Modulation of temperature-induced tone by vasoconstrictor agents

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Masset, Michael P., Stephen J. Lewis, James N. Bates, and Kevin C. Kregel. Modulation of temperature-induced tone by vasoconstrictor agents. J. Appl. Physiol. 86(3): 963–969, 1999.—One of the primary cardiovascular adjustments to hyperthermia is a sympathetically mediated increase in vascular resistance in the viscera. Nonneural factors such as a change in vascular tone or reactivity may also contribute to this response. Therefore, the aim of this study was to determine whether vascular smooth muscle tone is altered during heating to physiologically relevant temperatures (>37°C). Gradually increasing bath temperature from 37°C (normothermia) to 43°C (severe hyperthermia) produced graded contractions in vascular ring segments from rat mesenteric arteries and thoracic aortae. In untreated rings these contractions were relatively small, whereas hyperthermia elicited near-maximal increases in tension when rings were constricted with phenylephrine or KCl before heating. In phenylephrine-treated mesenteric arterial rings, the contractile responses to heating were markedly attenuated by the Ca2+ channel antagonists nifedipine and diltiazem. Diltiazem also blocked the contractile responses to heating in thoracic aortic rings. These results demonstrate that hyperthermia has a limited effect on tension generation in rat vascular smooth muscle in the absence of vascular tone. However, in the presence of agonist-induced tone, tension generation during heating is markedly enhanced and dependent on extracellular Ca2+. In conclusion, these data suggest that local regulation of vascular tone can contribute to the hemodynamic adjustments to hyperthermia.

VASOCONSTRICTION in the splanchnic region is a crucial hemodynamic adjustment during hyperthermia in the rat (9, 10). Preventing this adjustment alters the arterial blood pressure response to heating and hastens the onset of circulatory failure due to hyperthermia (9). The majority of the cardiovascular adjustments to heating are mediated by the sympathetic nervous system. However, neither celiac ganglionectomy nor adrenal demedullation completely abolishes the increase in mesenteric resistance and arterial blood pressure that occurs during hyperthermia (9), suggesting that nonneural factors may also play a role in mediating this response. One factor that may contribute to the vasoconstrictor response observed after removal of sympathetic innervation to the region is a temperature-induced change in vascular smooth muscle tone. In isolated venous tissue, Cooke et al. (1) demonstrated that heating increases isometric tension in unstimulated vascular smooth muscle. Moreover, Winqvist and Bevan (26) reported that stretch-dependent myogenic tone in rabbit facial veins is augmented during heating, suggesting that the contractile process in smooth muscle is thermosensitive. During heating, this temperature-induced change in vascular tone may be enhanced by the presence of circulating catecholamines and locally released endothelium-derived constricting factors. Therefore, the vasoconstrictor response observed after removal of sympathetic innervation to the region may be due to an interaction between the remaining systemic and local vasoconstrictor stimuli and the temperature dependence of vascular tone, comparable to the effect of cooling on vascular smooth muscle observed in vivo and in vitro (20).

A temperature-induced change in vascular tone is an important feature of the thermoregulatory responses to cooling (20). Systemic or local cooling of dog cutaneous veins has only a small effect on perfusion pressure or vascular tone in the absence of sympathetic innervation (23–25). However, decreasing temperature during sustained contractions induced by electrical stimulation or exogenous norepinephrine elicits marked vasoconstriction (23–25), which is frequency or concentration dependent (21, 22). A similar change in contractility may occur during hyperthermia, but the effect of physiologically relevant increases in temperature on vascular tone and reactivity has not been clearly established. On the basis of the vasoconstrictor response observed in the splanchnic region during heating in vivo (10, 12), it is tenable to postulate that tension generated during a sustained contraction in the mesenteric artery is enhanced by heating. This postulate is consistent with the reported effects of heating on vasoconstrictor responses in the rat thoracic aorta (8, 16). Therefore, we hypothesized that heating would elicit an increase in isometric tension in rat mesenteric arterial and thoracic aortic rings and that this contraction would be enhanced in rings constricted with an adrenergic agonist before heating. To test this hypothesis, isometric tension was recorded in untreated or phenylephrine (PE)-treated vascular rings from rat mesenteric arteries and thoracic aortae during heating from 37°C (normothermia) to 43°C (severe hyperthermia). Pharmacological blockade of voltage-sensitive Ca2+ channels was used to assess the role of Ca2+ in the responses to heating.

