonidine, trimethobenzamide (with antiemetic effects) and 50mg of hydroxyzine. An ECG was performed again, noting a prolongation of the QT segment to 612ms.

Overnight, the patient developed *torsade de pointes* arrhythmia. A check of the ICD device was performed, which revealed 19 episodes of R on T phenomenon leading to arrhythmia. Two episodes were terminated by antitachyarrhythmic pacing (ATP), and the patient received a total of 17 defibrillation shocks.

150 mg of amiodarone was given as an intravenous bolus, and an amiodarone infusion was started; after persistent polymorphic ventricular tachycardia (VT), 100 mg of lidocaine was also given as an intravenous bolus and a lidocaine infusion was started. Due to persistent polymorphic VT, refractory to treatment with amiodarone and lidocaine, the decision was made to intubate and sedate the patient to control the arrhythmia. Sedation was performed with propofol and midazolam, and bolus fentanyl was also used for analgesia. Amiodarone and lidocaine infusions were gradually discontinued after the persistent VT subsided. The patient was extubated, and the ICD device was reprogrammed, setting the pacing rate to 75 beats per minute. Transthoracic echocardiography showed a left ventricular ejection fraction of 35-40%, a small pericardial effusion and mitral valve regurgitation. After the acute episode subsided and hemodynamic stabilization was achieved, the patient was discharged from the hospital with a recommendation for cardiac follow-up to determine further treatment.

The above case demonstrates the need for extreme caution when including QT prolonging drugs, including hydroxyzine. In each case, the benefit/risk ratio should be evaluated, electrolyte levels should be assessed in laboratory tests, and ECGs should be monitored several times to assess possible QT prolongation. In addition, the lowest effective dose of hydroxyzine should be used in patients with a history of arrhythmias.

The use of hydroxyzine and other QT prolonging drugs significantly increases the risk of arrhythmias, as evidenced by the case of a 65-year-old female patient treated with flecainide and hydroxyzine.

The patient was admitted to the hospital due to a feeling of palpitations and a sensation of shortness of breath, aggravated especially at night, and orthopnoe. An ECG showed atrial fibrillation (AF) with a rhythm of 137 beats per minute with narrow QRS complexes, without repolarization abnormalities. Transthoracic echocardiography showed normal left and right ventricular size and contractility, mild left atrial dilatation (44 mm) with no other significant abnormalities.

With treatment with anticoagulants and diuretics, the patient's condition was stabilized, satisfactory control of symptoms and spontaneous return of sinus rhythm were achieved. After the patient's condition was stabilized, treatment with 2.5mg of bisoprolol and 50mg of flecainide was started. During hospitalization, the patient reported symptoms of severe pruritus of the lower extremities, which required loratidine 10mg and hydroxyzine 25mg.

On the fourth day of concomitant administration of flecainide and H1 receptor antagonists (hydroxyzine and loratidine), the patient experienced sudden cardiac arrest due to QT prolongation and the development of *torsade de pointes* arrhythmia. The patient required defibrillation six times and intubation. Normal heart rhythm was restored after 15 minutes of resuscitation. A CT scan of the head showed no ischemic changes, and coronary angiography showed coronary lumen lesions. The patient was extubated after 72 hours and was discharged home in good condition, with a recommendation to take bisoprolol 2.5mg/12 hours. During the month after discharge, she reported no symptoms.

Concomitant administration of flecainide with H1 receptor antagonists results in a significant increase in the risk of QT prolongation, resulting in cardiac *torsade de pointes* arrhythmia.

The effect of hydroxyzine on QT prolongation is also confirmed by a meta-analysis by Schlitz et al. conducted in 2017. The authors took into account data made available by the manufacturer of hydroxyzine on the safety of the drug (*pharmacovigilance* reports) from 1955 to 2016, as well as non-clinical electrophysiological studies collected in scientific databases.

Between 1955 and 2016, a total of 59 adverse events involving QT prolongation or episodes of *torsade de pointes* were reported in patients using hydroxyzine. Except for cases of intentional overdose, all cases involved patients with other risk factors, such as the use of other QT prolonging drugs or the presence of comorbidities. The highest cumulative risk was found in patients with cardiovascular disease and concomitantly taking drugs with known QT prolongation potential.

In parallel, electrophysiological studies were conducted, which showed concentration-dependent inhibition by hydroxyzine of ion channels in myocardial cells, including potassium channels, resulting in QT segment prolongation. The results of the above analysis support the classification of hydroxyzine as a drug with the potential to induce cardiac *torsade de pointes* arrhythmias, and are consistent with recommendations to limit its use in patients with other arrhythmia risk factors.

