Diphenhydramine Does Not Reduce Infusion-Related Ventricular Arrhythmias in Dogs Treated with Doxorubicin

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Introduction

Doxorubicin (DOX) is one of the most widely used and effective chemotherapy agents for treatment of canine lymphoma[1]. Cardiac side effects of DOX can be divided into those that are acute and chronic. For acute side effects, ventricular arrhythmias during or shortly after drug infusion are a significant concern[2].

Histamine levels have been shown to increase following DOX infusion, and are proposed to play a role in the acute side effect of arrhythmogenesis[3]. Many oncologists include diphenhydramine as an antihistamine premedication for dogs receiving DOX, although the efficacy has never been tested for the suppression of infusion-related arrhythmias. Randomized, prospective studies are needed to support the inclusion or exclusion of diphenhydramine in standard canine DOX-based chemotherapeutic protocols.

The objectives of this study are: 1. To evaluate the incidence and severity of DOX infusion related cardiac arrhythmias in clinical canine patients with lymphoma. 2. To evaluate the effect of diphenhydramine premedication on cardiac arrhythmia number and severity during and shortly after DOX infusion.

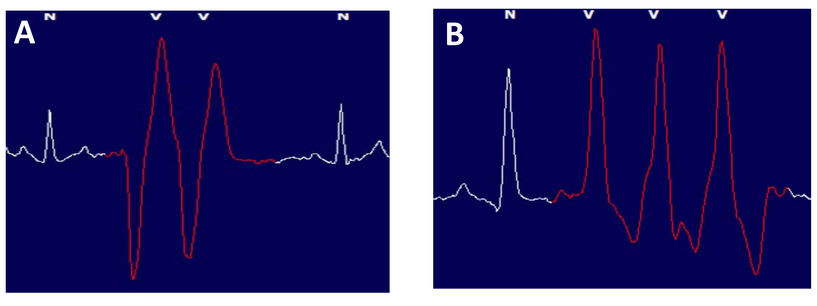
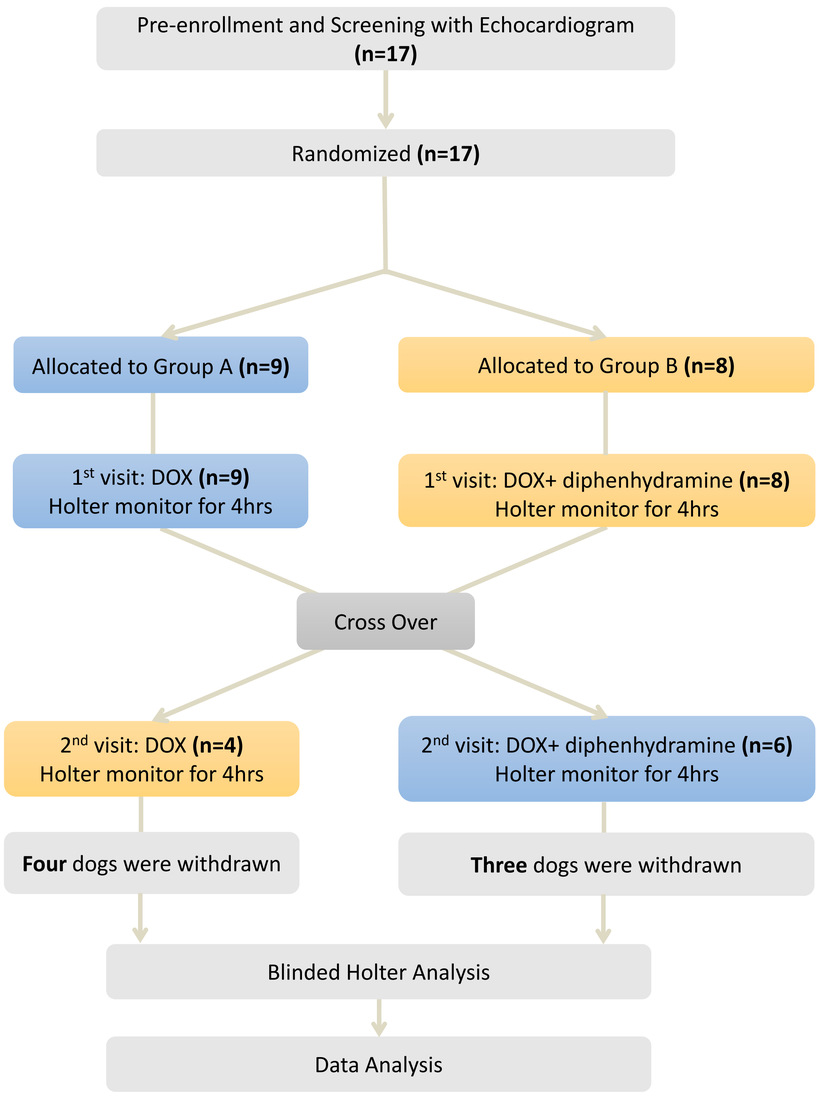


Figure 1: Holter data from Burdick Holter Analysis Software showing cardiac arrhythmias. A) Ventricular premature complex couplet; B) ventricular premature complex triplet.

