Clinical Neurophysiology Practice 3 (2018) 91–95

Contents lists available at ScienceDirect

Clinical Neurophysiology Practice

journal homepage: www.elsevier.com/locate/cnp

Research paper

Cerebral blood flow changes during tilt table testing in healthy volunteers, as assessed by Doppler imaging of the carotid and vertebral arteries

C. (Linda).M.C. van Campen [a], Freek W.A. Verheugt [b], Frans C. Visser [a,*]

[a] Stichting CardioZorg, Planetenweg 5, 2132 HN Hoofddorp, The Netherlands
[b] Radboud UMC, Geert Grooteplein Zuid 10, 6525 GA Nijmegen, The Netherlands

ARTICLE INFO

Article history:
Received 19 January 2018
Received in revised form 17 February 2018
Accepted 20 February 2018
Available online 23 March 2018

Keywords:
Cerebral blood flow
Head-up tilt table test
Healthy volunteers
Internal carotid artery blood flow
Vertebral artery blood flow
PetCO2

ABSTRACT

Objectives: Using different techniques, reduction of cerebral blood flow (CBF) during orthostatic stress were demonstrated. One study reported flow reduction of the right internal carotid (ICA) and vertebral (VA) artery during orthostatic stress by Doppler imaging, with different effects on the 2 vessels. Global CBF changes, using this technique, have not been reported. Therefore, flow of the ICA, VA and global CBF were measured during head-up tilt testing.
Methods: 33 healthy volunteers underwent tilt testing. At three time points (supine, half way and at the end of the test) Doppler imaging of the ICA and VA was performed, as well as PetCO2 measurements.
Results: Global CBF was significantly reduced by 4.5 ± 2.8% halfway the test and by 6.0 ± 3.4% at the end. All 4 artery flows were significantly reduced during the tilt, without differences between them. Despite small changes in PetCO2 there was a significant relation between de CBF decrease and PetCO2 decrease ($p < 0.05$).
Conclusions: Orthostatic stress in HV results in a small but significant reduction of CBF by a homogenous reduction in the four cerebral vessels and is modulated by PetCO2 changes.
Significance: CBF changes can be measured during tilt testing using Doppler VA and ICA imaging.

1. Introduction

Positional changes from supine to sitting or standing result in a decrease of cerebral blood flow (CBF) as demonstrated by different techniques (Yoshimoto et al., 1994; Ouchi et al., 2001; Oblak et al., 2002; Alperin et al., 2005; Wang et al., 2010; Bronzwaer et al., 2014). CBF measurements by extracranial Doppler echography of the internal carotid and vertebral arteries (ICA and VA) in the supine position have been described in a number of studies (Schoning et al., 1994; Deane and Markus, 1997; Seidel et al., 1999; Dorfler et al., 2000; Scheel et al., 2000; Yazici et al., 2005; Oktar et al., 2006; Albayrak et al., 2007; Nemati et al., 2009; Nevo et al., 2010; Sato et al., 2012; Liu et al., 2013). Using this technique the decrease in CBF during head up tilt table testing was also demonstrated in one small study (Sato et al., 2012) of healthy volunteers (HV). The authors studied only the right ICA and VA before and during tilt testing and reported a difference in vasculature response to the orthostatic stress of the right ICA and VA: the decrease in right VA blood flow after tilting was not significant from supine, in contrast to the significant decrease of the right ICA blood flow of 9.4% (Sato et al., 2012).

As total CBF changes during tilting have not been reported before, the aim of the study was to measure both left and right ICA and VA blood flows in a large group of HV before and during tilting, allowing assessment of total CBF changes during tilting.

