Sympathetic Vasomotor Response Of The Radial Artery In Patients With End Stage Renal Disease

L Galea, M Schembri, M Debono

Citation

L Galea, M Schembri, M Debono. *Sympathetic Vasomotor Response Of The Radial Artery In Patients With End Stage Renal Disease*. The Internet Journal of Nephrology. 2004 Volume 2 Number 1.

Abstract

Background: A novel way to assess the autonomic vascular functional unit of the upper extremity is the sympathetic vasomotor response of the radial artery using continuous wave Doppler ultrasonography. We used this method to determine whether such response is impaired in patients with end stage renal disease (ESRD).
Methods: 43 patients with ESRD on renal replacement therapy(Ga), 48 normal healthy subjects(Gc1) and 28 patients with diabetes mellitus and/or hypertension, serum creatinine levels <1.13mg/dL (100µmol/l) and with no evidence of nephropathy(Gc2) underwent continuous wave Doppler examination of the radial artery before and after cough using Bidop ES-100V3® (8MHz probe). The maximal change in waveform after cough was recorded. The resistance index was calculated as systolic velocity minus diastolic velocity/systolic velocity. The pulsatility index was calculated as peak to peak change/mean flow velocity.
Results: The resistance index after cough as a ratio of the baseline (RI) in Gc1 increased significantly (0.21±0.19) as opposed to Ga (0.02±0.07), the mean difference between the two groups being 1.93±0.29 (CI: 1.36,2.51 p<0.001). The pulsatility index after cough as a ratio of the baseline (PI) in the Gc1 increased significantly (1.93±2.09) as opposed to Ga (0.36±0.56), the mean difference between the two groups being 1.56 SD 0.31 (CI: 0.94,2.19 p<0.001). There was no significant difference in RI and PI between Ga and Gc2.
Conclusion: Patients with ESRD have impaired sympathetic vasomotor response of the radial artery after cough.

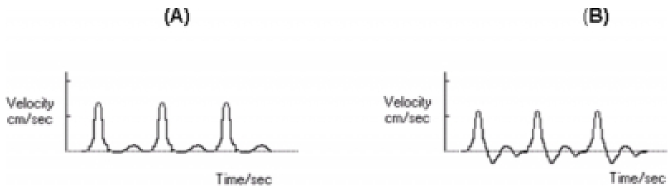
BACKGROUND

Neurophysiological assessment of the peripheral autonomic system is characterized by various limitations (1). A novel approach to assess the autonomic vascular functional unit of the upper extremity makes use of continuous wave Doppler ultrasonography (CWD) by assessing the sympathetic vasomotor tone of the radial artery (2).

The sympathetic vasomotor response can be tested reliably at an easily accessible superficial artery such as the radial artery using basic Doppler equipment. After adequate sympathetic stimulation (cough, inspiration, acoustic, or electric) and transmission by an intact peripheral sympathetic system, an age-independent vasoconstrictor response is observed in the Doppler waveform being sampled at the radial artery (3). Figure 1 below shows the difference in blood flow velocity waveforms before and after stimulation in a normal sympathetic vasomotor response. Note the reversed diastolic flow after cough.

Figure 1

Figure 1: The normal sympathetic response at the radial artery. A) before stimulation, B) after stimulation.



The aim of this study was to assess the sympathetic response of the radial artery in patients with ESRD after sympathetic stimulation. The data obtained were compared with normal healthy volunteers and control patients who suffer from diabetes mellitus and/or hypertension.

PATIENTS AND METHODS

PATIENTS AND SUBJECTS

43 patients with end stage renal disease (Ga) who have started renal replacement therapy (RRT) were included in the study. 25 were males and 18 were females (mean age 63

, range 29-81).17 were on chronic haemodialysis and 17 were on chronic ambulatory peritoneal dialysis. The mean number of months on RRT was 19, range 1-98. 16 patients suffered from diabetes mellitus (DM) and hypertension (HT), 12 patients had HT but no DM, 5 patients had DM but no HT, and 10 patients had neither DM nor HT.

