Acute changes in bladder volume produce minimal cardio-respiratory responses in lightly anesthetised humans

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Purpose: To examine whether changes in bladder volume elicit reflex cardiovascular and respiratory responses in humans under general anesthesia with sevoflurane and nitrous oxide.

Methods: Fourteen patients free of autonomic disorders were anesthetized with sevoflurane 0.5% and nitrous oxide 60% in oxygen that were approximately equivalent to 0.9 MAC. Warmed saline (6 $ml \cdot kg^{-1}$, 37°C) was instilled into the pre-emptied urinary bladder, and then the bladder was kept distended for five minutes. Following the distension, the instilled saline was drained to the pre-instilled volume of the bladder. Arterial blood pressure, respiratory flow, and intra-vesicle pressure were continuously measured, and mean arterial pressure, pulse rate, respiratory rate, tidal volume, and minute ventilation were estimated offline from these signals.

Results: Bladder emptying produced small decreases in mean blood pressure (from 83.4 ± 4.3 to 80.0 ± 4.4 mmHg, mean ± SE, P =0.017) and pulse rate (from 72.2 ± 2.9 to 69.4 ± 2.7 bpm, mean ± SEM, P =0.004). Only minimal respiratory reflexes were invoked by the bladder volume changes.

Conclusion: In lightly anesthetized humans, the acute changes in bladder volume produce only mild cardiovascular and respiratory responses.

Objectif : Vérifier si des changements volumiques de la vessie entraînent des réactions cardiovasculaires et respiratoires réflexes chez les humains sous anesthésie générale avec du sévoflurane et du protoxyde d'azote.

Méthode : Quatorze patients, sans trouble neurovégétatif, ont été anesthésiés avec du sévoflurane à 0,5 % et un mélange de protoxyde d'azote (60 %) et d'oxygène équivalant à environ 0,9 CAM. Une solution salée réchauffée (6 $ml \cdot kg^{-1}$, 37 °C) a été introduite dans la vessie, préalablement vidée, qu'on a gardée distendue pendant cinq minutes. On a ensuite drainé la solution pour retrouver le volume vésical initial. La tension artérielle, le débit respiratoire et la pression intravésicale ont été mesurés continûment et la tension artérielle moyenne, la fréquence du pouls, le débit respiratoire, le volume courant et la ventilation minute ont été estimés en différé à partir de ces données.

Résultats : La vidange de la vessie a produit de faibles baisses de la pression sanguine moyenne (de 83,4 ± 4,3 à 80,0 ± 4,4 mmHg, moyenne ± erreur type, P = 0,017) et de la fréquence du pouls (de 72,2 ± 2,9 à 69,4 ± 2,7 bpm, moyenne ± erreur type de la moyenne, P = 0,004). Seuls des réflexes respiratoires minimaux ont été provoqués par les changements de volume de la vessie.

Conclusion : Chez les humains légèrement anesthésiés, les changements de volume soudains de la vessie ne produisent que de faibles réactions cardiovasculaires et respiratoires.

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In additions to the measurement of urine output, urinary bladder catheterization prevents the bladder from over- distension which may lead to undesirable autonomic reflexes, such as the dramatic increase in blood pressure, especially in patients with high spinal lesions.[1–3] Sudden emptying of the bladder may result in severe hypotension.[4,5] Attenuation of these responses by spinal or epidural anesthesia[2] suggests involvement of afferent input from the urinary bladder in the cardiovascular reflexes. In the absence of block of the afferent pathway, inadequate anesthesia may produce an unstable cardiovascular status when stimuli are applied[2,6]

In addition to the cardiovascular reflexes, both spontaneous contraction and passive distension of the bladder may produce inhibition of respiratory motor neurone activity in anesthetized or decerebrate cats.[7–10] These findings may indicate that changes in bladder volume could produce abnormal breathing during light general anesthesia.

Therefore, we examined whether passive distension and voiding of the bladder caused autonomic responses in cardiovascular and respiratory systems during light general anesthesia in humans.

Methods

Subjects

After obtaining ethics approval and informed consent, patients for elective minor surgery under general anesthesia were recruited. Fourteen patients (six female and eight male; age, 42 ± 14 yr; weight, 60.4 ± 11.5 kg; height, 163.6 ± 10.4 cm) participated in this study. They were undergoing minor surgery of the head & neck,(n=11) plastic,(n=2) or breast surgery.(n=1) All subjects were ASA status I - II. None had any neurological and urological disorders. Patients with possible autonomic dysfunction or diabetes were also excluded.

