Plasma arginine vasopressin during neck suction in upright sitting man

P. Norsk¹, F. Bonde-Petersen¹ and J. Warberg²

Laboratory for Human Physiology¹, August Krogh Institute, and
Institute of Medical Physiology C², Panum Institute, University of Copenhagen, Copenhagen, Denmark

Abstract. In order to examine the influence of carotid baroreceptor stimulation on arginine vasopressin secretion, 8 normal healthy males were subjected to static neck suction of -3.3 kPa for 20 min in the upright sitting position after overnight food and fluid restriction. The plasma concentration of arginine vasopressin did not change significantly during neck suction. However, in 3 subjects the termination of neck suction induced large increases in plasma arginine vasopressin from 1.8 to 63.7 ng/l, from 0.7 to 34.3 ng/l and from 2.1 to 19.0 ng/l, respectively. Two subjects experienced symptoms such as nausea and paleness during neck suction. Systolic arterial pressure increased slightly but significantly during neck suction from 15.3 ± 0.3 to 15.7 ± 0.4 kPa (N = 7, P < 0.05), whereas mean arterial pressure, diastolic arterial pressure, central venous pressure, heart rate, plasma osmolality, plasma sodium and potassium were unchanged. Haemoglobin concentration in blood and haematocrit increased significantly during and after neck suction, whereas plasma volume decreased. We conclude that neck suction with a negative pressure of 3.3 kPa in upright sitting man does not significantly affect plasma arginine vasopressin. However, termination of the stimulation induces large increases in some subjects. This may be explained by a direct effect on the vagus nerve or by a selective unloading of carotid baroreceptors.

Based on experiments in dogs (Johnson et al. 1969; Gauer & Henry 1976; Schultz et al. 1982), it has been suggested that cardiopulmonary mechanoreceptors play an important role in extracellular volume homeostasis and in the regulation of arginine vasopressin (AVP). However, in a recent review, Gilmore (1983) proposed that in the primate, the volumetric control of salt and water homeostasis and of AVP has shifted from the low pressure to primarily high pressure receptors when compared with quadrupeds. This is supported by experiments in man, as Convertino et al. (1984) in heart transplanted patients found a suppression of plasma AVP (pAVP) during -6° head down tilt compared with upright sitting of a magnitude similar to the response in normal subjects.

During water immersion (WI) to the neck, pAVP was suppressed and central venous pressure (CVP) simultaneously increased in human subjects (Epstein et al. 1981; Norsk et al. 1985). As systolic arterial pressure (SAP) also increased and heart rate (HR) decreased (Norsk et al. 1985), this indicated that arterial baroreceptors were stimulated as well as cardiopulmonary mechanoreceptors.

For a further study of the role of arterial baroreceptors in the regulation of AVP secretion the following experiment was set up. Neck suction (NS) was applied selectively to stimulate carotid baroreceptors.

Materials and Methods

Eight healthy males, age 26 ± 2 years (mean ± SE), weight 79 ± 3 kg and height 186 ± 3 cm, participated in the experiment. All had a negative history of arterial hypertension, cardiovascular or kidney diseases. Informed consent was obtained after the subject had read a description of the experimental protocol.

The subjects were studied one at a time according to...
the following protocol: All had been told not to smoke, drink coffee, tea or alcohol all day before experimentation and were fasting (no food or drink) from 19.00 h until the end of the experiment the following noon. Thus, the subject was mildly dehydrated during the experiment. This was necessary to obtain an adequately high level of pAVP during standard conditions and to avoid interference from possible oropharyngeal or gastrointestinal receptors (Geelen et al. 1984). Prior to experimentation the subject slept at the laboratory from 22.00 h and was awakened at 07.00 h and allowed to wash and urinate. The central venous catheter was then placed during ECG surveillance with the subject in the supine position. One ml of heparin solution in saline (50 IU per ml) was used to fill the catheter after each blood sampling. The catheter dead space was emptied before each sampling. The amount of isotonic saline given during the experiment equaled the amount of blood taken.

At 08.15 h the subject was placed in a specially constructed chair, sitting upright with an angle of 90° between body axis and thighs and with his arms resting on leans. The NS device was placed around the neck at 08.30 h after which the subject was unable to move his head during the experiment. From immediately after measurements at 09.00 h to immediately after the measurements at 09.20 h, NS was effected. Measurements were carried out every 5 min from 08.50 to 09.35 h in the following sequence: Blood sampling (5 ml for the determination of pAVP; additional 5 ml of blood just before NS, after 20 min of NS, and 15 min after termination of NS for the determination of plasma osmolality (pOSM), plasma sodium (pNa), plasma potassium (pK), haemoglobin concentration (Hb), and haematoctrit (Hct)), CVP and HR. Just before NS, after 20 min of NS and 15 min after termination of NS, SAP and diastolic arterial pressure (DAP) were measured.

