An automated computerized method using Finapres for measuring cardiovascular reflexes


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(Received 17 December 1991/18 March 1992; accepted 31 March 1992)

INTRODUCTION

Cardiovascular reflex tests based on heart rate and blood pressure variability during forced breathing, standing up, the Valsalva manoeuvre and sustained handgrip are most commonly used to detect diabetic autonomic neuropathy [1, 2]. Because much time is required to elaborate the test results, automated programs have been developed, so far on a limited scale, using heart rate variability recorded with an ECG [3, 4]. Using a Finapres (from FINger Arterial PRESSure) instrument, heart rate (beats/min) and blood pressure (mmHg) can continuously be recorded from the finger non-invasively. The Finapres is based on servopletysmomanometry, employing the volume clamp technique [5–7]. The total finger arterial volume under an unloading finger cuff is measured with an infrared plethysmograph and despite changes in intra-arterial pressure this volume is clamped by modulating cuff pressure in parallel with intra-arterial pressure using a wide bandwidth electro-pneumatic servo-system. During actions such as the Valsalva manoeuvre, sustained handgrip and postural changes, the brachial to finger pressure differs only quantitatively, but the pattern of blood pressure changes is similar [8, 9].

By connecting the Finapres to a personal computer, the opportunity exists to develop an automated program for the calculation of the test results within a short period of time.

METHODS

The Finapres (Finapres model 5; TNO, Amsterdam, The Netherlands) was connected to an IBM-compatible computer using normal co-axial or shielded cable with a standard BNC connector. In Turbo Pascal 3.0 (Borland International Inc, Scotts Valley, CA, U.S.A.) a program was written based on a timeclock. Before each test the clock was started and the recorded digital signal of the Finapres was used to calculate the programmed test results. The manoeuvres were performed after rest and in the posture described by Wieling and co-workers [10, 11]. Before the start of the test, the subjects were trained to perform the manoeuvres correctly. The Finapres cuff was wrapped around the middle finger of the non-dominant arm, which was fixed at heart level. Control systolic blood pressure, diastolic blood pressure, mean blood pressure and heart rate were calculated as the mean values during the 30 s before the onset of each manoeuvre.

Forced breathing

The subjects performed six consecutive maximal respirations in the supine position at a rate of six breaths/min after 5 min of supine rest. Within 1 s of
Inspiration - H - H-

Fig. 1. Finapres recording during forced breathing. The systolic blood pressure and diastolic blood pressure are measured in mmHg. The heart rate is computed by the Finapres instrument by measuring the time between two upstrokes. The graph of the heart rate variability recorded by the personal computer is shown as the upper part of the Figure. The mean difference between the highest and lowest heart rate during each of the six respirations is calculated (I-E difference).

the start of inspiration the heart rate rises quickly to a peak at about 3s before maximal inspiration and a minimal heart rate is reached about 6s after the beginning of expiration (Fig. 1). During this test the subjects synchronized inspiration and expiration with the program clock on the computer monitor. The difference between maximal and minimal heart rate thereafter (inspiration—expiration difference, I-E difference) during each 10s cycle was measured and averaged for six cycles [1, 12, 13].

Standing up

Standing up was started on a verbal command, after 5min of supine rest. The manoeuvre was performed in 2–3s and the subjects remained in the upright position for 2min.

The blood pressure response to standing is shown in the lower part of Fig. 2. After an initial jump following the performance of the manoeuvre, the blood pressure decreases to a minimum at about 8–10s after standing up. Thereafter a blood pressure overshoot is seen [14]. The program calculated the difference between averaged systolic (ΔBPsys.) and diastolic (ΔBP dias.) blood pressure between 50 and 80s after standing up and during the control period.

Standing up evoked an immediate sharp increase in the heart rate to a peak occurring at about 15–20s. Thereafter heart rate decreased rapidly to the control level [15] (Fig. 2, upper part). The difference between maximum heart rate after standing up and control heart rate (ΔHRmax.) and the quotient of maximum heart rate and minimum heart rate after standing up (tachycardia/brady-cardia ratio, T/B ratio) were calculated [16, 17].