Anesthesia

Famotidine, 20 mg *iv*, was administered two hours prior to induction of anesthesia. The subjects received 50 mg hydroxyzine and 0.5 mg atropine *im* 45 min before induction. After a small dose of vecuronium (0.02 $mg \cdot kg^{-1}$ *iv*), anesthesia was induced with 5 $mg \cdot kg^{-1}$ thiopental (*iv*) and tracheal intubation was facilitated with 1.5 $mg \cdot kg^{-1}$ succinylcholine (*iv*). Anesthesia was maintained with sevoflurane in nitrous oxide and oxygen. A three-lumen balloon tipped silicon catheter (14 Fr.) was inserted via the urethra into the urinary bladder. In addition to routine monitoring, continuous measurement of arterial blood pressure (ABP) was performed via a catheter placed in the radial artery. The concentration of sevoflurane was adjusted to establish an adequate anesthetic depth for the surgical procedures.

Measurements

As well as measurement of ABP, airflow ($\dot{V}$) was measured with a Fleisch type pneumotachograph (#2) placed at the proximal end of the endotracheal tube. We also performed continuous measurement of intra-vesicle pressure (*P*vs) through a lumen of the three-lumen bladder catheter. All the signals were lowpass filtered at 50 Hz by a three-pole Butterworth filter (SPA-3, TechnoService, Urayasu, Japan) and digitized at 100 Hz by an analogue to digital converter (DT2801-A, Data Translation, Marlboro, NJ). Data acquisition was performed with a data logging software package (LAB-DAT 5.2 RHT-InfoDat, Montreal, Quebec, Canada), on an IBM compatible personal computer, and stored on an internal hard disk for offline analysis.

Experimental protocol

At the termination of surgery, end-tidal sevoflurane and nitrous oxide concentrations were set at 0.5 and 60%, respectively, which were confirmed a pre-calibrated infrared gas analyzer (Anesthetic Gas Monitor Type 1304, Brüel & Kjær, Norcross, GA). The depth of anesthesia was approximately equivalent to 0.9 MAC and was considerably lighter than the depth required to inhibit autonomic responses. Roizen *et al.* showed that about 1.5 times MAC was necessary to prevent cardiovascular responses to skin incision.[6] The subjects were allowed to breathe spontaneously in the supine position. The urinary bladder was emptied as much as possible by gentle compression of the lower abdomen. After obtaining stable respiratory and circulatory conditions, the following protocol was started. While measuring *Pvs*, warmed saline (37°C, 6 $ml \cdot kg^{-1}$) was infused into the bladder through another lumen of the bladder catheter. The saline was allowed to flow into the bladder with 100 cm hydrostatic pressure gradient. The instillation took approximately five minutes. The volume was chosen according to previous work with suggestion that the maximum bladder volume that was acceptable in awake humans was about 300 to 420 ml.[11] At the completion of the infusion, the infusion line was clamped to keep the bladder distended for another five minutes to observe the adaptation to the distension. Following this, the infusion route was reopened for the infused saline to drain freely. Although the fluid was usually voided within two minutes, we continued the measurement for another five minutes from the start of the evacuation to observe the changes during stabilization phase.

