Hemodynamics Following Real and Hypnosis-Simulated Phlebotomy

Edoardo Casiglia, Alberto Mazza, Giuliana Ginocchio, Caterina Onesto, Achille C. Pessina
Department of Clinical and Experimental Medicine of the University of Padova, Italy

Augusto Rossi
Italian Centre for Clinical and Experimental Hypnosis, Torino, Italy

Gianni Cavatton and Alberto Marotti
Blood Transfusion Centre of the General Hospital of Padova, Italy

Forearm arterial flow was measured in 22 healthy first-time blood donors during a 300-ml. blood letting and during the subsequent recovery. Blood pressure (BP) was also taken simultaneously and forearm peripheral resistance calculated. Following a transient BP and flow increase due to tachycardia related to needle insertion, both systolic BP and flow progressively and significantly decreased, while resistance increased. In a further 22 sex- and aged-matched highly hypnotizable subjects, blood donation was simulated by means of verbal hypnotic suggestions. The BP, flow and resistance curves were similar to those obtained with the real blood letting, without any between-subject difference or group/time interaction. Mere hypnosis without suggestion of phlebotomy and the simple bed resting did not produce any effect. These results indicate that the hemodynamic changes observed during and after a blood loss are partly due to mental involvement rather than merely to the hydraulic effects of the removal of blood.

Blood letting is an interesting human model of acute experimental hemorrhage, but little is known about its hemodynamics. Blood pressure (BP) has been found to increase (Kuchel, Avorn, Reed & Fields, 1992), decrease (Kirwan, Chir, Scurr & Brindle Smith, 1981) or not to change at all (Abraham et al., 1992) after a blood loss of 250-500 ml., and information on peripheral flow and resistance during and after phlebotomy are even more sparse. Besides, the question of whether the hemodynamic response to phlebotomy depends directly on the loss of blood or rather on the mental involvement in the ritual of blood letting remains unanswered.

For reprints write to: Edoardo Casiglia, M.D., Department of Clinical and Experimental Medicine, University of Padova, Via Giustiniani, 2 - 35128 Padova, Italy.

This study was aimed 1) at evaluating whether phlebotomy was capable of inducing peripheral hemodynamic variations, and 2) at identifying the role of the mental component involved in relation to simply the hydraulic component. Previous experiments by Whorwell, Houghton, Taylor and Maxton (1992) documented that hypnosis is a safe and reproducible way of inducing specific emotional states in selected subjects and may help in the investigation of the effects of emotions on the physiological function. Thus, the hypnotic approach was used to simulate the emotional state accompanying phlebotomy.

Methods

Real Blood Letting (Group A)

Twenty-two blood donors (11 men) aged 27±3 years, were studied. The procedure included three distinct phases: stabilization (variable length), blood letting (6 minutes), and a recovery period (18 minutes).

For stabilization, subjects were placed in bed in a comfortable room at a temperature of 23 C, in semi-darkness to minimize the effect of external stimuli. Repeated BP and heart rate measurements were made until hemodynamic stability was reached (<5% variation of both these parameters in two subsequent readings at 2-minute intervals). Thereafter, basal values of BP and peripheral flow were recorded with the methods described below. Then, each patient underwent a 300-ml. blood-letting, carried out by the very same male doctor, in 6 minutes. BP and flow were measured every 3 minutes, i.e. at the beginning, in the middle and at the end of the blood letting. Immediately after the end of phlebotomy (at the 6th minute from baseline) the needle was removed (see arrows in Figure 1). Patients remained in bed for a further 18 minutes and measurements of BP and flow were repeated every 3 minutes.

Hypnosis-Simulated Blood Letting (Group B1)

In another 22 subjects age and sex-matched with group *A*, the ritual of phlebotomy was simulated by way of hypnosis in order to evaluate the role of the mind in determining the hemodynamic variations accompanying phlebotomy, i.e. to separate the mental from the hydraulic effects.