Valsalva manoeuvre

The subjects were instructed to maintain an expiratory pressure of 40mmHg during 15s, by means of forced expiration into a mouthpiece connected to a sphygmomanometer. Closure of the glottis was prevented by a small leak to maintain a flow of air. The manoeuvre was performed three times in the sitting position, each after 1min rest.

The cardiovascular responses to a Valsalva manoeuvre can be divided into four phases [18] (Fig. 3). Immediately after the onset of the manoeuvre, a brisk rise in systolic and diastolic arterial blood pressure and a reduction in heart rate are seen (phase I). After 4s a fall and subsequent partial recovery of arterial blood pressure and an increase in heart rate characterize phase II. Immediately after the release of straining a sudden, brief (1–2s) further reduction in arterial blood pressure and an elevation of heart rate occur (phase III). In phase IV, an elevation of systolic and diastolic arterial blood pressure above control level (overshoot) is seen, accompanied by a bradycardia relative to the control heart rate.

Although the cardiovascular responses to a Valsalva manoeuvre are complex, the computer program calculated only the Valsalva ratio, defined by the maximum heart rate during the manoeuvre divided by the minimum heart rate after the manoeuvre [19, 20].
Fig. 2. Finapres recording and graph of the variation in heart rate recorded by the personal computer during standing up. The highest heart rate after standing up divided by the lowest thereafter is the T/B ratio. The arrow indicates the beginning of the standing up manoeuvre.

Fig. 3. Finapres recording and graph of the heart rate variability recorded by the personal computer during the Valsalva manoeuvre. The highest heart rate during the manoeuvre (A) divided by the lowest heart rate after the manoeuvre (B) is the Valsalva ratio (I, II, III and IV indicate the four different phases, see the text).
Sustained handgrip

Three minutes of squeezing a calibrated handgrip dynamometer at 30% of maximal voluntary contraction in the sitting position was performed, 2 min after the last Valsalva manoeuvre. During this isometric exercise, heart rate, systolic blood pressure and diastolic blood pressure increase. The difference between the average maximum diastolic blood pressure over 5 s during the handgrip and baseline value (delta BPdias.) was calculated [21].

Statistics

Statistical analysis was performed using the SAS software package (Statistical Analysis Systems, Cary, NC, U.S.A.). Methods included a two-sample t-test to determine the difference in test results between men and women. Calculation of a Pearson correlation coefficient was used to assess the relationship between parameters of autonomic function and age. For each test parameter, a mean and 5th and 95th percentiles were calculated.

The reproducibility of repeated tests was determined as the coefficient of variation (CV) = 100% × seSO/[[(1 × (mean first test + mean second test)], where seSO is the standard error of a single observation and is calculated by the formula:

\[ \text{seSO} = \sqrt{\frac{\sum_{i=1}^{n} (X_{1i} - X_{2i})^2}{2n}} \]

in which \( X_{1i} - X_{2i} \) is the difference between the first and the second test \( X \) in subject \( i \) and \( n \) is the number of paired observations.

RESULTS

Reproducibility

In 21 healthy subjects (age 22–32 years) the tests were performed on two different occasions, under standardized conditions in a climate room (mean temperature 24.3 ± 0.3°C). The subjects had normal blood pressure (<130/80 mmHg), regular heart rate and were without medication. Each subject was tested at the same time of the day. All the subjects refrained from caffeine- or alcohol-containing beverages for 12 h before the test, and the three smokers also refrained from smoking on the day of the test. The seSO and CV of the control blood pressure and heart rate before each manoeuvre were respectively between 2.6 and 7.0% and 4.4 and 9.1%. In eight normal subjects the tests were performed by the conventional method, using an ECG and a sphygmomanometer. The seSO and CV of the test parameters in these two groups are shown in Table 1. With the exception of \( \Delta \text{BPsys.} \) during the standing up test, reproducibility was moderate to good. Although the blood pressure parameters were slightly more reproducible with the automated program, no significant differences were noted.

Normal values

A total of 124 healthy normal subjects (66 males and 58 females) were studied. The subjects were reasonably distributed according to age and sex, except that in the age category over 80 years there were only three men. Diabetic patients were excluded, as were those with cardiovascular disease and those taking drugs known to affect heart rate or blood pressure. The blood pressure was normal according to WHO criteria and all subjects had a regular pulse. None of the subjects complained of Raynaud’s phenomenon or had other abnormalities of the hand and fingers.