Static NS was effected with a 50 × 10 cm lead plate formed to a chamber body constructed and fitted to the subject according to Eckberg et al. (1975). The edges of the chamber were bent to conform to the anatomy of the subject’s neck, sternum, jaw and clavicles. The chamber was held in place by securely wrapped paper tape. The subject had his head fixed, slightly bent backwards and was not able to move it. The chamber was supported by a leather strap hanging from a rack so that it would not compress the neck by its own weight. A vacuum cleaner powered by a variable transformer created subatmospheric pressure in the space between the skin of the neck and the chamber. At the start of NS, the pressure was regulated within 20–30 sec to the desired pressure of −3.3 kPa controlled by a mercury manometer connected by a tube to a valve on the right side of the chamber. NS was terminated over 1 min in order not to unload the carotid baroreceptors too quickly. According to Ludbrook et al. (1977), a subatmospheric pressure of 3.3 kPa corresponds to an increase in the transmural pressure in the carotid sinuses of

\[0.64 \times 3.3 \text{ kPa} = 2.1 \text{ kPa}.\]

Ambient temperature was measured by an ordinary thermometer and was between 23.7 ± 0.1 and 23.9 ± 0.1°C.

pAVP was measured by radioimmunoassay (Bie & Warberg 1983). Blood samples of mixed venous blood taken through the central venous catheter were collected in prechilled, disposable polypropylene syringes (10 ml, Brunswick) and transferred to polyethylene test tubes (10 ml, Minisorp) containing 12.5 IU heparin per ml blood. The blood samples were immediately separated by centrifugation at 4°C for 10 min and 2 ml of plasma was stored at −20°C for later analysis. Synthetic AVP (Ferring 800513), a diacetate, dihydrate compound with a molecular weight of 1239 daltons, served as reference preparation. The least detectable quantity of AVP was 0.3–0.6 pg/tube. Within-assay coefficient of variation at the middle-sensitivity range of the standard curve was 7.8% (N = 15). Between-assay coefficient of variation at the same range was 12%. pAVP was determined twice on each sample.

pOSM was measured with an osmometer (Advanced Osmometer, model 3L) using freezing point depression. Plasma, 2 ml, was cooled on ice and measured immediately after the experiment.

pNa and pK were measured in a flame photometer (Radiometer FLM 3). Samples were taken from the cooled plasma for pOSM and frozen at −20°C until time of measurement.

Hct was measured in Na-heparinized tubes (Micro-Haematocrit) on an autocrit centrifuge (Clay-Adams). Raw Hct values were collected for trapped plasma and for whole-body Hct by multiplication by a factor of 0.96 and 0.93, respectively.

Hb was measured by spectrophotometry (Zeiss, M4 QII) with a cyanid method.

Relative changes in plasma volume (dPV) were calculated from concomitant changes in Hct and Hb using the first supine value as baseline (Dill & Costill 1974).

CVP was measured through an indwelling 60 cm long catheter (Intracath) introduced through a cubital vein until the tip was situated in an intrathoracic vein. The catheter was connected to a pressure transducer (Siemens Elema AB, E033E) by a 180 cm plastic tube. The pressure transducer was placed at level with the 4th intercostal space at the left border of the sternum. Via a pressure amplifier (Siemens 863) and a strip chart recording (Clevite Brush, mark 220), mean CVP values were measured with an accuracy of ± 0.03 kPa. Position of the catheter in an intrathoracic vein was confirmed by typical waveforms and by characteristic responses to respiratory manoeuvres.

HR was measured simultaneously with CVP from ECG recordings by electrodes on the chest connected to an oscilloscope (Diascope DS 521, S&W) and a strip chart recorder (Clevite Brush, mark 220).
SAP and DAP were measured with a mercury sphygmomanometer (Erkameter 300) and a stethoscope. The beginning of the 4th sound of Korotkoff indicated DAP. MAP was calculated by adding one third of the pulse pressure to DAP.

Data are presented as means ± SE and evaluated statistically by paired, twosided t-tests. A significance level of 0.05 was accepted.

The protocol was in compliance with the principles set forth in the declaration of Helsinki. No complications occurred.

Results

The mean pAVP values did not change significantly during NS. Two subjects experienced nausea and became pale during NS resembling orthostatic intolerance symptoms and the experiment was stopped (J. S. P. and S. T., Fig. 2). These two subjects had increases in pAVP during NS. Measurements were not performed after termina-

![Graph](image-url)

Fig. 1.

Concomitant changes in 4 upright sitting male subjects (C. A., M. I., L. E. and J. N.) of plasma arginine vasopressin (pAVP) in ng/l, central venous pressure (CVP) in kPa, systolic (SAP) and diastolic (DAP) arterial pressure in kPa, and heart rate (HR) in bpm measured at 5-min intervals before, during and after neck suction (NS) of −3.3 kPa for 20 min.
Concomitant changes in 4 upright sitting male subjects (P. S. F., N. R., J. S. P. and S. T.) of plasma arginine vasopressin (pAVP) in ng/l, central venous pressure (CVP) in kPa, systolic (SAP) and diastolic (DAP) arterial pressure in kPa, and heart rate (HR) in bpm measured at 5-min intervals before, during and after neck suction (NS) of -3.3 kPa for 20 min. Subjects J. S. P. and S. T. experienced nausea and became pale during NS, whereafter the experiment was stopped.