Subjects of group *B1* were chosen on the grounds of their susceptibility to hypnosis according to Harvard A test (Shor & Orne, 1962) which implied a selection of the candidates. Following a precise explanation of the procedure involved and after informed consent had been obtained, each subject in turn was made to relax in response to verbal commands. Through the voice of the hypnotist, subjects were guided toward focussing their attention on a single idea. A traditional hypnotic induction followed by standard deepening procedures was used, consisting in a brief enumeration coupled with a series of commands suggesting in the subject a general sense of well-being, inducing palpebral heaviness and regular deep breathing, and inviting the subject to stare at a fixed point. After spontaneous eyelid closure was obtained, subjects were invited to concentrate on their own body from the feet to the head, whilst a feeling of heaviness and muscular relaxation was continuously being suggested. The verification of trance and exclusion of simulators was based on evidence of eyelid closure, left arm levitation, the easing of facial tension, a drop in the lower jaw with a mild opening of the mouth, on the slowing down of the breathing rate, and on the experience of the hypnotist in interpreting these signals.

Under such conditions, hypnotized patients are able to live out any imaginary situation that assumes all the subjective characteristics of reality which, in our case, was that of a blood letting. The ritual and timing of a real phlebotomy was simulated with suggestions like: *«...now the needle is being inserted into your arm... you can feel the pain due to the needle... now your blood is beginning to be drawn, you can see it in the tube..., (...) now the donation is complete... the needle has*

been removed...». This lasted 6 minutes. The feeling of reality of that experience was, thereafter, confirmed *a posteriori* by all subjects.

An 18-minute simulated recovery period followed the simulated phlebotomy. The same BP and flow measurements were performed as in group *A* subjects. At this point, they received the order to wake up.

Hypnosis Control (Group B2)

The same 22 subjects of group *B1* were hypnotized once more. They were simply given the suggestion that they were present in the room and were asked to lie on the same bed for the same period of time as they would have if venepuncture had been performed, without any mention whatsoever of a phlebotomy being made in that particular instant. This dealt with the likelihood that the induction of hypnosis itself was able to produce BP, flow or peripheral resistance changes.

No-Intervention Control (Group B3)

The same 22 subjects of group *B1* also underwent a BP and flow measurement with the same timing as described above, without any intervention (either phlebotomy or hypnosis). This was aimed at showing the effects of ongoing time and those due to cuff inflation and measurements taken.

Randomization Sequence

The sequence by which the different groups participated in the experiment was randomized according to a random-number list, and the interval which lapsed between one phase and the next was sufficient in order to avoid any knock-on effect (at least 2 weeks).

Hemodynamic Measurements

BP was measured with a normal Riva-Rocci sphygmomanometer. Mean BP was calculated as *diastolic BP + pulse BP / 3*. Arterial flow was measured on the left forearm with an automatic venous-occlusion strain-gauge plethysmographic fluximeter (Angiomed©, *Microlab Inc.*, Padova, Italy). At each 3-minute interval, 4 automatic measurements were performed and averaged automatically. We have validated and used this method in several of our clinical studies (Casiglia, et al., 1996; Casiglia et al., 1991; Casiglia, et al., 1994). Forearm peripheral resistance was calculated as mean BP / flow ratio and expressed as units of resistance (UR= mmHg•min•dl•ml-1).

Statistics

BP, flow and resistance values were averaged and expressed as mean± SD. Baseline values were first compared with analysis of variance (ANOVA). Then, both within-group and between-group differences in BP, flow and resistance were analyzed with repeated-measures ANOVA, after demonstrating that data satisfied the conditions of compound symmetry; the test for violation of the sphericity condition was not significant.

Results

The four groups had comparable values of BP, flow, and resistance at baseline (table 1).

In both *A* and *B1* groups, *systolic BP* mildly, briefly and insignificantly increased at the first minute (+2% and +1%, respectively), then significantly decreased both during real and simulated phlebotomy and during recovery, reaching -5% and -3% respectively at the 15th minute, without any between-groups dif-

Table 1

Blood pressure (BP, mmHg), forearm flow (ml•min-1•dl-1) and forearm peripheral resistance (mmHg•ml•min•dl-1) in 22 subjects who underwent a real 300-ml phlebotomy (group A), and other 22 age- and sex-matched who underwent a hypnosis-simulated phlebotomy (group B1), a control hypnosis without any suggestion of phlebotomy (group B2), and a simple bed rest (group B3).