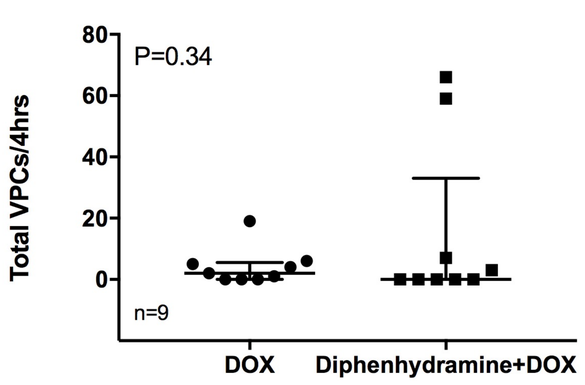
Hypothesis

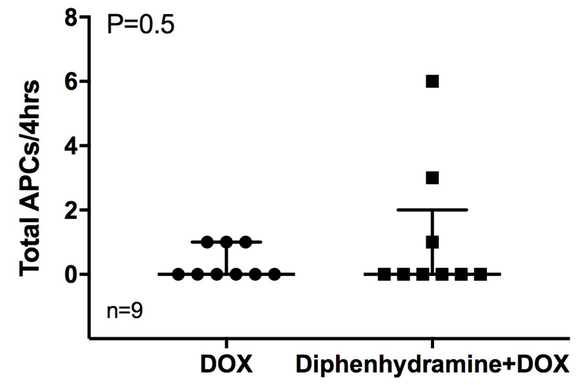
Diphenhydramine will **not impact** the number or severity of cardiac arrhythmias observed during DOX infusion in canine lymphoma patients.

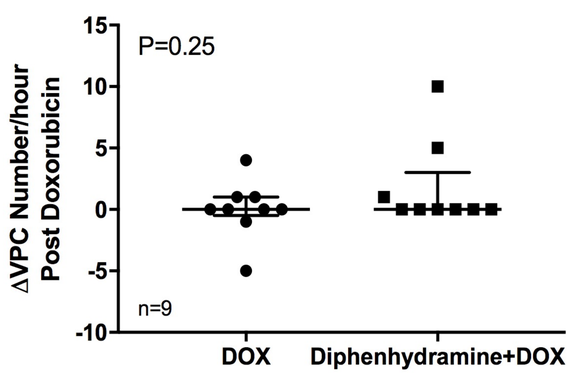
Materials & Methods

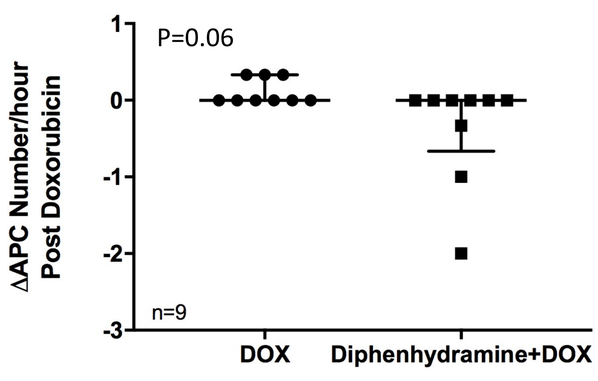


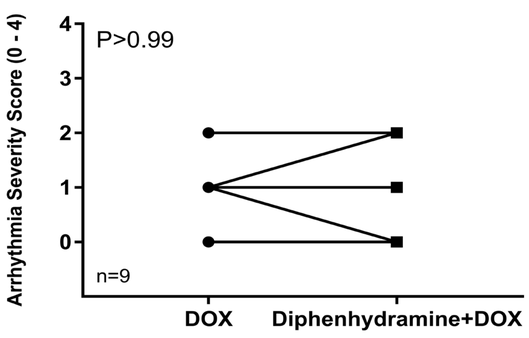
Results











- No significant differences were identified between the two treatments groups
- Post-hoc power analysis showed this experiment had a 90% power to detect a difference between pairs of 25 VPCs. This data supports that changes secondary to use of diphenhydramine in DOX protocols for treatment of lymphoma are likely clinically irrelevant for modulation of cardiac arrhythmogenesis.

Discussion

- Dox has been used for decades in canine lymphoma patients, yet the mechanism of acute arrhythmogenesis and how to best alleviate this side effect is incompletely understood. Our study demonstrates that in canine patients with appropriate pretreatment cardiovascular screening (echocardiogram and ECG), DOX infusion does not commonly induce acute, severe cardiac arrhythmias. Furthermore, these data support that the inclusion of diphenhydramine as a premedication for the acute cardiac effects of DOX has no appreciable benefit on arrhythmia number or severity.
- A potential next step for this study would be to analyze the histamine release pattern of canine patients receiving DOX with and without diphenhydramine. Perhaps significant histamine release is not routinely encountered in canine patients receiving DOX and diphenhydramine can be eliminated as a premedication.
- Care should be exercised when applying the data of this study to other patient populations. In particular, the study group had a relatively low number of total arrhythmias at baseline. This is likely due to the best practices screening protocol used in this study. In an environment where echocardiographic and electrocardiographic screening is not routinely performed prior to DOX administration, the findings may not be directly comparable.

References & Acknowledgements:

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