Smooth Muscle Mechanics: Implications for Airway Hyperresponsiveness

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Abstract

Human bronchial smooth muscle preparations from 10 freshly dissected pneumonectomy samples were evaluated for their mechanical characteristics and compared with results obtained for similar samples obtained from porcine tracheae. **Length-tension** relationships of in vitro smooth muscle were evaluated for passive stretching as well as active isometric force generation and isotonic shortening using electrical field stimulation. At the length ($L_{\max}$) producing maximal force ($P_{\max}$) resting tension was very high ($60.0 \pm 8.8\% P_{\max}$) compared with porcine trachealis ($5.2 \pm 2.3\% P_{\max}$). Maximum shortening was $25.0 \pm 9.0\%$ at a length of $75\% L_{\max}$ with suboptimal shortening occurring at $L_{\max}$ ($12.0 \pm 3.4\%$) for the human bronchus, whereas optimal shortening of porcine trachealis ($71.4 \pm 3.6\%$) occurred at $L_{\max}$. Morphometric evaluation revealed threefold less muscle per **cross-sectional** area of tissue for human ($8.7 \pm 1.5\%$) versus porcine ($24.8 \pm 1.9\%$) preparations. We conclude that the high passive tension and the decreased maximum shortening are produced by a relatively large load which must be overcome for the muscle to shorten, presumably provided by the greater connective tissue elastic component present in the airway. We suggest that a decrease in airway wall elastance would increase smooth muscle shortening, thereby leading to excessive responses to contractile agonists as seen in vivo in asthma.

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Introduction Methods

Airway hyperresponsiveness is a well-documented component of bronchial asthma [1]. Few studies have evaluated human asthmatic airways in vitro with only two laboratories demonstrating increased responses [2, 3]. A significant limitation in all studies has been the lack of measurements of isotonic shortening and the failure to ensure that maximal force generation was evaluated at optimal length ($L_{\max}$) (a greater criticism of studies showing no change in responses).

The load placed upon the muscle by surrounding elements will alter the shortening (the greater the load which must be overcome to shorten, the lesser the shortening). We have recently [4] shown that adding a relatively small elastic load to porcine trachealis produces a striking decrease in the shortening. Because we had previously noted that human airways contained less smooth muscle per cross-sectional area, we postulated that the increased connective tissue around and between muscle fibres would place a greater parallel elastic load upon human airways versus porcine or canine airways and therefore any decrease in this load would produce airway hyperresponsiveness.

Mainstem bronchial smooth muscle was obtained from freshly resected pneumonectomy samples from nonasthmatics. Strips approximately $1 \times 1 \times 5$ mm were dissected and suspended in a 37°C organ bath containing Krebs-Henseleit solution continuously bubbled with $95\% \text{O}_2$ – $5\% \text{CO}_2$. Measurements of tension and shortening were performed using a unique force/position transducer

[4]. Muscle and cross-sectional areas of glutaraldehyde-fixed strips were determined by a digitizer.

Results

Human airway smooth muscle (ASM) differed from porcine trachealis in the following: (1) Passive tension at optimal length for force generation (L_{max}) was much greater for human ASM. When expressed as a percent of the maximal active force at L_{max} (% P_{max}), the human passive tension was $60.0 \pm 8.8\%$ P_{max} versus $5.2 \pm 2.3\%$ for porcine. (2) The degree of shortening at L_{max} was strikingly less for human ASM. Porcine ASM shortened 70–80% from L_{max} whereas human ASM contracted only $12.0 \pm 3.4\%$. Maximal muscle shortening of $25.0 \pm 9.0\%$ occurred at a length

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of 75% L_{max} for human bronchus. (3) Morphometric analysis of the airway strips revealed that the amount of muscle expressed as percent cross-sectional area was threefold less for human than porcine airways ($8.7 \pm 1.5\%$ vs. $24.8 \pm 1.9\%$).

Discussion

The present results demonstrate that human ASM must overcome large loads in order to shorten, and that under normal circumstances shortening is approximately two-thirds less than that of porcine ASM. This corresponds with twelvefold higher passive tension at L_{max} and threefold less muscle per cross-sectional area of tissue. These findings suggest human ASM has a greater connective tissue parallel elastic load which must be overcome for shortening to occur. As a result of the unique mechanical properties of human airways, we would anticipate that decreases in

load would produce much greater increases in shortening for human than porcine ASM. We suggest that this may be brought about in human asthmatic airways by inflammatory mediators.

References

- Cockcroft, D.W.; Ruffin, R.E.; Dolovich, J.; Hargreave, F.E.: Clin. Allergy 7: 503–513(1977).
Schellenberg, R.R.; Foster, A.: Int. Archs Allergy appl. Immun. 75: 237–241 (1984).
DeJongste, J.C.; Mons, H.; Bonta, I.L.; Kerrebijn, K.F.: Eur. J. Respir. Dis. 70: 23–29(1987).
Ishida, K.; Pare, P.D.; Blogg, T.; Schellenberg, R.R.: J. Appl. Physiol. 69: 1033–1039(1990).