2. Subjects, material and methods

2.1. Subjects

Initially 41 HV underwent head up tilt table testing (HUT). None had signs or symptoms of cerebral- and cardiovascular disease, the electrocardiogram (ECG) and echocardiogram were normal. One HV with a delayed orthostatic hypotension (OH) and profound hypocapnia and 1 with a vasovagal syncope were excluded. Furthermore, 3 HV were excluded because of an insufficient Doppler image quality. In three HV the right or left VA were hypoplastic (2 right and 1 left VA) defined by a supine flow <30 ml/min (Schoning et al., 1994). These HV were also excluded, leaving 33

* Corresponding author.
E-mail address: fransvisser@stichtingcardiozorg.nl (F.C. Visser).

https://doi.org/10.1016/j.cnp.2018.02.004
2467-981X/© 2018 International Federation of Clinical Neurophysiology. Published by Elsevier B.V.

HV included in this study. Three times after tilting (directly post tilt, at 10 and 20 min post tilt) HV were asked for dizziness/light-headedness. Seven (21%) reported dizziness/light-headedness directly post tilting, at 10 min complaints were present in 3 (9%), and after 20 min these complaints were absent in all. All had a normal heart rate and blood pressure response during HUT, none had a postural orthostatic tachycardia syndrome (POTS) (Task Force for the et al., 2009; Freeman et al., 2011). The study has been carried out in accordance with Declaration of Helsinki. All HV gave informed consent, the study was approved by the MEC of the Slotervaart hospital in Amsterdam.

2.2. Methods

HV underwent HUT with 20 min in the supine and 25–30 min in the upright position (70 degrees). They were investigated in the morning, at least 3 h after a light breakfast or in the afternoon 3 h after a light lunch. No formal hydration protocol was applied, but subjects were asked to ingest an ample amount of fluid.

Heart rate (HR), systolic, diastolic and mean blood pressures (SBP, DBP and MAP) were continuously recorded by finger plethysmography using the Nexfin device (BMeye, Amsterdam, NL). Using an independent radio-controlled clock the starting time of HR and BP recording as well as the time of the start of tilting was noted. HR and blood pressures were extracted from the Nexfin device and imported into an Excel spreadsheet. HR and blood pressures at the radio clock corrected echo time intervals (see below) were averaged.

ICA and VA Doppler frames were acquired by one operator (FCV), using a Vivid-I system (GE Healthcare, Hoevelaken, NL) equipped with a 6–13 MHz linear transducer. Flow data of the ICA were obtained ~1.0–1.5 cm distal to the carotid bifurcation and of the VA at the C3–C5 level. Care was taken that the insonation angle was less than 60 degrees, that the sample volume was positioned in the center of the vessel and that it covered the width of the vessel. High resolution B mode images, color Doppler images and the Doppler velocity spectrum (pulsed wave mode) were recorded in one frame. The order of imaging was fixed: left ICA, left VA, right ICA, and right VA. At least 2 consecutive series of 6 s per artery were recorded. Moreover the recording time of the first and last analyzed artery was noted. These times were corrected to the times of the radio clock.

In the supine position image acquisition started 8 ± 1 min prior to tilting (supine data) and during the upright position 2 series were acquired: one series was started at 13 ± 3 min (mid HUT data) and one at 24 ± 3 min. (end HUT data). Image acquisition lasted 4.0 ± 1.5 min.

During the study period end-tidal PCO2 (PetCO2) was monitored using a Lifesense device (Nonin Medical, Minneapolis USA).

2.3. Data analysis

Calculations of blood flow were performed by one operator (CMCvC). Automated mean blood flow velocities (MFV) were obtained. Vessel diameters were manually traced by CMCvC and FCV independently on B-mode images, from the intima to the opposite intima. Differences in vessel diameter were resolved by consensus. Surface area was calculated as proposed by Sato et al. (2011): the peak systolic and end diastolic diameters were measured, and the mean diameter was calculated as: mean diameter = (peak systolic diameter × 1/3) + (end diastolic diameter × 2/3). Arterial flow was calculated from the mean blood flow velocity × the surface area. Flow in the individual arteries was calculated in 3–6 cardiac cycles and data were averaged. Total CBF was calculated by adding the flow of the 4 arteries.

End tidal CO2 measurements were imported into an Excel spreadsheet and PetCO2 data at the radio clock corrected echo time intervals were averaged.