48 healthy normal volunteers (Gc1) were included for comparison of data. 28 were males and 20 were females (mean age 32, range 22-57). 28 patients with diabetes mellitus and/or hypertension, serum creatinine levels <1.13mg/dL (100μmol/l) and with no evidence of diabetic and/or hypertensive nephropathy formed group Gc2. 18 of these were males and 10 were females (mean age 63, range 40-78). Patients in the latter group were matched with patients in Ga for age, gender, DM, HT and side –dominant or nondominant- were the Doppler examination was carried out.

Patients who had already failed bilateral wrist arteriovenous fistulas, had valvular heart disease, uncompensated heart failure, atrial fibrillation or were on Beta blockers were excluded from the study. Current smokers or who stopped smoking one month or less from index examination were also excluded. Informed consent was obtained from all patients and subjects. The study was approved by the local research ethics committee.

METHOD

A continuous wave Doppler ultrasound machine (Bidop ES-100V3 ®) with an attached 8MHz probe was used for the study. It was calibrated once at the beginning of the study. Its accuracy is up to ±10% or less. All the examinations were carried out by a single author who had a month period of training in the procedure before the commencement of the study.

Continuous wave Doppler examination of the radial artery before and after cough was performed on all patients and subjects. The maximal change in waveform after cough was recorded. Where possible, the non-dominant upper extremity (ND) was used for the examination. If patients had failed or had functioning wrist arteriovenous fistula in the ND, the dominant upper extremity was used for the examination.

Patients were in the sitting position with the forearm to be examined resting on the thigh. The Doppler probe was held at a 60o angle to the skin. The systolic velocity (cm/sec), mean flow velocity (cm/sec), diastolic velocity (cm/sec), resistance index (systolic velocity minus diastolic velocity divided by systolic velocity), pulsatility index (peak to peak change divided by mean flow velocity), the pulse rate (bpm) were recorded three times in successive manner from the radial artery at the wrist near the level of the radial styloid process at the point of maximal pulsation. The average of the three sets of readings was used for data analysis.

Patients were then asked to cough without moving their hands The same parameters were recorded at the point of maximal change in waveform after cough. This was repeated after another two more coughs, each separated by one minute. The average of the three sets of readings was used for data analysis.

The independent student t-test for equal and unequal variances was used for analysis of data using SPSS version 12.0. Statistical significance was assumed if the P value was <0.05.

RESULTS

BASELINE

Before cough, subjects in Gc1 had significantly higher systolic velocity (S), diastolic velocity (D) and mean flow velocity (MV) than group Ga as shown in table 1. However, patients in Ga had a significantly higher pulsatility index (PI) and a higher resistance index (RI) than Gc1 (Table 1).

Figure 2

Table 1: Baseline systolic velocity (S) / cm sec-1, diastolic velocity (D) / cm sec-1, mean flow velocity (MV) / cm sec-1, pulsatility index (PI) and resistance index (RI) in Ga and Gc1. Data are means ± standard deviation.

	Ga	Gc1	P value
S	17.6 +/- 7.5	21.4 +/- 7.0	0.015
D	0.5 +/- 3.6	4.5 +/- 4.1	<0.001
MV	2.8 +/- 2.2	8.1 +/- 5.2	<0.001
PI	11.9 +/- 9.2	3.6 +/- 2.8	<0.001
RI	1.0 +/- 0.1	0.8 +/- 0.1	<0.001

There was no significant difference in baseline S, D, PI and RI between Gc2 and their controls from Ga as shown in table 2. However, patients in Gc2 had a significantly higher MV than their controls from Ga (table 2).

Figure 3

Table 2: Baseline systolic velocity (S) / cm sec-1, diastolic velocity (D) / cm sec-1, mean flow velocity (MV) / cm sec-1, pulsatility index (PI) and resistance index (RI) in Ga (matched patients) and Gc2. Data are means ± standard deviation.

