Lidocaine Does Not Affect Conducted Vasodilation in Humans

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Introduction
Rapid vasodilation is studied extensively in skeletal muscle contractions, and vasodilation responses resulting from the action of muscle contractions can be conducted via the microcirculation starting in the small arteries close to the capillaries and ascending into upstream feed arteries1,2,3. There are no current pharmacological tools that dependably block or attenuate vascular conducted responses in humans, but there is some evidence that propagated dilation was blocked by the local anesthetic lidocaine in animal studies4. If lidocaine can successfully block conducted dilation in humans, it could be used to address many issues related to skeletal muscle blood flow and metabolic control during exercise. This is significant because the mechanisms for skeletal muscle blood flow in response to exercise are poorly understood5. The aim of the study was to determine if lidocaine administration alters the vasodilator response to a brief forearm contraction. Three different doses of lidocaine at 1, 2, and 5 µg/100mL/min were infused into the brachial artery via a 20 ga catheter. A single muscle contraction (SMC) at 40% of maximum voluntary contraction (MVC) was performed and forearm blood flow (FFB) was determined from brachial artery diameter and mean blood velocity measured using Doppler ultrasound. Forearm vascular conductance (FVC) was calculated from blood flow (ml/min) and blood pressure (mmHg). Total vasodilator responses with and without lidocaine did not show any significant differences at any dose. Change (∆) in FVC with saline vs. 5 µg/100mL lidocaine infusion values (206 ± 33, 210 ± 27 ml/min/100mmHg)2, respectively) suggests that there was no significant change between differing drug doses.

Experimental Timeline

When a single contraction is performed using a handgrip dynamometer, the maximum voluntary contraction was performed using a handgrip device set to 40% of MVC. For each contraction at 40% of MVC, followed by 5 minutes of recovery. Doses were increased after each 5 minute session and repeated SMC.

Reference

Methods

- 10 healthy human participants between the ages of 18-40 years old who fasted for 4 hours prior to the study were instrumented with a 3-lead ECG to measure heart rate. A 20 ga catheter was placed in the brachial artery under asptic conditions for beat-by-beat blood arterial monitoring and drug infusions.
- A Doppler ultrasound image was taken of the brachial artery in the subject’s arms. Forearm volume was also measured via volume displacement and a maximum voluntary contraction was performed using a handgrip dynamometer.
- FBF was determined by measurements of brachial artery mean blood velocity (MBV) and vessel diameter. The echo-Doppler, a hand-held 10.5 MHz linear probe operating in B-mode, was positioned over the brachial artery and blood flow was calculated as FBF = MBV x r², where r is the vessel radius. FVC was then calculated as FVC = FBF/MBV x 100, expressed in ml/min/100mmHg.
- Forearm tissue volume (FAV) was used to determine the rate for drug infusion and a maximum voluntary contraction was performed using a handgrip dynamometer.
- Change in FVC after a brief SMC during sustained drug infusion was not significantly different between saline and lidocaine doses. Deltas were calculated by subtracting resting baseline FVC from post-contraction FVC.

Discussion
- There is a possibility that vasodilation occurs via the myogenic response of vascular smooth muscle or within the perivascular nerve plexus, but results do not lead to a definitive conclusion.
- Lidocaine as a pharmacological tool could potentially play a role in exploring skeletal muscle blood flow in response to exercise, but the mechanisms for this are poorly understood4.
- Exercise hyperemia in conjunction with the drug lidocaine may not be the answer in order to see the effects of vasodilation in human subjects.
- The vasodilator responses to exercise during lidocaine and saline infusion were not similar to the animal model findings and should be investigated further to make any conclusions6.

Conclusions
- Rapid dilation is not blocked or attenuated by lidocaine in humans and further studies are needed to understand regulation of skeletal muscle blood flow.

Acknowledgements
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Acknowledgements

References

Hemodynamic Responses

<table>
<thead>
<tr>
<th></th>
<th>Saline (µg/dL)</th>
<th>Lidocaine 1 (µg/dL)</th>
<th>Lidocaine 2 (µg/dL)</th>
<th>Lidocaine 5 (µg/dL)</th>
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<tbody>
<tr>
<td>Baseline</td>
<td>52.09 ± 9.57</td>
<td>40.00 ± 4.58</td>
<td>45.83 ± 3.97</td>
<td>43.02 ± 3.41</td>
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<td>Peak</td>
<td>258.1 ± 41.59</td>
<td>223.0 ± 25.67</td>
<td>269.6 ± 37.37</td>
<td>259.2 ± 28.02</td>
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<tr>
<td>FVC</td>
<td>206.0 ± 33.49</td>
<td>183.0</td>
<td>223.8 ± 34.5</td>
<td>209.8 ± 26.57</td>
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<tr>
<td>Area under the Curve (AUC)</td>
<td>5820 ± 1110</td>
<td>4933 ± 580</td>
<td>6116 ± 1055</td>
<td>4821 ± 512</td>
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</tbody>
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Table 1. Values are means ± SEM for all 10 subjects. Lidocaine administration had no statistically significant effects on FVC or FBF during exercise.
Methods

Healthy human participants between the ages of 18-40 years old who fasted for 4 hours prior to the study were instrumented with a 3-lead ECG to measure heart rate. A brachial artery catheter was placed under aseptic conditions for beat-by-beat blood arterial monitoring and drug infusions.

A Doppler ultrasound image was taken of the brachial artery in the subjects’ arms. Forearm volume was also measured via volume displacement and a maximum voluntary contraction was performed using a handgrip dynamometer.

Forearm blood flow (FBF) was determined by measurements of brachial artery mean blood velocity (MBV) and vessel diameter. The echo-Doppler, a hand-held 10.5 MHz linear probe operating in B-mode, was positioned over the brachial artery and blood flow was calculated as $\text{FBF} = \text{MBV} \times \pi \times r^2$, where $r$ is the vessel radius. Forearm vascular conductance (FVC) was then calculated as $\text{FVC} = \frac{\text{FBF}}{\text{MAP}} \times 100$, expressed in mL/min/100mmHg.

Forearm tissue volume (FAV) was used to determine the rate for drug infusion for saline and lidocaine. Subjects performed a single 1 second contraction at 40% of MVC three times over the study period with 5 minutes of rest between the respective lidocaine infusions of 1, 2, and 5 $\mu$g/100mL (Figure 3).

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