2.4. Statistical analysis

Data were analyzed using SPSS 21. Distribution of data was tested by the Mann Whitney test. As all data were normally distributed, the data are presented as the mean ± SD. A p value < 0.05 was considered significantly different. HUT mid data and HUT end data were compared to supine date using paired-samples t-tests. Linear regression analysis was performed between the change in PetCO2 and the %CBF change at the end of the study. For reproducibility measurements intraclass correlation coefficients (ICC's) were calculated using SPSS. Both ICA and VA mean flow velocities, diameters and flows were recalculated for 21 ICA and for 10 VA cycles. For intra-observer variation data were analyzed at least 3 month after the first assessment by CMCvC, for inter-observer variation FCV also performed the measurements.

3. Results

33 healthy volunteers participated. Included were 9 males and 24 females with a mean age of 41 ± 16 years. BMI was 25 ± 5 kg/m^2, BSA (Du Bois) 1.87 ± 0.18 m^2. No differences were found between morning and afternoon sessions (data not shown).

The ICC's for intra-observer variation of the ICA flow velocity, diameter and flow were 0.99, 0.78 and 0.86, respectively. For the VA these values were 0.97, 0.91 and 0.92, respectively.

The ICC's for inter-observer variation of the ICA flow velocity, diameter and flow were 0.99, 0.82 and 0.87, respectively. For the VA these values were 0.97, 0.80 and 0.91, respectively.

Table 1 shows the measurements of hemodynamics, PetCO2 data, and cerebral flow data in the supine position, at 13 min post tilt (mid HUT data) and at end of the tilt period (end HUT). Heart rate significantly increased by mean 16 bpm during tilting, systolic blood pressure decreased mean 8 mmHg at the end of HUT. Dias-

Table 1
Hemodynamic and cerebral flow measurements during tilt testing.

	Supine	Mid HUT	End HUT
Heart rate (bpm)	61 ± 10	78 ± 16****	77 ± 16****
SBP (mmHg)	135 ± 14	128 ± 15*	127 ± 15***
DBP (mmHg)	78 ± 7	81 ± 9 ns	80 ± 8 ns
MAP (mmHg)	100 ± 10	97 ± 12 ns	98 ± 11 ns
PetCO2 (mmHg)	37 ± 3	35 ± 3****	36 ± 3***
Total CBF (ml/min)	638 ± 77	609 ± 75****	599 ± 74****
ICA-L blood flow (ml/min)	245 ± 47	234 ± 50****	232 ± 44****
ICA-R blood flow (ml/min)	237 ± 41	225 ± 37****	220 ± 41****
VA-L blood flow (ml/min)	88 ± 27	85 ± 28	83 ± 28*
VA-R blood flow (ml/min)	68 ± 24	65 ± 23**	64 ± 23**
ICA-L flow velocity (cm/s)	24.7 ± 5.1	23.3 ± 5.6	24.9 ± 5.3
ICA-R flow velocity (cm/s)	25.2 ± 5.2	25.0 ± 4.8	24.2 ± 4.9
VA-L flow velocity (cm/s)	16.8 ± 3.4	17. ± 3.7	16.6 ± 4.4
VA-R flow velocity (cm/s)	15.5 ± 4.3	14.7 ± 3.6*	14.8 ± 3.8
ICA-L diameter (mm)	4.63 ± 0.46	4.47 ± 0.58**	4.49 ± 0.50*
ICA-R diameter (mm)	4.50 ± 0.50	4.40 ± 0.46	4.43 ± 0.51
VA-L diameter (mm)	3.29 ± 0.45	3.24 ± 0.54	3.25 ± 0.52
VA-R diameter (mm)	3.06 ± 0.49	3.05 ± 0.52	3.05 ± 0.50

CBF = cerebral blood flow, DBP = diastolic blood pressure, ICA = internal carotid artery, MAP = mean arterial pressure, SBP = systolic blood pressure, VA = vertebral artery.
* p < 0.05 versus supine.
** p < 0.01 versus supine.
*** p < 0.005 versus supine.
**** p < 0.001 versus supine.