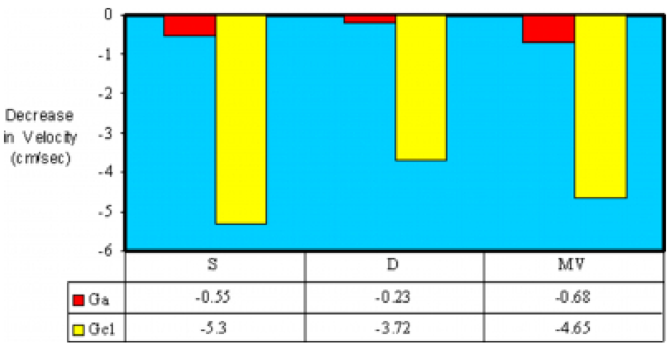
	Ga	Gc2	P value
S	20.5 +/- 7.1	17.5 +/- 8.2	0.230
D	3.1 +/- 2.1	1.6 +/- 2.4	0.116
MV	0.5 +/- 1.0	4.2 +/- 3.9	0.024
PI	11.9 +/- 8.9	9.2 +/- 8.2	0.058
RI	1.0 +/- 0.1	0.9 +/- 0.1	0.126

STIMULATION

After cough there was a significant difference in the decrease in S in Ga compared to Gc1 (0.55 ± 3.81 vs. 5.03 ± 6.03, P <0.001, 95% CI 2.40, 6.56). Also, the decrease in D was much less in Ga than Gc1 after cough (0.23 ± 0.99 vs. 3.72 ± 3.57, P <0.001, 95% CI 2.41, 4.56). After cough, MV decreased much less in Ga than in Gc1 (0.68 ± 1.20 vs. 4.65 ± 4.53, P <0.001, 95% CI 2.61, 5.33) (Figure 2).

Figure 4

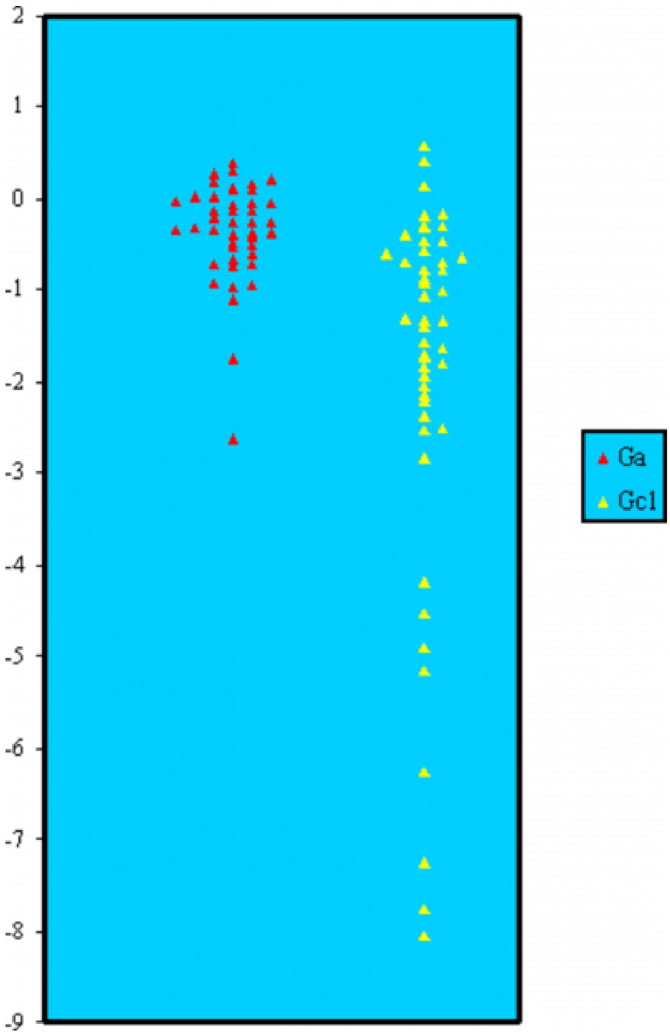
Figure 2: Decrease in systolic velocity (S) / cm sec-1, diastolic velocity (D) / cm sec-1 and mean flow velocity (MV) / cm sec-1 after cough in Ga and Gc2.