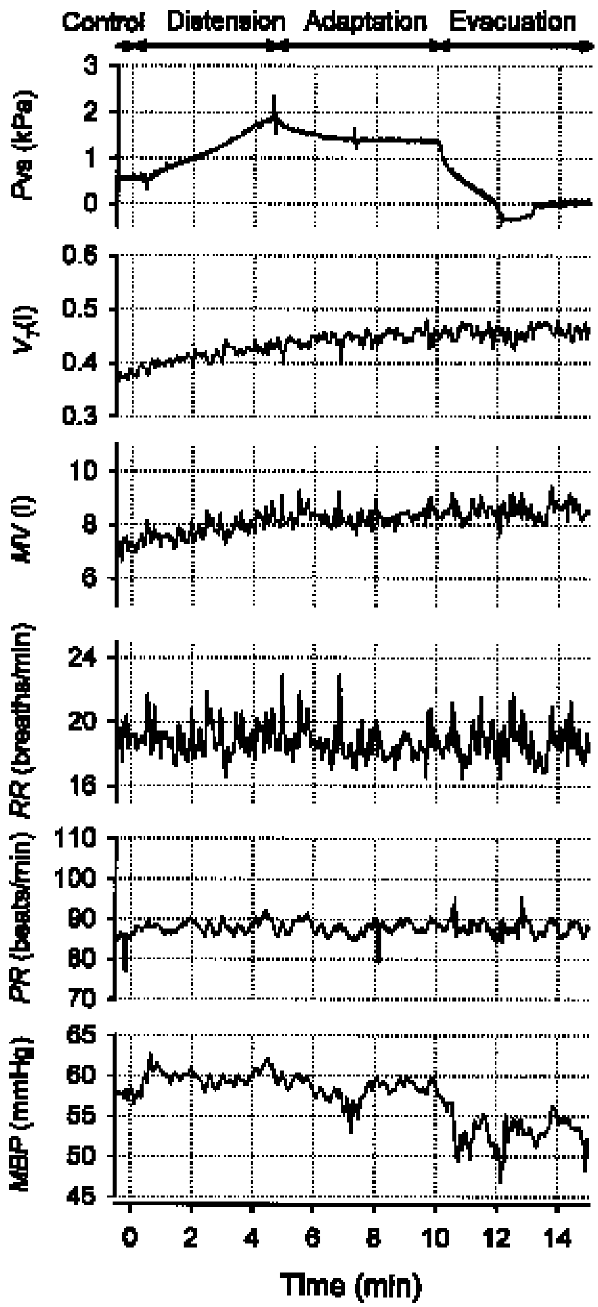

FIGURE 1 An example of offline analysis. From the top, panels indicate temporal changes in intra-vesicle pressure (*P*vs), tidal volume (V_T), minute ventilation (*MV*), respiratory rate (*RR*), pulse rate (*PR*), and mean arterial blood pressure (*MBP*).

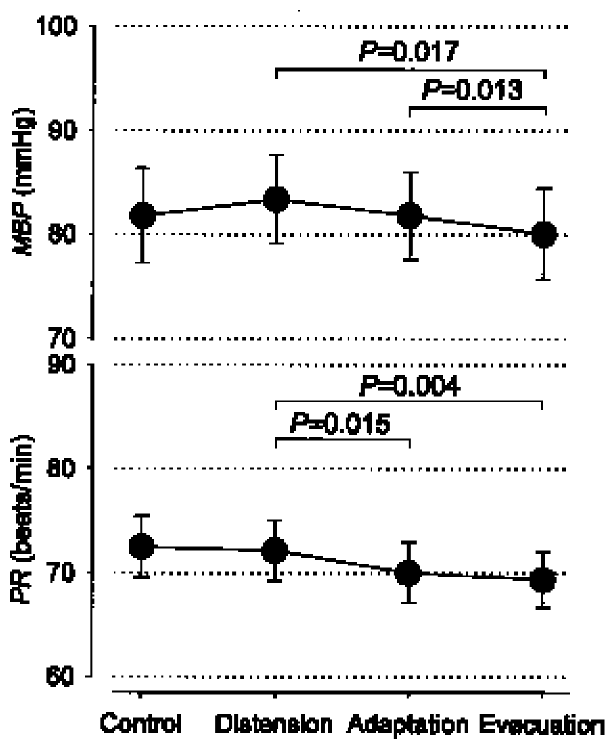

FIGURE 2 Changes in cardiovascular variables. Values are presented as mean ± SEM. Square brackets with *P* values indicate pairs whose difference in means are significant.

Offline analysis

An example of the analysis is shown in Figure 1. The ventilatory volume (*V*) was calculated by numerical integration of $\dot{V}$ signals. Respiratory frequency (*RR*), tidal volume (V_T), and minute ventilation (*MV*) were calculated on a breath-by-breath basis from $\dot{V}$ and *V* signals. Beat-wise trends in mean ABP (*MBP*) and pulse rate (*PR*) were calculated from the ABP signals. Signal processing and other numerical analysis were performed by a house made software written in S language (S-Plus 4, MathSoft, Seattle, USA).