	Group A Real Phlebotomy	Group B1 Simulated Phlebotomy	Group B2 Control Hypnosis	Group B3 Staying in Bed	Between Groups ANOVA
Systolic BP	130.8±9.1	130.6±8.8	130.2±8.9	130.0±7.9	N.S.
Diastolic BP	80.2±7.5	80.1±7.6	80.0±7.7	80.4±7.5	N.S.
Flow	3.30±1.22	3.40±1.30	3.45±1.28	3.35±1.55	N.S.
Resistance	29.4±11.6	28.8±10.9	28.0±13.5	28.9±12.2	N.S.

ference (F=0.13, p=0.71); after a brief increase, *diastolic BP* also significantly decreased in both groups without between-groups differences (F=0.31, p=0.58) (data not shown).

In both groups *A* and *B1*, *forearm flow* significantly decreased during the experiment as well as during recovery time (within-analysis for real phlebotomy: F=11.35, p<0.0001; for simulated phlebotomy: F=8.72, p<0.0001) without any between-groups difference (F=2.16, p=0.15) (figure 1, upper panel).

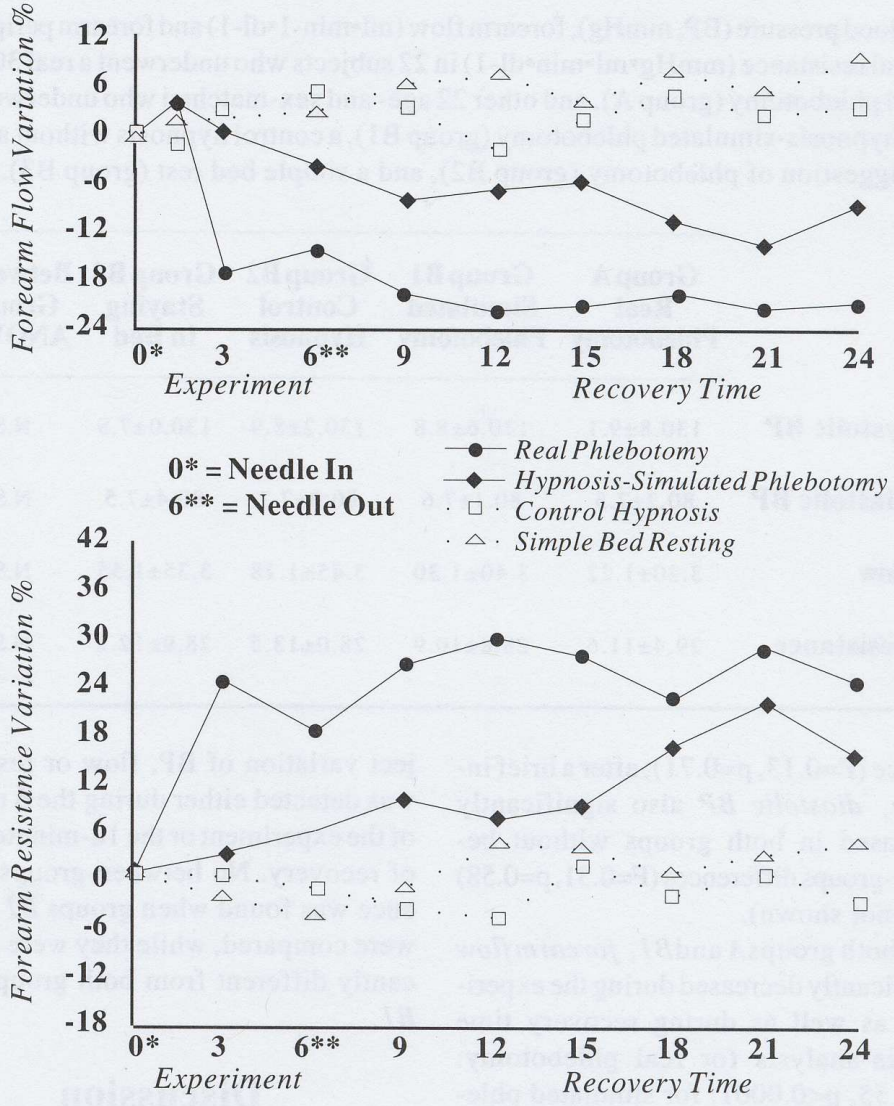
Forearm resistance progressively and significantly increased during the experiment and the recovery time in both groups *A* and *B1* (real phlebotomy: F=5.49, p<0.0001; simulated phlebotomy: F=4.46, p<0.0001), showing no between-groups difference (F=0.38, p=0.07) (figure 1, lower panel).