There was a significant difference in the increase in PI after cough as a ratio of the baseline in Ga when compared with Gc1 (-0.36 ± 0.56 vs. -1.93 ± 2.09, P <0.001, 95% CI 0.94, 2.19) (Figure 3).

Figure 5

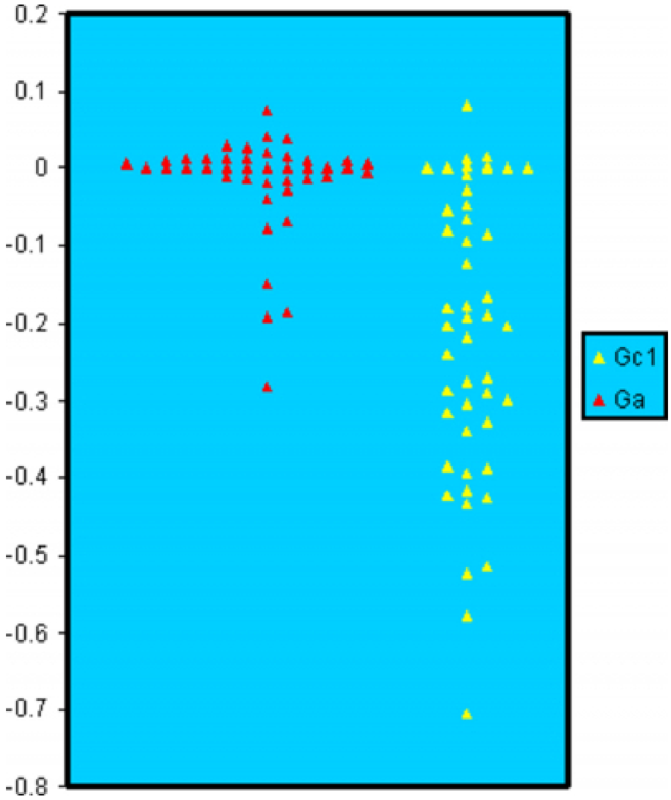
Figure 3: Change in Pulsatility Index (PI) after cough as a ratio of the baseline in Ga and Gc2.



Also, there was a significant difference in the increase in RI after cough as a ratio of the baseline in Ga when compared with Gc1 (-0.02 ± 0.07 vs. –0.21 ± 0.19, P <0.001, 95% CI 1.36, 2.51) (Figure 4).

Figure 6

Figure 4: Change in Resistance Index (RI) after cough as a ratio of the baseline in Ga and Gc2.



There was no significant difference in the change in S (P=0.09, 95% CI 0.03, 4.14), D (P=0.06, 95% CI 0.03, 1.39), MV (P=0.06, 95% CI 0.03, 2.00), PI as a ratio of the baseline (P=0.07, 95% CI 0.07, 1.52) and RI as a ratio of the baseline (P=0.08, 95% CI 0, 0.10) between Gc2 and their controls from Ga (data not shown).

CONCLUSIONS

Our results show that patients with ESRD have flow velocity profiles which differ considerably from the healthy controls. The baseline flow profile of patients with ESRD revealed a lower diastolic velocity and a higher pulsatility index than the normal controls. This may be due to the greater rigidity of the vessels due to arterial calcification of the media which has been observed in diabetic patients ([4]).

The value of neurophysiological tests of the autonomic nerve system is limited. The sympathetic skin response (SSR), one of the routinely employed methods for evaluating the autonomic function of peripheral nerves is more of a qualitative technique. Eicke BM et al compared SSR with CWD of the radial artery in healthy subjects. The stimulus was a loud and unexpected acoustic signal or a cough. They showed a decrease in systolic velocity and diastolic velocity, and an increase in resistance index in 85% of subjects and SSR was observed in 88% of subjects. They concluded that CWD allows an additional approach to autonomic nerve evaluation ([3,5]). Wenderhold et al concluded that CWD can be used to allow easy quantitative assessment of autonomic nerve lesions. They showed a reduction of systolic, diastolic and mean flow velocity in most of the healthy subjects after electrical and acoustic stimulation as well as after inspiratory cough. However, changes in blood flow could not be observed in patients with lower brachial plexus lesions ([6]).