METHODS

Male Sprague-Dawley rats (Harlan Laboratories, Indianapolis, IN) weighing 300–350 g were housed in individual...
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cages on a 12:12-h light-dark schedule and allowed standard rat chow and water ad libitum before experimentation. Experiments were performed in accordance with guidelines approved by the Institutional Animal Use and Care Committee.

Rats were anesthetized with an intraperitoneal injection of pentobarbital sodium (50 mg/kg ip) and exsanguinated. The thoracic aorta (TA) and a proximal segment of the superior mesenteric artery (SMA) were excised, placed in ice-cold (4°C) physiological saline solution (PSS), cleaned of fat and connective tissue under a stereomicroscope, and cut into 2.5-mm-long rings.

Segments were mounted on two stainless steel triangles and suspended horizontally between a Grass force-displacement transducer (Grass Instrument, Quincy, MA) and a fixed support. Each ring was placed in an organ chamber filled with 25 ml of oxygenated (95% O2-5% CO2) PSS, stretched to 1.0 g of tension for SMA and TA, respectively, and allowed to equilibrate for 45 min at 37°C. These resting tensions were considered to be optimal for force generation on the basis of the results of preliminary experiments in which a separate group of rings was used. The output from the force transducer was passed through a signal conditioner (model B434C, University of Iowa, Bioengineering Resource Facility), and tension (mg) was recorded on a chart recorder (Gould, Cleveland, OH).

Before each experiment, smooth muscle function and endothelial cell integrity were determined in each ring. Contractile responses to 30 mM KCl were used to assess vascular smooth muscle function, whereas relaxation responses to Ach (10⁻⁶ M) in rings preconstricted with PE (10⁻⁷ M) were used to test endothelial integrity. Rings were washed several times after smooth muscle and endothelium tests, then allowed to equilibrate at resting tension for 15–20 min before one of the experimental protocols was started.

Effect of heating. To determine the effect of increasing temperature on vascular tone, untreated control rings were stretched to the appropriate tension and allowed to equilibrate for 15 min. Bath temperature was then increased in 2°C increments to 43°C. After each 2°C increase in bath temperature, rings were allowed to stabilize for 10 min at that temperature. In preliminary experiments, contractile responses to heating plateaued by the end of each 10-min period. To determine the effect of α-adrenergic agonists on the contractile responses to heating, separate groups of vascular ring segments were preconstricted with a half-concentration of PE (10⁻⁷ and 3 × 10⁻⁸ M for SMA and TA, respectively) eliciting ~30–40% of maximal contraction before bath temperature was increased. Additional groups of rings were preconstricted with KCl (10–20 mM) to determine whether the contractile responses to heating were agent specific. This heating protocol was used in all the experimental interventions.

Endothelium removal and the responses to heating. To address the role of the endothelium in changes in vascular responsiveness during heating, the experimental protocol outlined above was repeated using vascular rings pretreated with the nitric oxide synthase inhibitor N⁵-nitro-L-arginine methyl ester (L-NAME, 10⁻⁵ M) or after removal of the endothelium by gently rubbing the luminal surface of the rings with a fine wire. Nitric oxide synthase blockade and endothelium denudation were considered complete if the relaxation responses to Ach (10⁻⁶ M) in PE-constricted rings were <5% of maximal. L-NAME was added to the organ chamber bath 20 min before preconstriction with PE.

Effect of Ca²⁺ channel antagonists on the responses to heating. The voltage-sensitive Ca²⁺ channel antagonists nifedipine (10⁻⁵ M), diltiazem (10⁻⁴ M), and verapamil (10⁻⁴ M) were used to determine the role of Ca²⁺ influx on the contractile responses to heating in PE-treated rings. After vascular ring segments were preconstricted with a half-maximal dose of PE, one Ca²⁺ channel inhibitor was added to each bath and tension was allowed to stabilize. When tension was stable, bath temperature was increased to 43°C as outlined above. KCl (30 mM) was added to the bath at the end of the heating protocol to verify channel blockade. Antagonists were administered after constriction with PE to better approximate the level of preconstriction tension in rings used in previous experiments that were treated with PE only.

Effect of removing extracellular Ca²⁺ on the responses to heating. Variable responses to the Ca²⁺ channel antagonists were obtained in rings from the thoracic aorta; therefore, additional experiments were conducted to assess the role of extracellular Ca²⁺ on the responses to heating. Before heating, thoracic aortic rings were incubated for 15 min in a Ca²⁺-free PSS with 2.0 mM EGTA (see Drugs and solutions) and then constricted with PE (10⁻⁴ M). The contraction to PE in a Ca²⁺-free PSS is due to intracellular release of Ca²⁺ only. Therefore, responses were somewhat attenuated. After responses plateaued, rings were heated as outlined above.

