Impact of Abnormal Electrolytes on Dofetilide (Tikosyn®) Initiation: A Pilot Study

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Background

- Dofetilide (Tikosyn®) is an antiarrhythmic medication commonly prescribed for supraventricular arrhythmias such as atrial fibrillation and atrial flutter
- Due to the risk of serious ventricular arrhythmias, the manufacturer requires dofetilide be initiated in a hospital setting and patients must be observed for a minimum of 3 days[1]
- The risk of ventricular arrhythmias increases if a patient has a prolonged QTc interval, severe renal impairment, low heart rate, or hypokalemia or hypomagnesemia
- Current practice at Mercy Hospital Springfield; pharmacists act as a double-check using process below

Pharmacist assess baseline labs and vitals → Relay abnormal findings to cardiologist → Cardiologist orders electrolyte replacement

- Previous research and anecdotal experience at this facility has shown this process of relaying electrolyte values can delay electrolyte replacement and potentially delay dofetilide administration, ultimately leading to hospital stays beyond the 72-hour observation period[4]
- Pharmacist managed programs for antibiotic dosing regimens, stress-ulcer prophylaxis protocols, and warfarin dosing services have been shown to improve clinical outcomes and patient safety[6,7,8]
- Pharmacist-driven antiarrhythmic drug protocols significantly improve adherence to recommended baseline monitoring parameters but no study to date has specifically assessed the impact of a pharmacist-managed electrolyte replacement for dofetilide initiation[2,3,5]

Objectives

Primary

Compare time from hospital admission to first dose of dofetilide in patients with normal electrolytes at baseline to those with abnormal electrolytes at baseline

Secondary

- Compare hospital length of stay of patients admitted for dofetilide treatment with normal electrolytes at baseline to those with abnormal electrolytes at baseline
- Compare the number of dofetilide doses received prior to discharge between patients with normal electrolytes and abnormal electrolytes at baseline
- Compare readmission rates of patients admitted for dofetilide treatment with normal electrolytes at baseline to those with abnormal electrolytes at baseline

Methods and Materials

Power: 44 patients in each group are needed to achieve 90% power. Alpha will be set at 0.05.

Design: Retrospective chart review of patients admitted for dofetilide initiation from January 1st, 2017, to January 1st, 2020.

Study Population:
- Control Group: Normal electrolytes level at baseline: potassium ≥4 mEq/L and magnesium ≥2 mg/dL
- Study Group: Abnormal electrolyte levels at baseline: potassium <4 mEq/L and/or magnesium <2 mg/dL

Inclusion Criteria: Adult patients with diagnosis of supraventricular arrhythmia admitted for initiation of dofetilide

Exclusion Criteria:
- Continuation of home dofetilide regimen
- QTc prolongation >440 msec at baseline
- Creatinine clearance <20 ml/min at baseline
- Heart rate <50 beats per minute at baseline

Results

- After review of 143 patient charts, 46 patients were eligible for study analysis
  - 24 patients had abnormal electrolytes at baseline and 22 patients had normal electrolytes at baseline
  - 97 patients were excluded, most commonly because of continuation of home dofetilide regimen
- Power was not met
- The primary outcome was not statistically significant (p=0.181)
- Only one patient in the study group was readmitted, no patient in the control group was readmitted

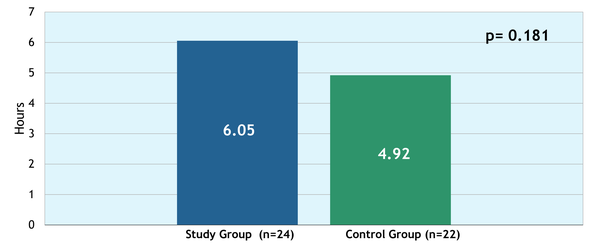

Figure 1: Average Time to First Dose of Dofetilide. On average, patients with abnormal electrolytes had an hour delay in time to the first dose compared to those with normal electrolyte levels at baseline.