The aforementioned impairment of ion channels was also evaluated in a study by Lee et al. back in 2011. In an in vitro study conducted on animal cells, they showed a significant prolongation of action potential duration after administration of hydroxyzine at concentrations of both 0.2 and 2 µmol/L. The prolongation of the action potential was dependent on both the concentration and duration of the drug. In addition, it was found that hydroxyzine affects both active and inactivated ion channels, but not closed ion channels. Hydroxyzine has also been shown to affect hERG ion channels, which, with a rare mutation in their structure, may be an additional risk factor for arrhythmias. Therefore, special attention should be paid to patients' genetic predisposition to QT prolongation before initiating hydroxyzine therapy.

Due to numerous cases of arrhythmias in patients using hydroxyzine, in 2015 the EMA issued a warning regarding hydroxyzine's potential to prolong the QT segment and induce *torsade de pointes*.

The published warning influenced the frequency of initiation of hydroxyzine therapy in many European countries and the UK.

A study by Morales et al. reported a significant decrease in initiation of hydroxyzine therapy in England and Scotland. Before the warning was issued, in the first quarter of 2009, hydroxyzine therapy was initiated in 91.5 patients per 100,000 in Scotland, while in England it was initiated in 35.9 patients per 100,000. After the warning was issued, these values dropped to 58.9/100,000 and 30.8/100,000 in 2018, respectively. There was also an increase in the number of hydroxyzine therapy discontinuations in England. However, similar changes were not observed in Denmark or the Netherlands. Hydroxyzine discontinuation was also not associated with a change in treatment to other antihistamines, benzodiazepines or antidepressants.

The study by Morrow et al. reports similar results obtained in the United Kingdom. During the year after the warning was issued, the number of patients starting hydroxyzine therapy dropped by 21% compared to before the warning was issued. No higher dropout rates were observed in patients with additional risk factors for QT prolongation or the development of cardiac arrhythmias. The study also reported statistics from Canada, but did not see a significant decrease in the number of cases of initiation of hydroxyzine treatment in that country.

Conclusions

Analysis of clinical cases and the available literature clearly indicates that one of the side effects of hydroxyzine is QT prolongation and the risk of inducing cardiac *torsade de pointes* arrhythmia.

Hydroxyzine is very commonly used in the relief of pruritus and urticaria symptoms, as premedication for surgical procedures and to relieve anxiety symptoms. It shows high efficacy, so it is used in both outpatient, inpatient and prehospital care. Despite its relatively good safety profile, one of the most important risks associated with the administration of hydroxyzine is its potential to induce cardiac arrhythmias.

Patients with other risk factors for QT prolongation, such as comorbidities, electrolyte abnormalities, advanced age or taking other drugs with arrhythmogenic potential, are particularly vulnerable to this complication. Drugs whose interactions increase the risk of *torsade de pointes* include digoxin, moxifloxacin, propafenone and flecainide in particular. The chance of ventricular arrhythmias is also increased when combined with clarithromycin, quetiapine, theophylline, papaverine or phenothiazide neuroleptics. Taking hydroxyzine concomitantly with amiodarone or haloperidol can, in turn, lead to sudden cardiac death.

Numerous cases of *torsade de pointes* following hydroxyzine use in patients at high risk for arrhythmias have been reported in the literature. In 2021, a case was described of a patient in whom administration of hydroxyzine 12.5mg as premedication preoperatively led to QT prolongation and *torsade de pointes*. The patient's diagnosed atrioventricular block and bradycardia were significant comorbidity risk factors.

In a case reported in 2023, administration of hydroxyzine led to sudden cardiac arrest in a patient treated for symptoms of withdrawal syndrome after opioid abuse. A dose of 50mg of hydroxyzine caused QT prolongation, against which a *torsade de pointes* heart rhythm disturbance developed. The patient required sedation to control the arrhythmia, but was discharged from the hospital in good general condition after a recovery period.

A similar case occurred in a patient, treated with flecainide, who developed urticaria symptoms during hospitalization for atrial fibrillation. To relieve pruritus, the patient received hydroxyzine and loratidine. On the fourth day of therapy, the patient developed QT prolongation, developed cardiac *torsade de pointes* arrhythmia, and eventually sudden cardiac arrest. The patient required defibrillation and intubation six times. After 72 hours, she was discharged home in overall good condition.

Cases of cardiac arrhythmias during hydroxyzine use have also been reported as side effects of the drug and included in safety reports published by manufacturers. Despite the fact that hydroxyzine has been in use for more than sixty years, by 2016 only 59 such events had been reported in safety reports. The actual number of cases of *torsade de pointes* following hydroxyzine use is certainly higher.

