Research Article

Rate Control in Atrial Fibrillation by Cooling: Effect of Temperature on Dromotropy in Perfused Rabbit Hearts

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Background. Cooling has emerged as a therapeutic option in critically ill patients (especially after cardiac resuscitation) and might also have a negative dromotropic effect in atrial fibrillation. We sought to determine the impact of cooling on electrophysiologic properties of Langendorff-perfused rabbit hearts.

Methods and Results. In 20 isolated Langendorff-perfused rabbit hearts, the temperature of the tissue bath was changed between 17 and 42°C. With decreasing temperature, significant increases of the spontaneous sinus cycle length, decreases of the mean ventricular heart rate during atrial fibrillation, and relevant increases of atrial and ventricular refractory periods were observed (ANOVA P < .01).

Conclusions. Cardiac hypothermia leads to a significant drop of mean ventricular heart rate during atrial fibrillation. Negative chronotropy and dromotropy induced by moderate cardiac hypothermia might be a feasible therapeutic approach in patients with hemodynamically relevant tachyarrhythmias in a CCU/ICU setting.

1. Introduction

Therapeutic hypothermia has been used in survivors of cardiopulmonary resuscitation, patients with brain trauma and with acute myocardial infarction [1–3]. Mild systemic hypothermia might theoretically be used for rate control in critically ill patients with supraventricular tachycardias instead of or on top of drug therapy.

Many drugs with negative dromotropic effects also decrease left ventricular inotropy and are thus contraindicated in patients with significant heart failure and supraventricular tachycardias. In this animal study, we sought to investigate the effect of negative chronotropy and especially dromotropy in Langendorff-perfused rabbit hearts.

2. Materials and Methods

Animal care and euthanasia were performed according to the guidelines of the American Society of Physiology with institutional approval and permission of the competent authorities (Bezirksregierung Köln). Female New Zealand white rabbits aged 3–6 months were euthanized and the beating hearts removed. After cardioplegia, Langendorff-perfusion was performed in 20 isolated hearts. The tyrode used for perfusion consisted of 130 mM NaCl, 5.6 mM KCl, 24.2 mM NaHCO3, 2.2 mM CaCl2, 0.6 mM MgCl2, 1.2 mM NaH2PO4, and 12.2 mM glucose and was equilibrated with 95% O2 and 5% CO2.

Bipolar electrodes were positioned on the surface of right and left atrium and right ventricle. The temperature of tyrode and tissue bath was changed in 5-degree steps between 17 and 42°C (constant temperature Bath T1000, P.M. Tamson, Netherlands) (Figure 1).

The pacing threshold was determined at each temperature level. We measured the atrial and ventricular refractory period (AERP and VERP) by extrastimulus testing. The antegrade and retrograde Wenckebach periods (AWB and RWB) were determined by decremental pacing. Stimulation were performed at twice the pacing threshold. Atrial fibrillation was induced by continuous high-frequency burst stimulation with 100 ms. If atrial fibrillation could not be induced, it was simulated by continuous stimulation with...
100 ms. During atrial fibrillation, the mean ventricular heart rate was determined by averaging all cycle lengths during intervals of 30 sec.

2.1. Statistical Analysis. Results are presented as mean ± 1 standard deviation. Two-sided student’s t-test was used to compare spontaneous cycle length, refractory periods, AWB, RWB, and mean ventricular rate during atrial fibrillation. P values < .05 were considered significant.

3. Results and Discussion

3.1. Results. With decreasing temperature, significant increases of the spontaneous sinus cycle length, the mean ventricular heart rate during atrial fibrillation, and relevant increases of AERP, VERP, AWB, and RWB were observed (ANOVA P < .01).

At moderate hypothermia of 32°C, a 25–40% decrease of cardiac chronotropy and dromotropy could be obtained (Figures 2 and 3).

The effects of temperature on atrial and ventricular refractory periods as well as AWB and RWB are shown in Figure 4.

3.2. Discussion. The activity of biological tissue depends on its temperature. The rate of biological processes usually decreases by half to two-thirds with a decrease in temperature of 10°C [4].

Supraventricular tachycardias often complicate acute heart failure or sepsis in critically ill patients. The deleterious effect of tachycardia on cardiac output cannot be well addressed by pharmacological approaches as many drugs which exert significant negative dromotropic effects also decrease left ventricular inotropy and may decrease systemic vascular resistance.

Cardiac hypothermia has been used as a therapeutic option in patients after cardiac arrest and in patients with brain injury [1–3, 5, 6].