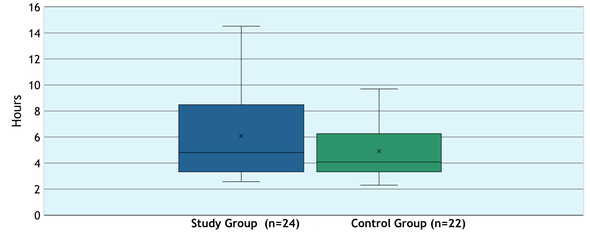

Figure 2: Number of Hours to First Dose of Dofetilide. The range of time to the first dose was longer in the study group (11.95 hours) compared to the control group (7.4 hours).

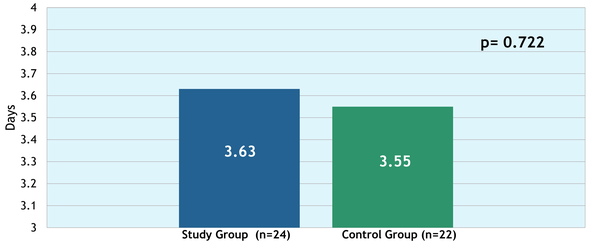

Figure 3: Average Hospital Length of Stay. The average hospital length of stay was similar between both groups.

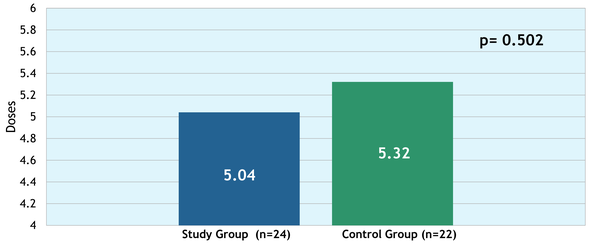

Figure 4: Average Number of Dofetilide Doses. The average number of dofetilide doses received prior to discharge was similar between both groups.

Discussion

The goal of this study was to determine if patients with abnormal baseline electrolytes have a delay in administration of the first dose of dofetilide when compared to patients with normal baseline electrolyte levels. The results did not show a significant difference between the two groups but did show that the study group had a slight delay in dofetilide initiation compared to the control group. Not meeting power leads to a risk for beta-error and with more patients in a larger study a significant difference may exist, so a chance of a significant difference cannot be ruled out. The results also indicated that the range of time to the first dose was wider in the study group vs the control group, which signifies the variability in how dofetilide is initiated and the need for standardization of this process.

Limitations
- Retrospective design limited ability to control variables
- Small sample size
- Study did not reach *a priori* power, leading to a beta error

Future Directions
- This study showed a trend towards slower time to initiation of dofetilide in study group indicating a need to change the current monitoring process for dofetilide initiation. As shown by the wide range in time to the first dose of dofetilide for the study group, some patients had long delays in initiation of dofetilide awaiting electrolyte replacement. This delay could be negatively impacting patient satisfaction with the management of their care.
- Development and implementation of an electrolyte replacement protocol allowing pharmacists to order potassium or magnesium supplementation for patients admitted for dofetilide initiation
- Evaluation of the effects of the pharmacist-driven protocol on decreasing time to first dose of dofetilide
  - Comparing patients with abnormal electrolytes after initiation of pharmacist-driven protocol to patients with abnormal electrolytes prior to protocol initiation

Conclusion

Because power was not met, there may be a significant difference in time to first dose of dofetilide in patients with abnormal electrolytes compared to those with normal electrolytes that was not identified with this study. While this study did not show that abnormal baseline electrolytes had a statistically significant impact on hospital length of stay or patient outcomes, it did show that the current monitoring process for dofetilide initiation at this institution can be improved to standardize how and when electrolytes are replaced. By standardizing electrolyte replacement, time to first dose of dofetilide will be consistent between patients and prevent the long delays some patients with abnormal electrolytes experienced. A pharmacist-driven protocol for electrolyte replacement in setting of dofetilide initiation would allow pharmacists to act as physician extenders, relieving the burden on the cardiology team and could provide standardization to this process.

Disclosures

The personnel involved in this study have nothing to disclose at this time.

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