

REFLEX INFLUENCE OF CAROTID BARORECEPTOR INACTIVATION ON RESPIRATORY RESISTANCE IN HUMANS

J. J. Klawe¹, M. Tafil-Klawe², A. Lewandowski³, P. Zalewski¹

¹Department of Hygiene and Epidemiology, Faculty of Health Sciences, ²Department of Human Physiology, Medical Faculty and ³Department of Basis of Physical Education, Faculty of Health Sciences, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Torun, Poland

Abstract

Our previous study demonstrated that selective carotid baroreceptors activation decreases airway resistance. The aim of the present study was to evaluate the effect of carotid baroreceptor inactivation on the reflex change of respiratory resistance. Twenty healthy men aged between 20 and 25 were included in the study. Selective inactivation of carotid baroreceptors was induced by generating a positive pressure of 40 mmHg for 5 s in two capsules placed bilaterally on the neck over the bifurcation of the carotid arteries. The oscillatory method (Siregnost FD5, Siemens) was used to measure continuously respiratory resistance. Inactivation of carotid baroreceptors produced a short increase in respiratory resistance by 0.39 ± 0.01 (SE) mbar/l/s, i.e., 21.7% above the resting level. We conclude that in humans, carotid baroreceptors might have a background contribution to bronchodilator tone. This observation seems to be important for clinical situations of impairment of baroreflex function. *Key words:* airway resistance, carotid baroreflex, bronchodilation

INTRODUCTION

The main baroreceptive areas are in the carotid sinuses and these are the regions which have been most studied in humans. Various non-specific stimuli can be used to examine reflex control. The use of an airtight chamber applied to the subject's neck allows application of either a negative pressure which increases carotid transmural pressure and activates of the baroreceptors, or a positive pressure which has the opposite effect and inactivates the receptors [1]. It is plausible that this stimulus (positive or negative) alters the firing of other mechanoreceptors located in the neck region beside the carotid baroreceptors, which includes the upper airway receptors in the trachea and larynx. A new more selective method of activation and inactivation of carotid baroreceptors in humans has been described [2]; namely, instead of one neck chamber, two separate capsules placed on the surface of the skin over the carotid bifurcations. The use of two separate capsules (chambers) makes it possible to apply stimuli to the left and right carotid sinus, without activation or inactivation of the other neck's mechanoreceptors. It is known from studies in animals that the reflex effects of activating the carotid sinus barorecep-

tors involve breathing and bronchomotor tone [3, 4, 5]. Our previous study in man has demonstrated that carotid baroreflex activation is not confined to the cardiovascular system (produces bradycardia), but also decreases airway resistance. The aim of the present study was to evaluate the opposite, i.e., the influence of carotid baroreceptors inactivation on respiratory resistance in humans.

MATERIAL AND METHODS

Twenty healthy male volunteers aged between 20 and 25 were included in the study. The study protocol was approved by a local Ethics Committee and the subjects gave informed consent to study procedures. All experiments were performed at rest, in the seated recumbent position.

INACTIVATION OF CAROTID BARORECEPTORS

In order to inactivate carotid baroreceptors a two-neck-chamber method was applied. The selective inactivation of carotid baroreceptors was induced by generating a positive pressure of 40 mmHg for 5 s in two capsules placed bilaterally on the neck over the bifurcation of the carotid arteries. The stimuli were applied 250 ms after the R-wave during the expiratory phase of breathing. The maximal rate of air pressure increase was 300 mmHg per second.

The following variables were recorded continuously:

1. R-R intervals, measured from ECG;
2. Respiratory phase and the rate of breathing by means of a termistor placed at a nose orifice;
3. Air pressure in the neck chambers;
4. An average R-R interval was calculated from a 10-s recording preceding the onset of stimulus and is referred to as the baseline. The cardiac baroreflex response was expressed as a gain of heart response (GHR) and calculated as the peak value of the R-R shortening during the 5 s after the onset of stimulus, compared with the baseline level, and divided by the neck pressure change.

MEASUREMENT OF RESPIRATORY RESISTANCE

The oscillatory method (Siregnost FD5, Siemens, Germany) was used to measure continuously respiratory resistance, as described in detail elsewhere [6].

RESULTS

We took the calculated GHR as the expression of a cardiac response to carotid baroreceptors inactivation. The mean GHR was $-4.013 \pm 0.030(\text{SE})$ ms/mmHg. Inactivation of carotid baroreceptors produced a short increase in respiratory resistance by $0.39 \pm 0.01(\text{SE})$ mbar/l/s, i.e., 21.7% above the resting level.

DISCUSSION

Although the use of neck chambers seems to provide a discrete baroreceptors stimulus, there are some limitations and considerations to take into account. The immediate response of pulse interval is likely to be due mainly to baroreceptor inactivation. There is evidence that about 86% of the applied positive pressure is transmitted to the deep structures of the neck [7]. However, this response rapidly becomes smaller due presumably to some adaptation of the receptors but also to 'buffering' by the resulting response which exerts an effect on other baroreceptors [8]. This consideration limits the use of this technique in the study of vasomotor responses. These, being sympathetically mediated, occur more slowly than vagally mediated effects on the heart [8]. In the present study, only the heart response to baroreceptor inactivation, calculated as a gain in the heart response, was measured. The maximum shortening of the pulse interval observed during the 5 s of stimulus action seems to be vagally mediated (inhibition of vagal activity) with a small component of sympathetic activation and may be considered as a relatively pure cardiac response to carotid baroreceptors inactivation.