Therefore, it is of utmost importance to report all adverse reactions occurring after the administration of already registered drugs. This action will allow a better estimation of the incidence of most of them, and as a result will contribute to improving the safety of pharmacotherapy.

Hydroxyzine's potential to induce cardiac arrhythmias has also been demonstrated in non-clinical, *in vitro* studies. Hydroxyzine has been shown to have time- and concentration-dependent effects on the flow of potassium ions through ion channels in myocardial cells. It affects hERG channels in both active and inactivated forms, prolonging the duration of the action potential and, as a result, prolonging the QT segment, which can lead to the development of arrhythmias.

Despite numerous reports of hydroxyzine side effects, it was not until 2015 that the EMA issued a warning advising of the drug's possible induction of cardiac arrhythmias. [16] The issuance of the warning influenced clinical practice regarding the use of hydroxyzine. There was a clear downward trend in the number of patients starting hydroxyzine treatment in some European countries.

Despite this, hydroxyzine remains an effective drug with a relatively good safety profile that has a well-established place in clinical practice. In patients without comorbid risk factors, it remains the drug of first choice for the treatment of anxiety, pruritus and sleep disorders.

The above analysis of the literature and clinical cases underscores the important role of a detailed history in preventing serious complications of pharmacotherapy. Extreme caution should be exercised when including hydroxyzine in elderly patients and in situations where contraindications cannot be established.

In situations where there are contraindications to hydroxyzine, the benefit/risk ratio should be analyzed and alternative therapy should be considered. It is also extremely important to check the interaction of medications taken by the patient with hydroxyzine each time, due to the fact that the combination with many commonly used preparations can significantly increase the risk of adverse reactions and, in some cases, even sudden cardiac death.

It is also important to increase the knowledge of health care professionals about drugs that can cause cardiac arrhythmias. Informed and prudent selection of treatment according to a patient's medical history is a key element of safe pharmacotherapy and avoids numerous, often dangerous complications.