Statistics

The effects of bladder volume changes were analyzed by comparing representative values of the cardiovascular (*MBP*, *PR*) and respiratory (*RR*, V_T, *MV*) variables among four different phases: Control, Distension, Adaptation, and Evacuation (Figure 1). The phase Control was defined as the period before infusing the saline into the bladder. Distension was a phase during which the saline was instilled into the bladder: the volume of the bladder was increasing. Adaptation was the phase during which the bladder was kept distended but the volume did not change. Evacuation was the phase during voiding of saline from the bladder. The values of the last 30 sec of each phase were averaged as the

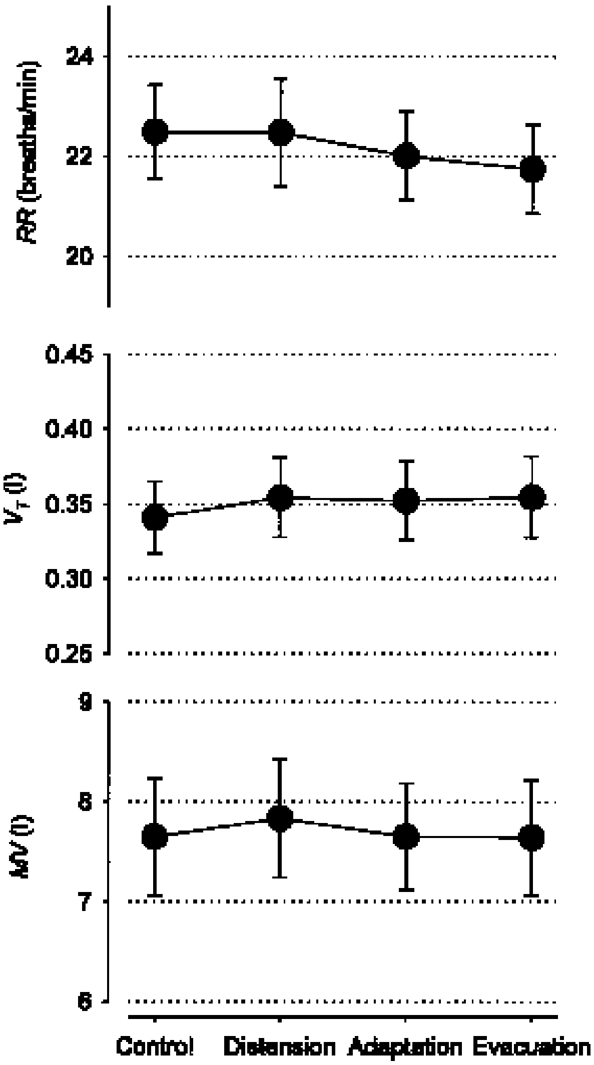

FIGURE 3 Changes in respiratory variables. Values are presented as mean ± SEM. No significant changes are observed in respiratory parameters.

representative values. Abnormal breaths such as sighs and arrhythmia such as premature contractions were discarded for statistical comparison. Data were analyzed using multivariate ANOVA followed by a contrast analysis to reveal which two specific sets were significantly different. We analyzed circulatory and respiratory variables separately. $P < 0.05$ was considered significant. Descriptive statistics were expressed as mean ± SD or median (range), unless otherwise stated.

Results

Anesthetic time before the start of the experiment was 205 (110-665) min. The amount of crystalloid administered and bleeding were 6.5 (1.7-12.6) $ml \cdot kg^{-1} \cdot hr^{-1}$ and 2.3 (0.4-7.9) $ml \cdot kg^{-1}$ respectively. Although the amount of surgical bleeding was relatively small, it was corrected by administering larger amounts of crystalloid fluids to the patients with greater bleeding. No cardiovascular or respiratory events were reported during the surgery.

Although the bladder distension tended to cause an increase in *MBP*, it did not reach statistical significance (P =0.169, Control *vs* Distension). Evacuation of the bladder resulted in a decrease in *MBP* (P =0.017, Distension *vs* Evacuation; P =0.013, Adaptation *vs* Evacuation). Similarly, a small decrease in *PR* was also observed during adaptation and evacuation (P =0.015, Distension *vs* Adaptation; P =0.004, Distension *vs* Evacuation) (Figure 2).

No consistent response was detected in respiratory variables (Figure 3).

Discussion

The main findings of this study are that rapid changes in bladder volume 1) produced only minimal cardiovascular reflexes, that 2) did not produce respiratory reflexes in humans lightly anesthetized with nitrous oxide and sevoflurane.