Cardiovascular responses
CVP varied between 0.31 ± 0.21 and 0.37 ± 0.25 kPa without being affected by NS. Only one subject (P. S. F., Fig. 2) had an increase in CVP during NS from 0.85 to 1.17 kPa and a decrease after termination of NS from 1.12 to 0.80 kPa. HR

Fig. 2.
increased during NS only in the two subjects who experienced nausea and paleness during NS (J. S. P. and S. T., Fig. 2). The mean value of SAP increased slightly but significantly from 15.3 ± 0.3 to 15.7 ± 0.4 kPa (P < 0.05, N = 7). DAP and MAP did not change significantly during the experiment.

Blood and plasma composition

pOSM (286 ± 1 mosm/kg), pNa (143 ± 1 meq/l) and pK (4.3 ± 0.1 meq/l) did not change significantly during the experiment. Hb increased from a prestudy level of 9.7 ± 0.2 mmol/l to 9.9 ± 0.2 (P < 0.01) after 20 min of NS and Hct increased from 40.4 ± 0.8% to 41.2 ± 0.8% (P < 0.01). PV decreased by 3.3 ± 0.6% (P < 0.01) during 20 min of NS and was still decreased after termination of NS by 2.9 ± 0.9% (P < 0.05).

Discussion

This study indicated that stimulating the carotid baroreceptors by NS with a negative pressure of 3.3 kPa in upright sitting man after overnight food and fluid restriction did not suppress pAVP. However, three subjects showed large increases in pAVP after termination of NS which were not related to changes in systemic arterial blood pressure or CVP.

Static NS is known to increase carotid transmural pressure (Eckberg et al. 1975; Ludbrook et al. 1977; Mancia et al. 1978; Skagen et al. 1985). According to Ludbrook et al. (1977), 64% of the negative pressure is transmitted to the neck vessels. NS is therefore a unique tool in selectively stimulating carotid baroreceptors. To our knowledge, pAVP has not been measured during NS before. Mancia et al. (1978) measured renin release during NS and during neck positive pressure for 5 min in hypertensive subjects lying supine and found no effect of either procedure. We found no effect of NS on AVP secretion in normal upright sitting man except when the procedure was terminated.

Share & Levy (1966) concluded from dog experiments that carotid baroreceptors may participate in the regulation of antidiuretic hormone activity in plasma (pADH). By changing carotid sinus perfusion pressure from pulsatile to non-pulsatile in the vagotomized dog, they increased pADH. Data regarding AVP secretion during manipulation of carotid baroreceptors in humans are limited. Hammer & Engell (1982) demonstrated an increase in pAVP during operative manipulation of the left common carotid artery on a patient undergoing surgery. This indicated that in man, carotid sinus baroreceptors may directly influence the AVP secretion.

As previously mentioned, it has been discussed in the literature whether cardiopulmonary mechanoreceptors and/or arterial baroreceptors may influence AVP secretion. In man, several lines of evidence suggest that a decrease in arterial pressure stimulates AVP secretion (Baylis & Heath 1977; Wiggins et al. 1977; Robertson 1983). This is in compliance with our discovery that termination of NS in three subjects induced increases in pAVP of the same magnitude as observed during hypotensive states. Other factors than unloading of the carotid baroreceptors might have accounted for this increase. If e.g. the vagus nerve was directly affected in some way during termination of NS this could have induced cardiovascular reflexes eliciting profound AVP secretions.

In our study there were no consistent changes in cardiovascular parameters before, during and after termination of NS except for a very small increase in SAP after 20 min of NS compared to prestudy values (Fig. 1 and 2). Abboud et al. (1979) measured a decrease in HR during NS for 60 to 120 sec with the subjects in the supine position. We measured HR every 5 min and did not measure this parameter within the first 5 min after start of NS. It is therefore conceivable that an initial drop in HR occurred during NS, but that it was abolished after a few minutes.

The symptoms resembling a condition of orthostatic intolerance occurring in two of our subjects during NS may be explained by a decrease in total peripheral vascular resistance due to dilation of vessels in the skeletal muscles and the splanchnic area (Abboud et al. 1979; Skagen et al. 1985). This is supported by the decrease in plasma volume of 3.3% after 20 min of NS. However, arterial pressures were affected very little by NS, but this should be cautiously interpreted as we did not measure these parameters continuously by intraarterial means.

In conclusion, NS with a negative pressure of 3.3 kPa in upright sitting and slightly dehydrated man did not suppress pAVP. There were no concomitant changes in plasma electrolytes,
pOSM, HR, DAP or CVP. SAP increased very little and PV decreased compared to prestudy values. In three subjects, termination of NS increased pAVP considerably. This may be explained by a direct effect on the vagus nerve or by a selective unloading of carotid baroreceptors.

Acknowledgments

This investigation was supported by the Danish Space Board grant No. 1112-12/85. The assistance of Karsten W. Hartmann, Søren Toubrø, Marianne Hemmingsen, and Elsa Larsen is gratefully acknowledged.

References