REFERENCES

- Summary of product characteristics: Hydroxyzinum Hasco 10mg, Hydroxyzinum Hasco 25mg.
- Drug database: Hydroxyzine. (2025, April 18). Retrieved from <http://www.mp.pl>
- Woroń, J., Drygalski, T., Lonc, T., Wordliczek, J., Gupało, J., Sanak, T., Putowski, M. (2024). Causes of drug complications in emergency medicine, practical aspects only - top 10. *Anesthesiology and Emergency Medicine*, 18, 147–153.
- Editorial. Woroń, J. (2023). Meanders of modern pharmacotherapy. *Medical Tribune Poland*.
- Editorial. Tyminski, R., & Woroń, J. (2020). Adverse drug interactions: Clinical and legal aspects. *Medical Tribune Poland, Warsaw*.
- Woroń, J., Siwek, M., & Wasik, A. (2019). *Drug interactions in psychiatry*. Asteriamed Gdansk.
- Kaski, J. C., & Kjeldsen, K. P. (Eds.). (2019). *The ESC handbook on cardiovascular pharmacotherapy*. Oxford University Press.
- Shear, N. H. (2023). *Drug Eruption & Reaction Manual*. CRC Press.
- Kaito, K., Akihiro, E., Nobuhide, W., Koichi, O., & Kazuaki, T. (2021). Hydroxyzine-induced Torsade de Pointes in a patient with complete atrioventricular block. *Internal Medicine*, 60(20), 3257–3260.
- Pitak, M. (2017, July 13). Ventricular arrhythmias part 2: ECG testing in pediatric practice. Indication, performance, and interpretation. Retrieved April 21, 2025, from <http://www.mp.pl>
- Afzal, M., Khalid, N., Abdullah, M., et al. (2023, July 9). Hydroxyzine-induced Torsade De Pointes: A case report and a literature review. *Cureus*, 15(7), e41588. <https://doi.org/10.7759/cureus.41588>
- Acosta-Materán, C., Díaz-Oliva, E., Fernández-Rodríguez, D., & Hernández-Afonso, J. (2016). QT interval prolongation and torsade de pointes: Synergistic effect of flecainide and H1 receptor antagonists. *Journal of Pharmacology and Pharmacotherapeutics*, 7(2), 102–105.
- Schlitt, A.-F., Delaunois, A., Colomar, A., Claudio, B., Cariolato, L., Boev, R., Valentin, J.-P., Peters, C., Sloan, V. S., Bentz, J. W. G. (2017). Risk of QT prolongation and torsade de pointes associated with exposure to hydroxyzine: Re-evaluation of an established drug. *Pharma Res Per*, 5(3), e00309. <https://doi.org/10.1002/prp2.309>
- Lee, B., Lee, S., Chu, D., et al. (2011). Effects of the histamine H1 receptor antagonist hydroxyzine on hERG K⁺ channels and cardiac action potential duration. *Acta Pharmacologica Sinica*, 32, 1128–1137. <https://doi.org/10.1038/aps.2011.66>
- Sakaguchi, T., Itoh, H., Ding, W. G., Tsuji, K., Nagaoka, I., Oka, Y., Ashihara, T., Ito, M., Yumoto, Y., Zenda, N., Higashi, Y., Takeyama, Y., Matsuura, H., & Horie, M. (2008). Hydroxyzine, a first-generation H1-receptor antagonist, inhibits human ether-a-go-go-related gene (HERG) current and causes syncope in a patient with the HERG mutation. *Journal of Pharmacological Sciences*, 108(4), 462–471. <https://doi.org/10.1254/jphs.08178FP>
- European Medicines Agency. (2015). New restrictions to minimize the risks of effects on heart rhythm with hydroxyzine-containing medicines. Retrieved April 23, 2025, from <https://www.ema.europa.eu>
- Morales, D. R., Macfarlane, T., MacDonald, T. M., et al. (2021). Impact of EMA regulatory label changes on hydroxyzine initiation, discontinuation, and switching to other medicines in Denmark, Scotland, England, and the Netherlands: An interrupted time series regression analysis. *Pharmacoepidemiology and Drug Safety*, 30, 482–491. <https://doi.org/10.1002/pds.5191>
- Morrow, R. L., Mintzes, B., & Souverein, P. C. (2022). Hydroxyzine initiation following drug safety advisories on cardiac arrhythmias in the UK and Canada: A longitudinal cohort study. *Drug Safety*, 45, 623–638. <https://doi.org/10.1007/s40264-022-01175-2>
- Perry, L. T., Bhasale, A., Fabbri, A., Lexchin, J., Puil, L., Joarder, M., et al. (2020). A descriptive analysis of medicines safety advisories issued by national medicines regulators in Australia, Canada, the United Kingdom, and the United States: 2007 to 2016. *Pharmacoepidemiology and Drug Safety*, 29(9), 1054–1063. <https://doi.org/10.1002/pds.5072>
- Davila, I., Sastre, J., Bartra, J., Del Cuvillo, A., Jáuregui, I., Montoro, J., et al. (2006). Effect of H1 antihistamines upon the cardiovascular system. *Journal of Investigational Allergology and Clinical Immunology*, 16(Suppl 1), 13–23.
- European Medicines Agency. (2015). PRAC recommends new measures to minimize known heart risks of hydroxyzine-containing medicines. Retrieved February 13, 2015, from http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2015/02/WC500182462.pdf
- Gintant, G. A., Su, Z., Martin, R. L., & Cox, B. F. (2006). Utility of hERG assays as surrogate markers of delayed cardiac repolarization and QT safety. *Toxicologic Pathology*, 34, 81–90.

23. Hancox, J. C., McPate, M. J., El Harchi, A., & Zhang, Y. H. (2008). The hERG potassium channel and hERG screening for drug-induced torsades de pointes. *Pharmacology & Therapeutics*, 119, 118–132.
24. Redfern, W., Carlsson, L., Davis, A., Lynch, W. G., MacKenzie, I., Palethorpe, S., et al. (2003). Relationships between preclinical cardiac electrophysiology, clinical QT interval prolongation, and torsade de pointes for a broad range of drugs: Evidence for a provisional safety margin in drug development. *Cardiovascular Research*, 58, 32–45.
25. Sakaguchi, T., Itoh, H., Ding, W. G., Tsuji, K., Nagaoka, I., Oka, Y., et al. (2008). Hydroxyzine, a first-generation H1-receptor antagonist, inhibits human ether-a-go-go-related gene (HERG) current and causes syncope in a patient with the HERG mutation. *Journal of Pharmacological Sciences*, 108, 462–471.
26. Vigne, J., Alexandre, J., Fobe, F., Milliez, P., Loilier, M., Fedrizzi, S., et al. (2015). QT prolongation induced by hydroxyzine: A pharmacovigilance case report. *European Journal of Clinical Pharmacology*, 71, 379–381.
27. Zeltser, D., Justo, D., Halkin, A., Prokhorov, V., Heller, K., Viskin, S. (2003). Torsade de pointes due to noncardiac drugs: Most patients have easily identifiable risk factors. *Medicine*, 82, 282–290.
28. Valentin, J. P., Pollard, C., Lainée, P., & Hammond, T. (2010). Value of non-clinical cardiac repolarization assays in supporting the discovery and development of safer medicines. *British Journal of Pharmacology*, 159, 25–33