The cardiovascular responses observed in this study were similar to the results of previous studies conducted either in anesthetized animals[12,13] or in awake human subjects.[14] However, the magnitude of responses seen in this study was smaller than that in previous studies. Our results indicate that acute changes in bladder volume do not evoke serious cardiovascular instability in humans during light general anesthesia. Nevertheless, we observed unstable circulatory profiles in several subjects (Figure 4) indicating variable autonomic responsiveness among subjects. Kao *et al.* also reported a case who exhibited loss of consciousness probably due to hemodynamic decompensation associated with micturition.[4] The variability might be explained by the large variation in bladder capacity and a relatively small distension volume used in this study.

Several studies in anesthetized or decerebrate cats reported respiratory inhibition produced by bladder volume changes.[7,9,10] We did not observe any consistent responses in respiration. The discrepancy is probably due to the differences in species and experimental conditions. The magnitude of the respiratory reflex responses generally varies among species.[15] In some studies on cats,[7,10] the vagi were sectioned. The vagus

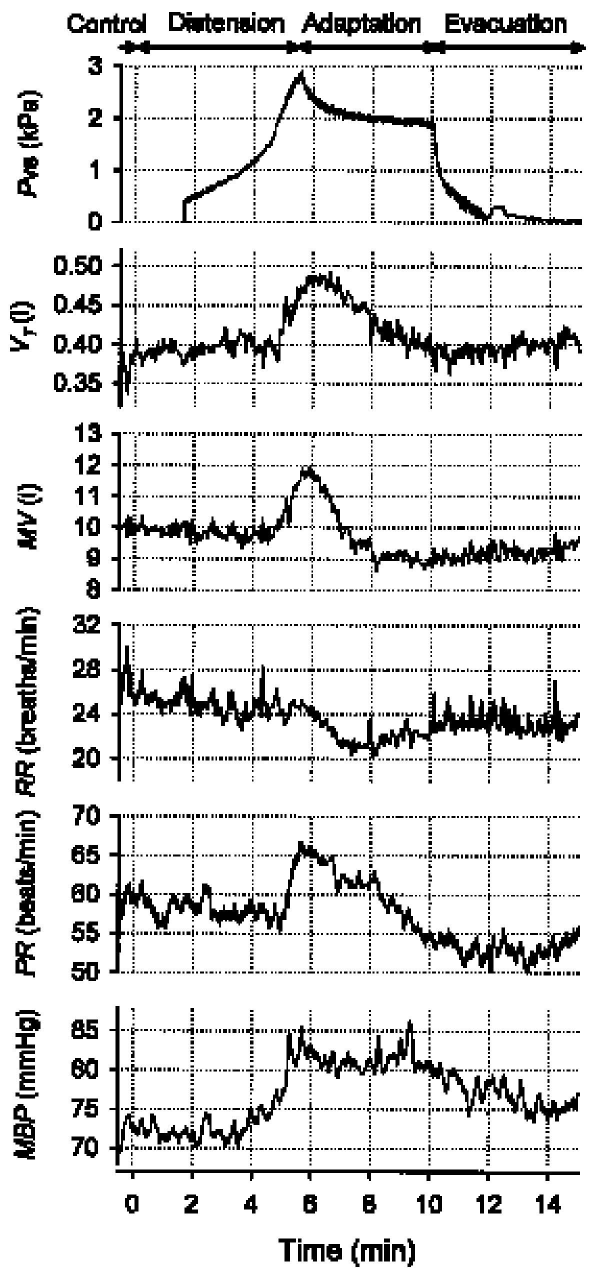

FIGURE 4 A subject who had clear responses both in cardiovascular and respiratory variables. Note the clear responses associated with changes in the bladder volume.

nerve may act as 'a buffer' which would blunt the respiratory responses as in the hemodynamic response.[1 6] Decerebration performed in the animal studies,[7,10] may also account for the discrepancy, since it can eliminate the influence of anesthesia, thus augments reflexes. With larger distension volume, we might have consistent responses in respiratory parameters, however, we imposed limits on the distension volume to avoid injury of the bladder due to over distension.

In conclusion, in lightly anesthetized humans, bladder distension and voiding produced minimal cardiovascular reflexes. These volume changes did not invoke respiratory reflexes. During light general anesthesia, as may seen during emergence from anesthesia, changes in the bladder volume are unlikely to produce appreciable cardiovascular and respiratory reflexes.

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