Effect of caffeine and ryanodine on temperature- and KCl-induced tone. Experiments were conducted in separate groups of vascular rings to address the importance of intracellular Ca²⁺ on the contractile responses to increasing temperature. Thirty minutes before preconstriction with KCl, rings were washed and incubated in normal PSS containing caffeine (20 mM) and ryanodine (10⁻⁵ M) to release and prevent the uptake and storage of intracellular Ca²⁺. After the constrictor responses to KCl (60–80 mM) plateaued, rings were heated to 43°C. Rings were constricted with KCl in this protocol, because application of PE under these conditions yielded only a minimal contraction. Caffeine and ryanodine were present in the organ chamber bath throughout the experiment.

Drugs and solutions. The normal PSS contained (in mM) 118.3 NaCl, 24 NaHCO₃, 4.7 KCl, 1.2 MgSO₄, 1.2 KH₂PO₄, 1.9 CaCl₂, and 11.1 glucose. In the Ca²⁺-free PSS, EGTA was substituted for CaCl₂, and all other components remained the same as in normal PSS. Nifedipine and verapamil were dissolved in ethanol (0.1% of total volume) and diluted with distilled water. Ethanol vehicle had no effect on tension generation in vascular rings in this preparation. All other drugs were dissolved in distilled water. All chemicals were purchased from Sigma Chemical (St. Louis, MO).

Data analysis and statistics. Values are means ± SE. The contractile responses to heating are expressed in milligrams of tension and were compared by repeated-measures ANOVA followed by a modified Student’s t-test with a Bonferroni correction for multiple comparisons. Linear regression analysis was also used to describe the changes in tension across temperatures as a means for correcting for any differences in baseline tension. A one-way ANOVA was used to compare slope and intercept data across agents. Paired t-tests were used to compare values for intact and denuded rings within each group. Statistical significance was set at P < 0.05.

RESULTS

Effect of heating. A representative response to heating in untreated control and PE-treated mesenteric arterial rings is presented in Fig. 1. In control rings, increasing bath temperature from 37 to 43°C significantly increased tension in rings from both vessels, indicating that heating can stimulate tension generation. However, the responses to heating were minimal (Fig. 2, Table 1). In mesenteric rings, tension increased...
93–190 mg above control by 43°C, whereas thoracic aortic rings generated 184–383 mg of tension during heating. The responses to heating were markedly enhanced in rings contracted with PE or KCl before heating. Baseline tension (tension after preconstriction) was 625–975 mg in PE- and KCl-treated mesenteric arterial rings. Heating increased tension in these rings to maximal values of ~1,400–1,900 mg. In thoracic aortic rings preconstricted with PE or KCl, heating increased tension from baseline levels of 550–1,200 to 2,000–2,800 mg. The responses in preconstricted rings were significantly greater at all temperatures than in untreated control rings.

The relationship between increasing temperature and the change in tension was also assessed using linear regression analysis. Slopes are presented in Table 1. PE- and KCl-treated mesenteric arterial rings had significantly steeper slopes than untreated rings. The changes in tension per degree centigrade were also smaller in untreated rings from the thoracic aorta than in rings that were preconstricted with PE or KCl before heating (Table 1).

Role of the endothelium. To determine whether endothelial factors modulate the response to heating, experiments were conducted in rings after endothelium removal or treatment with the nitric oxide synthase inhibitor L-NAME. Removal of the endothelium or treatment with L-NAME did not significantly alter the contractile responses to heating in rings from the mesenteric artery (Fig. 3), although responses tended to be greater in denuded than in intact KCl-treated rings. In contrast, heating-induced constriction was potentiated in denuded thoracic aortic rings from control and KCl-treated groups (Fig. 4). Removal of the endothelium or treatment with L-NAME in rings preconstricted with PE did not significantly alter the contractile responses to heating. Slopes were not altered after endothelium removal or L-NAME treatment for any group of rings.