The main finding of this study is that, in humans, carotid baroreceptors inactivation evoked reciprocal effects on vagal cholinergic control of the heart and airways: a decrease in cardioinhibitory tone and an increase in bronchoconstrictor tone. Our previous study showed a contrary effect of activation of carotid baroreceptors: an increase in cardioinhibitory tone and a decrease in bronchoconstrictor tone [2]. The motor neurons of the vagus nerve are situated in two nuclei: the dorsal vagal nucleus and the nucleus ambiguus, with the parasympathetic motor neurons innervating the sinus node and airway in the latter nucleus [9]. Cardioinhibitory cells tend to be more caudal and ventral than the presumed bronchoconstrictor neurons [10]. Thus, morphological and functional evidence is consistent with there being two separate vagal efferent pathways of the carotid baroreflex. Inactivation of the carotid baroreflex in the present study evoked both synergic reflex responses: circulatory response – increase in heart rate, and ventilatory response – increase in respiratory resistance, in effect resulting in increases in inspiratory effort and in venous return.

Numerous studies have shown that respiratory depression due to increased arterial blood pressure preferentially affects upper airway motor output in humans [11, 12]. Because increases in blood pressure increase the severity of upper airway obstruction by increasing pharyngeal collapsibility [13], "baroreceptors have been implicated in the regulation of upper airway patency" [14].

We conclude that in humans carotid baroreflex decreases respiratory resistance. This tonic bronchodilator influence, resulting in a decrease in inspiratory effort, may uphold the imbalance between the activities of the upper airway and diaphragm and chest wall inspiratory muscle groups. This observation seems noteworthy for clinical situations of impairment of baroreflex function.

Conflicts of interest: the authors reported no conflicts of interest in relation to this article.

REFERENCES

- [1] Ludbrook J, Mancia G, Ferrari A, Zanchetti A. The variable-pressure neck chamber method for studying the carotid baroreflex in man. *Clin Sci Mol Med* 1977; 53: 165-171.
- [2] Tafil-Klawe M, Raschke F, Hildebrandt G. Functional asymmetry in carotid sinus cardiac reflexes in humans. *Eur J Appl Physiol* 1990; 60: 402-406.
- [3] Brunner MJ, Sussman MS, Greene AS. Carotid sinus baroreceptor reflex control of respiration. *Circ Res* 1982; 51: 624-636.
- [4] Nadel JA, Widdicobme JG. Effect of changes in blood gas tension and carotid sinus pressure on tracheal volume and total lung resistance to airflow. *J Physiol* 1962; 163: 13-33.
- [5] Schultz HD, Pisarri TD, Coleridge HM, Coleridge JCG. Carotid sinus baroreceptors modulate tracheal smooth muscle tension in dogs. *Circ Res* 1987; 60: 337-345.
- [6] Von Korn V. Die Bestimmung des Atemwiderstandes mit dem oszillatorischen Messprinzip, Siregnost FD5. *Dustri Verlag*, 1979, pp. 16-40.
- [7] Mancia G, Ferrari A, Gregorini L, Valentini L, Ludbrook J, Zanchetti A. Circulatory reflexes from carotid and extracarotid baroreceptor areas in man. *Circulation Res* 1977; 41: 309-315.
- [8] Mary D, Hainsworth R. Methods for the study of cardiovascular reflexes. In: *Cardiovascular reflex control in health and disease*. Hainsworth R. and Mark AL. (eds) W.B. Saunders Company Ltd, 1993, pp. 1-34.
- [9] Mc Allen RM, Spyer KM. Two types of vagal preganglionic motoneurons projecting to the heart and lungs. *J Physiol* 1978; 282: 353-364.
- [10] Kalia M. Brain stem localization of vagal preganglionic neurons. *J Aut Ner Syst* 1981; 3: 451-481.
- [11] Garpestad E, Basner RC, Ringeler J, Lilly J, Schwarzstein R, Weineberger SE, Weiss JW. Phenylephrine-induced hypertension acutely decreases genioglossus EMG activity in awake humans. *J Appl Physiol* 1992; 72: 110-115.
- [12] Wasicko MJ, Knuth SL, Leiter JC. Response of genioglossus EMG to passive tilt in man. *J Appl Physiol* 1993; 74: 73-81.
- [13] Mayor AH, Schwartz AR, Rowley JA, Willey SJ, Gillespies MB, Smith PL, Robotham JL. Effect of blood pressure changes on air flow dynamics in the upper airway in the decerebrate cat. *Anesthesiology* 1996; 84: 128-134.
- [14] Stella MH, Knuth SL, Barlett D, Jr. Respiratory response to baroreceptor stimulation and spontaneous contractions of the urinary bladder. *Res Physiol* 2001; 124: 169-178.

Corresponding author:

Prof. Jacek J. Klawe
 Department of Hygiene and Epidemiology
 Faculty of Health Sciences of Collegium Medicum
 M. Skłodowskiej-Curie 9 St.
 85-094 Bydgoszcz, Poland
 Phone: +48 52 5853615
 Fax: +48 52 5853589
 E-mail: Jklawe@cm.umk.pl