In groups *B2* and *B3*, no within-subject variation of BP, flow or resistance was detected either during the 6 minutes of the experiment or the 18-minute period of recovery. No between-groups difference was found when groups *B1* and *B3* were compared, while they were significantly different from both group *A* and *B1*.

Discussion

The main results of our study are the following: 1) blood donation actually induced a rapid and transient BP rise followed by a long-lasting decrease, and a progressive increase in peripheral resistance during the whole of the blood donation and recovery period; 2) the same hemodynamic response was induced by a suggestion without the removal of blood; 3) the mere hypnotic procedure as well as simple bed rest

Figure 1



Legend to figure

Percent variations from baseline of forearm arterial flow (upper panel) and foream resistance (lower panel) in 22 subjects who underwent a real 300-ml blood letting (—●—) and in 22 age- and sex-matched subjects who underwent a hypnosis-simulated blood letting (—◆—). A comparable trend was shown in the two groups both during the procedure (lasting 6 minutes) and during the 18-min recovery time. Curves from a control group simply staying in bed (· □ ·) and from a group which underwent control hypnosis without any suggestion of phlebotomy (· △ ·) are also shown: note the absence of any variation in these two groups. Arrows indicate when needle was inserted and removed in group *A*, or when suggestion of insertion and removal was given in group *B* (this latter variation is less pronounced than that due to the real needle).

without suggestion did not produce any effect.

The removal of 300 ml of venous blood during a blood letting is an excellent experimental model of acute, controlled hemorrhage in man. As we previously demonstrated (Casiglia et al., 1989; Casiglia, et al., 1990), a blood loss is followed by an increase in plasma renin activity (+18%), aldosterone (+21%), ACTH (+55.5%) and norepinephrine (+11%), and it is likely that the hemodynamic variations that we observed in the present study were due to an increase of sympathetic discharge. Kuchel et al. (1992) and O'Shaugnessy and Slome (1934) are of the opinion that this may be attributed to hypovolaemia as similar effects are seen after diuretic treatment or plasmapheresis. We disagree with this hypothesis, as in our experience BP and peripheral flow decreased and peripheral resistance increased not only in subjects who actually underwent blood letting (hypovolemia), but also in those who simply believed that they were undergoing blood letting (no hypovolemia at all).

Despite the common belief that cardiovascular functions are partially controlled by the mind, very little information is available concerning the influence of subconscious mechanisms on cardiovascular system. Atkinsons (1994) stated that hypnosis is a scientifically acceptable and reproducible method to investigate this topic, provided that the study population is carefully selected. Actually, the efficacy of hypnosis has been validated not only in pain relief (Erickson, 1994) but also in many other pathologic situations ranging from hyperemesis to drug addiction, and some authors even demonstrated the possibility of obtaining with hypnotic suggestions certain physical effects, such as the elimination of warts, the production of blisters, modifications in colonic pressure, and the reduction of immune response (Kennedy, 1957; Ewin, 1992; Whorwell, Houghton, Taylor & Maxton 1992).

Hypnosis has been employed only occasionally in cardiovascular research: for example, Kraemer et al. (1992) found a greater oxygen consumption in hypnotized than in non-hypnotized subjects who underwent a submaximal exercise test; and Mittleman, Doubt and Gravitz (1992) found a faster rate of heat loss in subjects receiving suggestions of warmth. Data are too sparse to allow more than a vague idea about this topic, and the present study is probably the first to demonstrate that, at least in highly hypnotizable subjects, the hemodynamic response to blood letting may be due to the mental participation in the procedure and not only to the hydraulic changes following blood removal. It appears consistent with the hypothesis that central nervous system activity secondary to the perception of phlebotomy underlies at least part of the hemodynamic response to blood letting.

This study does not allow, of course, the generalization of the findings to all subjects, and does not show whether subjects of a lesser hypnotic capacity would have the same hemodynamic responses to an imagined phlebotomy; it simply demonstrates that hypnotizable subjects who are medically knowledgeable can register hemodynamic changes similar to those who are having phlebotomy. Other experiments, namely the suggestion of simple venepuncture and phlebotomy during no-phlebotomy suggestion, will be necessary for a better understanding of the problem.

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