Effect of Ca\(^{2+}\) channel antagonism on the responses to heating. Because \(\alpha\)-adrenoceptor agonists and KCl can stimulate Ca\(^{2+}\) influx through voltage-sensitive Ca\(^{2+}\) channels (6, 13, 15), a separate group of PE-treated rings was treated with one of three voltage-sensitive Ca\(^{2+}\) channel antagonists before heating. Nifedipine treatment significantly attenuated the contractile response to heating in mesenteric arterial rings (Fig. 5). These rings generated less tension and the rate of change in tension during heating was smaller than in PE- and KCl-treated rings from the same vessel (Table 1). Although the slight difference in tension between control and nifedipine-treated rings was maintained throughout heating, the maximal response to heating (Table 1) and the slopes were comparable, suggesting that the difference in baseline tension did not affect the response to heating. Similarly, verapamil and diltiazem blocked the contractile responses to heating in PE-treated rings from the mesenteric artery (data not shown). Slope and intercept values were also comparable to untreated and nifedipine-treated rings and significantly different from PE-treated rings (Table 1).

Unlike responses in the mesenteric artery, the voltage-sensitive Ca\(^{2+}\) channel antagonist nifedipine did not affect the contractile responses to heating in PE-treated rings from the thoracic aorta (Fig. 5, Table 1). Maximal tension generated and the rate of change in tension with increasing temperature were similar to values in PE- and KCl-treated rings. Likewise, verapa-
endothelium-intact and -denuded or L-NAME-treated rings in any untreated (control) or treated with PE (10 M). Heating increased tension in all rings. Tension in untreated rings was significantly less than tension in preconstricted rings at all temperatures (P < 0.05). There was no significant difference between endothelium-intact and -denuded or L-NAME-treated rings in any group. Table 1. Slopes and maximal changes in tension during heating from 37 to 43°C for mesenteric arterial and thoracic aortic rings from male Sprague-Dawley rats

<table>
<thead>
<tr>
<th></th>
<th>Mesenteric Artery</th>
<th>Thoracic Aorta</th>
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<tr>
<td></td>
<td>Slope, mg°C</td>
<td>Δ Tension, mg</td>
</tr>
<tr>
<td>Control Intact</td>
<td>16.2 ± 1.9</td>
<td>93 ± 12</td>
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<tr>
<td>KCl</td>
<td>175.3 ± 19.4*</td>
<td>1,063 ± 111*</td>
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<tr>
<td>+ Caffeine-ryanodine</td>
<td>67.4 ± 12.7†‡</td>
<td>396 ± 79†‡</td>
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<tr>
<td>PE</td>
<td>133.0 ± 11.5*</td>
<td>803 ± 67*</td>
</tr>
<tr>
<td>+ l-NAME</td>
<td>133.2 ± 16.5*</td>
<td>807 ± 101*</td>
</tr>
<tr>
<td>+ No Ca²⁺</td>
<td>38.6 ± 10.6†‡</td>
<td>225 ± 63†‡</td>
</tr>
<tr>
<td>+ Nifedipine</td>
<td>45.0 ± 7.1†‡</td>
<td>267 ± 43†‡</td>
</tr>
<tr>
<td>+ Diltiazem</td>
<td>41.5 ± 8.0†‡</td>
<td>247 ± 47†‡</td>
</tr>
<tr>
<td>+ Verapamil</td>
<td>33.6* 1,280</td>
<td>29.7* 1,449</td>
</tr>
<tr>
<td>Control Denuded</td>
<td>30.3 ± 6.2</td>
<td>190 ± 40§</td>
</tr>
<tr>
<td>PE</td>
<td>167.0 ± 20.3†</td>
<td>1,002 ± 124†</td>
</tr>
<tr>
<td>+ l-NAME</td>
<td>160.5 ± 21.0*</td>
<td>580 ± 121*</td>
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Values are means ± SE. Rings were untreated (Control) or treated with phenylephrine (PE) or KCl before heating. L-NAME, N⁶-nitro-L-arginine methyl ester; + no Ca²⁺, rings treated with PE in Ca²⁺-free physiological saline solution. *P < 0.05 compared with endothelium-matched control; †P < 0.05 compared with endothelium-matched PE; ‡P < 0.05 compared with endothelium-matched KCl; §P < 0.05 compared with agent-matched intact. Number of preparations for each condition is indicated in Figs. 1–5.

mil did not block the potentiating effect of PE on the contractile responses to heating. These responses were, however, significantly attenuated by diltiazem (Fig. 5, Table 1). Although the slope was threefold higher for diltiazem-treated rings, it was not significantly different from the value for untreated rings. The lack of an effect of nifedipine on the thoracic aorta was unexpected; however, differences in sensitivity to nifedipine have been demonstrated between the mesenteric artery and the thoracic aorta (3).