In our animal study, we have demonstrated a decline in ventricular heart rate of about 8% per degree C of cooling. A mild hypothermia of 32°C resulted in a significant decrease in ventricular heart rate from 267/min to 166/min (38%) during atrial fibrillation in this animal model. The spontaneous cycle length increased from 485 to 615 ms (27%) during mild hypothermia of 32°C. In addition, atrial and ventricular refractory periods increased significantly with a decrease in temperature. Appleton et al. studied cardiac electrophysiology properties in mice and used mild hypothermia (33-34°C) as well as hyperthermia [7]. The results of this in vivo mice study are congruent to our results with regard to refractory periods. Ventricular rate during atrial fibrillation, however, was not tested in the study by Appleton et al.
A high percentage of patients treated by mild hypothermia after resuscitation due to cardiac arrest suffer from acute myocardial infarction. Those patients are prone to develop arrhythmias including atrial fibrillation. The incidence of atrial fibrillation after cardiac arrest is around 15%, and atrial fibrillation is associated with a higher mortality rate [8, 9]. Hypothermia causes negative dromotropy and an increase in effective refractory periods. P < .05 for any temperature level.

4. Limitations

The results we obtained were from an isolated heart model, and no in vivo data are available. Data on repolarization, left ventricular refractory periods or inotropy were not gathered. Differences between human and rabbit electrophysiology may limit the applicability of the results of the study. Although we can only speculate on the effect of temperature. Hypothermia might reduce the ventricular rate during atrial fibrillation after resuscitation due to cardiac arrest. Hypothermia might reduce the ventricular rate during atrial fibrillation is associated with a higher mortality rate [8, 9].

5. Conclusions

Cardiac hypothermia induces a relevant decrease in ventricular heart rate during atrial fibrillation. Thus, moderate cardiac hypothermia might be used as a new therapeutic tool in critically ill patients nonresponding to electrical cardioversion or pharmacotherapy.

Conflict of Interest

The authors declared that there is no conflict of interests.

References

[1] S. A. Bernard, T. W. Gray, M. D. Buist et al., “Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia,” New England Journal of Medicine, vol. 346, no. 8, pp. 557–563, 2002.
[2] M. Holzer, F. Sterz, J. M. Darby et al., “Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest,” New England Journal of Medicine, vol. 346, no. 8, pp. 549–556, 2002.
[3] M. Holzer, “Targeted temperature management for comatose survivors of cardiac arrest,” The New England Journal of Medicine, vol. 363, no. 13, pp. 1256–1264, 2010.
[4] C. L. Prosser, “Temperature,” in Comparative Animal Physiology, Ed., C. L. Prosser, pp. 362–428, W.B. Saunders, Philadelphia, Pa, USA, 1973.
[5] R. J. Goldberg, D. Seeley, R. C. Becker et al., “Impact of atrial fibrillation on the in-hospital and long-term survival of patients with acute myocardial infarction: a community-wide perspective,” American Heart Journal, vol. 119, no. 5, pp. 996–1001, 1990.
[6] G. O. Appleton, Y. Li, G. E. Taffet et al., “Determinants of cardiac electrophysiological properties in mice,” Journal of Interventional Cardiac Electrophysiology, vol. 11, no. 1, pp. 5–14, 2004.
[7] R. J. Goldberg, D. Seeley, R. C. Becker et al., “Impact of atrial fibrillation on the in-hospital and long-term survival of patients with acute myocardial infarction: a community-wide perspective,” American Heart Journal, vol. 119, no. 5, pp. 996–1001, 1990.
[8] T. Sugita, T. Iwasaka, A. Ogawa et al., “Atrial fibrillation in acute myocardial infarction,” American Journal of Cardiology, vol. 56, no. 1, pp. 27–29, 1985.
[9] I. C. Van Gelder, H. F. Groenveld, H. J. G. M. Crijns et al., “Lenient versus strict rate control in patients with atrial fibrillation after resuscitation due to cardiac arrest is around 15%, and atrial fibrillation is associated with a higher mortality rate [8, 9]. Hypothermia might reduce the ventricular rate during atrial fibrillation is associated with a higher mortality rate [8, 9].

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fibrillation,” New England Journal of Medicine, vol. 362, no. 15, pp. 1363–1373, 2010.

[11] M. A. J. M. Huybregts, R. de Vroege, and W. van Oeveren, “A new system for right atrial cooling,” Annals of Thoracic Surgery, vol. 85, no. 4, pp. 1421–1424, 2008.

[12] N. Jost, J. G. Y. Papp, and A. Varró, “Slow delayed rectifier potassium current (I) and the repolarization reserve,” Annals of Noninvasive Electrocardiology, vol. 12, no. 1, pp. 64–78, 2007.

[13] A. O. Verkerk and R. Wilders, “Relative importance of funny current in human versus rabbit sinoatrial node,” Journal of Molecular and Cellular Cardiology, vol. 48, no. 4, pp. 799–801, 2010.