Forced breathing. The mean \( I-E \) difference was age-dependent. Fig. 4(a) shows the relation between age and mean with 5th and 95th percentiles.

Standing up. Heart rate variability during standing up was age-dependent. A sex difference was found for \( \Delta \text{HRmax.} \) (\( P<0.02 \), Fig. 4b), but not for the \( T/B \) ratio (Fig. 4c). The 5th percentiles of \( \Delta \text{BPsys.} \) and \( \Delta \text{BPdias.} \) were respectively -3.2 and 0.7 mmHg.

Valsalva manoeuvre. Fig. 4(d) shows the mean with 5th and 95th percentiles of the highest Valsalva ratio of the three Valsalva manoeuvres performed. The ratio appeared to be age-dependent.

Sustained handgrip. Delta BPdias. (\( P<0.0001 \)) was sex-dependent, but age did not influence the test results. The 5th percentile of the delta BPdias. for men was 7.8 mmHg and for women it was 6.8 mmHg.

Diabetic patients

Using this program 10 patients with longstanding (14–34 years) complicated diabetes were studied. Three patients (two females aged 29 and 30 years...
and a male aged 50 years complained of orthostatic hypotension. The other patients had severe diabetic neuropathy of the legs, no vibration sense and absent knee and ankle jerks. Each patient had more than four abnormal results (below the 5th percentile corrected for age and gender, Table 2). The heart rate parameters were more often abnormal than the results of tests based on the variability in blood pressure. In this group of diabetic patients the $I - E$ difference, $\Delta HR_{\text{max}}$, $T/B$ ratio and the
Valsalva ratio were always below the 5th percentiles of normal.

**DISCUSSION**

We have developed an automated program to detect diabetic autonomic neuropathy, using a personal computer and a Finapres to record blood pressure and heart rate variability during standard cardiovascular reflex tests. Within 25 min the tests can be performed and the results calculated.

The blood pressure profile is printed by the Finapres at the same time. This makes it possible for the investigator to detect irregularities caused by the time delay between starting the computer and initiating the manoeuvres, by extrasystoles or by artefacts. In 14 of the 124 subjects, a part of the program had to be repeated (forced breathing was repeated six times because of coughing). In 25 of the subjects tested it was necessary to correct the test results afterwards using the saved data. The most frequent reason for correction was the presence of premature beats in the elderly.

The reproducibility of the heart rate variability test parameters was comparable with results reported in the literature [8, 22–24], whereas reproducibility of the blood pressure variability was slightly better than with the conventional method.

The beat-by-beat blood pressure monitoring by the Finapres allows the possibility of analysing in detail the whole blood pressure curve after a given stimulus. Calculating the mean over 30 s (standing up) or a more precise detection of peak blood flow pressure changes (sustained handgrip) explains the slightly better reproducibility compared with the traditional sphygmomanometer approach.

The age-dependent 5th percentiles of the heart rate parameters were also reported by others using different methods for measuring heart rate and blood pressure [23–27]. However, the relation of ΔHRmax. with sex is in contradiction with the results in the literature [23, 25, 27]. The sex-related 5th percentile of delta BP dias. during handgrip was also found by Gauthschy et al. [27], although in their study the difference did not reach statistical significance.

The seven test parameters used are generally recommended for detecting diabetic autonomic neuropathy; moreover the program also calculates automatically the difference between the highest heart rate during and the lowest heart rate after the Valsalva manoeuvre [23, 28], the blood pressure overshoot [29] after the Valsalva manoeuvre and delta BPsys. and heart rate increase during handgrip [21, 30]. A number of less frequently used parameters can easily be programmed, for instance the expiration/inspiration ratio [12] and heart rate variation [31] during forced breathing or the 30:15 ratio after standing up [32]. As all data are saved on the disc, future calculation can be carried out at later convenience.

With this automated program, diabetic patients can easily be tested by a trained nurse for dysfunction of the autonomic nervous system. It creates the opportunity to study a large number of patients in a standardized way during a clinical trial or for screening diabetic patients before surgery [33].

**ACKNOWLEDGMENT**

This study was supported by a grant from the Diabetes Fonds Nederland.

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