Role of extracellular Ca²⁺ in the contractile responses to heating. Additional experiments using Ca²⁺-free PSS were conducted in rings from the thoracic aorta because of the inconsistent results obtained with the Ca²⁺ channel antagonists. Removing extracellular Ca²⁺ attenuated the contractile response to a single dose of PE at 37°C. Baseline tension was 183.3 ± 22.2 mg in thoracic aortic rings constricted with PE in Ca²⁺-free PSS compared with 635.8 ± 87.5 mg in rings preconstricted with PE in normal PSS. Heating-induced vascular constriction was also significantly blunted after Ca²⁺ removal (Fig. 5). The magnitude and pattern of the responses in these rings were comparable to those in untreated rings (Fig. 5, Table 1).

Effect of caffeine and ryanodine on temperature- and KCl-induced tone. Caffeine and ryanodine were utilized to assess the role of intracellular Ca²⁺ on temperature-induced tone in KCl-treated vascular rings. Addition of caffeine and ryanodine to the organ chamber bath caused a transient constriction in rings from both vessels, indicating that Ca²⁺ had been released from intracellular stores. Because this treatment virtually eliminated the constrictor response to PE, these rings were constricted with KCl. For vascular segments from the mesenteric artery, tension was greater at all temperatures in caffeine-and-ryanodine-treated rings than in untreated control rings (Fig. 5). However, the slope...
was not statistically different from untreated rings, despite being approximately fourfold greater (Table 1). Regression coefficients were also similar to those for PE-treated rings, but contractile responses were significantly less than those in PE-treated rings at all temperatures. Reduction of intracellular Ca\(^{2+}\) had a small, but significant, effect on the contractile responses during heating in thoracic aortic rings (Fig. 5). Tension generated in caffeine-and-ryanodine-treated rings was significantly lower at 41 and 43°C than in PE- and KCl-treated rings. Slope and intercept values were also smaller in rings treated with caffeine and ryanodine than in those treated with KCl (Table 1).

**DISCUSSION**

The purpose of this study was to determine whether heating could augment vascular tone in rat mesenteric arteries and thoracic aortae. The results of these experiments indicate that raising bath temperature from 37 to 43°C increases isometric tension in both vessels. However, this heating-induced tension generation is dependent on the presence of active vascular tone, as evidenced by the observation that changes in tension in untreated rings were relatively small compared with those contracted with KCl or PE before heating. The augmented responses in PE-treated rings are primarily due to an increase in Ca\(^{2+}\) influx through voltage-sensitive Ca\(^{2+}\) channels and are independent of receptor activation, inasmuch as responses to heating in KCl- and PE-treated rings were comparable.

The temperatures utilized in this study (37–43°C) were chosen to include body temperatures experienced during passive or exertional heating under physiological or pathophysiological conditions. For example, body temperatures can exceed 40°C in exercising rats (7), whereas body temperatures in excess of 41°C have been measured in conscious and anesthetized rats during passive heating (9, 12). Furthermore, conscious rats can tolerate heating to 41°C on 2 consecutive days (11). In general, the majority of the cardiovascular and thermoregulatory adjustments to heating have stabilized by 41°C (9, 12). The onset of heat stroke and circulatory collapse usually follows with continued heating (9, 12), and body temperatures >43°C are generally lethal (5, 7).

In conscious and anesthetized rats, mesenteric resistance can increase by >100% during moderate hyperthermia (9, 12). This compensatory increase in mesenteric resistance is mediated primarily by the sympathetic nervous system (9). However, removal of sympathetic input to this region does not completely...
eliminate this constrictor response (9), suggesting that circulating and local factors might also contribute to this increase in resistance. The results of this study provide a potential mechanism to explain this residual response, as well as a means for amplifying the normal vasoconstrictor response to neural input. As Webb-Peploe and Shepherd (24) demonstrated in dog cutaneous veins, sympathetically mediated vasoconstriction can be profoundly altered by a change in local temperature. In the present study the contractile response to the α1-adrenergic agonist PE progressively increased with increasing temperature (Fig. 2). This change in tension mimics the increase in vascular resistance observed during hyperthermia (9, 12) and implies that the sympathetically mediated vasoconstriction in the mesenteric artery may be augmented by a direct effect of heating on vascular smooth muscle contractility.