To our knowledge this is the first study that makes use of CDW to assess the autonomic vascular functional unit of the upper extremity in patients with ESRD. In our study we excluded patients with valvular heart disease, uncompensated heart failure and atrial fibrillation due to the great variation in subsequent waveforms which in turn reflected on the wide variation in blood velocity patterns including pulsatility index. For example a patient with aortic regurgitation had extremely high pulsatility index due to the large negative diastolic flow. Patients taking Beta blockers were excluded due to the effect of such medications on the sympathetic nerve endings. Current smokers or who stopped smoking one month or less from index examination were excluded to eliminate the eventual effect of nicotine on the sympathetic nervous system as a confounding factor.

The present study showed that patients with ESRD have an impaired sympathetic vasomotor response of the radial artery when compared with the normal controls. However, there was no statistically significant difference between patients with DM and/or HT when compared to patients with ESRD with DM and/or HT. This implies that the impaired sympathetic response in patients with ESRD is largely the effect of DM and possibly hypertension with the renal disease per se playing a less important role.

A primary recommendation of the National Kidney Foundation published as Dialysis Outcomes Quality Initiative is to maximize the number of primary arteriovenous fistula. Some studies showed that brachial plexus block increased blood flow through the brachial artery by giving a temporary sympathectomy type effect and helped in increasing primary patency rates ([7,8]). However, patients with ESRD who have impaired sympathetic vasomotor response of the radial artery, brachial plexus block may not prove to be helpful in this regard. A further study may help in proving or disproving this hypothesis.

CORRESPONDENCE TO

Laurence Galea 35, Visitation Street, Gharb, Gozo, Malta, GRB 102. E-mail : laurgalea@hotmail.com

References

1. Gilmore JE, Allen JA, Hayes J: A comparison of peripheral vasoconstrictor responses and cardiovascular autonomic function tests in diabetic patients. Diabetologia 33:350-356, 1990.
2. Muck-Weymann M, Kalb R, Heckmann J, von den Driesch P: Inspiration triggered vasoconstrictive episodes in healthy subjects, in patients with diabetes mellitus and in patients with clinically manifest polyneuropathy of variable origin. A simple Doppler ultrasound test to assess autonomic vascular unit of the upper extremity. Med Klin (Munich) 92:249-54, 1997.
3. Eicke BM, Bauer J, Mink S, et al : Sympathetic vasomotor response of the radial artery in patients with diabetic foot syndrome. Diabetes care 26:2616-21, 2003.
4. Bernardi D, Ferreri A, Bortoli P et al. : Use of Doppler flow velocity waveform analysis in detection of initial diabetic microangiopathy. Angiology 41:877-883, 1990.
5. Eicke BM, MinkS, Kullmer K, Krummenauer F : Comparison of the sympathetic skin response and continuous wave Doppler sonography of the radial artery. J Auton Nerv Syst 75:202-6. 1999.
6. Wenderhold W, Kunkel M, Eicke BM, Reimers CD: Continuous wave Doppler ultrasound in the evaluation of vasomotor tone of the radial artery. Eur J Ultrasound 10:11-20. 1999.
7. Mouquet C, Bitker MO, Bailliart O, et al :Anaesthesia for creation of a forearm fistula in patients with end stage renal failure. Anaesthiology. 70 : 909-914, 1989.
8. Shemesh D, Zigelman, Olsha O, Alberton J, Shapira J, Abramowitz H : Primary forearm arteriovenous fistula for hemodialysis access - an integrated approach to improve outcomes. Cardiovasc Surg. 11:35-41, 2003.

Author Information

Laurence Galea, M.D.
Senoir House Officer, Department of Surgery, St. Luke's Hospital

Mark Schembri, FRCS
Consultant General and Vascular Surgeon, Department of Surgery, St. Luke's Hospital

Miguel Debono, MRCP
Senior House Officer, Department of Medicine, St. Luke's Hospital