In addition to the enhanced responses observed in the mesenteric artery, heating also increased isometric tension in KCl- or PE-treated rings from the thoracic aorta (Fig. 2). This extends the findings of Price and Wilmoth (16), who reported that a small increase in temperature from 37 to 39°C increased tension generated in response to norepinephrine. Furthermore, using a protocol similar to that utilized in this study, Karaki and Nagase (8) reported that heating increased the contractile response to a single concentration of norepinephrine in the thoracic aorta. Heating to 43°C also significantly increased isometric tension in rings constricted with KCl to levels that were comparable to those in PE-treated rings (Fig. 2). This effect of warming or heating has been reported by several investigators (1, 16, 22) and is generally thought to reflect the direct effect of temperature on vascular smooth muscle (20, 22), because KCl-induced contractions are receptor independent. However, the direct effect of heating on vascular smooth muscle is small, as demonstrated by the responses to heating in unstimulated preparations in this study and others (16, 21). Although heating may stimulate Ca2+ release or facilitate changes in receptor activation (1, 2, 17) or enzyme activity (14), the difference between the effect of heating on stimulated and unstimulated vascular smooth muscle is likely due to Ca2+ influx mediated by the vasoconstrictor agents.

Adrenergic agonists and KCl can stimulate Ca2+ influx through voltage-sensitive Ca2+ channels (6, 13, 15). In the present study we found that the tension generated during heating was minimal in untreated rings but increased markedly in rings preconstricted with PE or KCl (Fig. 2). The difference between untreated control rings and rings preconstricted with PE was largely abolished by inhibiting Ca2+ influx through voltage-sensitive Ca2+ channels (Fig. 5). The Ca2+ dependence of this response was further verified by incubating thoracic aortic rings in nominally Ca2+-free PSS before constriction with PE. In these rings, PE elicited a transient constriction due to intracellular Ca2+ release, followed by a low level of constrictor tone. Aside from the initial level of tension due to the PE, the tension generated in these rings during heating was not significantly different from that in untreated rings incubated in normal PSS. Furthermore, depleting intracellular Ca2+ stores with the combination of caffeine and ryanodine slightly attenuated responses in both vessels (Fig. 5). These results suggest that the release of intracellular Ca2+ contributes, possibly by acting as a signal for Ca2+ channel activation (13), but is not the primary mechanism for the enhanced responses to heating in preconstricted vascular rings. Collectively, these data support the conclusion that the augmented response to heating in preconstricted rings is dependent on Ca2+ influx.

The endothelium could also influence the contractile responses during heating by releasing vasoconstrictor and vasodilator substances. In the present study, removing the endothelium did not influence vasoconstriction in rings from the mesenteric artery during heating (Fig. 3). However, tension generation was potentiated during heating in endothelium-denuded rings from the thoracic aorta (Fig. 4). Interestingly, this potentiating effect was observed in untreated and KCl-treated rings, but not in endothelium-denuded or L-NAME-treated thoracic aortic rings constricted with PE. Although tension generation was enhanced in the KCl-treated rings, the pattern of tension generation was not altered in endothelium-denuded rings. This suggests that the observed differences were due to a higher baseline (37°C) tension, and removing the endothelium did not affect the response to heating. In the untreated rings, tension at the two highest temperatures was greater in the denuded than in the intact rings, indicating some interaction between heating and the mechanism responsible for this increase in tension. Possible explanations include the absence of inhibitory effects of endothelium-derived hyperpolarizing factor on membrane potential (18) or of endothelium-derived relaxing factor on Ca2+ channels (4, 19).

In summary, heating stimulated tension generation in vascular rings from the mesenteric artery and thoracic aorta of rats when heating was initiated during active contraction with PE or KCl. Conversely, hyperthermia elicited relatively small contractions in unstimulated rings from both vessels. The potentiating effects of PE were inhibited by the Ca2+ channel antagonists nifedipine and diltiazem, suggesting a role for voltage-sensitive Ca2+ channels in this response. Although the contribution of this pathway to the vasoconstrictor responses to heating in vivo is unclear, the results from this study provide a potential mechanism for enhancing the vasoconstrictor responses to neural stimuli or endogenous catecholamines during heating. The data also imply that local regulation of vascular tone plays an important role in the hemodynamic responses to hyperthermia. However, further studies are necessary to determine whether Ca2+ channel blockade reduces compensatory vasoconstriction in the mesentery during hyperthermia or, conversely, whether stimulating Ca2+ channels would augment vasoconstriction in this region.

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REFERENCES


