Lower Blood Pressure Values in Blood Donors?

Edoardo CASIGLIA, MD, Renata BIASIN, MD,
Gianni CAVATTON,* MD, Marco CAPUANI, MD,
Alberto MAROTTI,* MD, Caterina ONESTO, MD,
Paolo TRAMONTIN, MD,
and Achille C. PESSINA, MD, PhD

SUMMARY

594 blood donors were studied to define the influence of regular blood donation on blood pressure. Blood pressures were compared at the first phlebotomy performed at the Padova Blood Unit, the 13-year phlebotomy, and the median between the two. As a control population, a cohort of 594 non-donors from the same general population similar to the blood donors was studied twice at a 15-year interval.

Subjects had made on average 7.3 ± 0.4 donations at the first step, 23 ± 0.6 at the second, and 30.9 ± 0.7 at the last step. Unadjusted systolic blood pressure regularly and significantly increased by 1.6% from the first phlebotomy to the second one and by 2.3% from the first to third. Adjusted systolic blood pressure, on the contrary, significantly decreased by 2.1% and by 2.7% respectively. Diastolic blood pressure tended to increase insignificantly, while the adjusted one did not change at all. The increase of systolic blood pressure from the first to second step directly correlated with the number of donations, and this also applied to differences between the first and the third. When the increase in age was introduced in the multiple regression analysis, systolic blood pressure rise from the first to third step showed an inverse correlation with the number of phlebotomies.

Our data render suspect the results of epidemiological investigations which took into consideration cohorts of blood donors; although these cohorts may be anagraphically representative of a general population, repeated phlebotomies introduce a bias leading to the detection of misleadingly low blood pressure values in regular blood donors. (Jpn Heart J 1996; 37: 897-903)

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From the Department of Clinical and Experimental Medicine, University of Padova, Padova, and the *Blood Transfusion Unit, General Hospital of Padova, Padova, Italy.

Address for correspondence: Edoardo Casiglia, MD, Department of Clinical and Experimental Medicine, University of Padova, Via Giustiniani, 2-35128 Padova, Italy.

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RELATIONSHIPS between blood pressure (BP) and blood donation are unclear. The subtraction of 300–500 ml of blood has an immediate hypotensive effect^{1–10)} and phlebotomy is considered to be a good way of inducing a rapid and transient BP fall.^{11,12)} On the other hand, the long-term effects of repeated phlebotomies on BP are essentially unknown.

This retrospective study was performed in a large group of normotensive blood donors whose BP history was recorded for 13 years in order to ascertain whether regular blood donation influences BP values. This could have practical importance as blood donation is widespread and involves millions of people worldwide: not only could the cardiovascular risk pattern of a great number of blood donors be modified by repeated blood lettings, but they could also require special attention to avoid misunderstandings when included in epidemiological studies.

METHODS

Data from 594 blood donors who were referred to the Blood Transfusion Unit of the General Hospital of Padova were used in this study. Three blood pressures were taken into consideration: that in occasion of the first phlebotomy performed at the Padova Transfusion Center (this was not necessarily the first phlebotomy ever carried out), that in occasion of the 13-year phlebotomy, and the median between the previous two.

Systolic and diastolic BP in mmHg, body weight in kg, body height in m, number of blood lettings performed, and the interval in years from the first phlebotomy were recorded at each step. Body mass index (BMI) was calculated in $\text{kg} \cdot \text{m}^{-2}$ as the weight/height ratio. It must be emphasized that the routine of blood letting at the Padova Transfusion Center is organized in order to minimize any reaction,^{13,14)} in particular, blood donors stay in bed for at least 20 minutes prior to phlebotomy, BP is measured repeatedly (3 to 5 times), and only the last value is taken into consideration as the BP value. Although high BP values are considered by a great number of transfusion centers to be a contraindication to phlebotomy, this is not the policy of the Padova Center except in the cases of severe hypertension; nevertheless, no subject was excluded from the present study because of hypertension, and this meant that no confounding effect was introduced.

As a control population, a cohort of 594 non-donors from the same general population, demographically similar to the blood donors, was studied. Their BP was measured with the same method described above at a 15-year interval.

All subjects included in this study were non-diabetic and normotensive at the moment of the first donation (BP < 140/< 90 mmHg) and had never re-

Figure 1. Blood pressure increase with age among the 594 blood donors. * $p < 0.05$, ** $p < 0.01$.

ceived antihypertensive therapy.

Values were averaged and expressed as mean $\pm$ standard error. As in blood donors, BP regularly increased with age (Figure 1). BP values of both cohorts were also age-adjusted. A repeated-measure analysis of variance was used in order to compare the means in the three steps, with Tukey's test as *post hoc* and Bonferroni's correction. Correlations were evaluated using the Pearson coefficient and Bonferroni's probability. The multiple correlation between the number of phlebotomies and systolic and diastolic BP was also performed using age as a covariate; results are expressed as multiple R and 2-tail p value.

RESULTS

Blood donors: Age of blood donors was 33.5 ± 0.3 years at the first step (95% confidence limits [C.L.] 32.8–34.3), 43 ± 0.4 at the second (C.L. 42.2–43.9), and 46.5 ± 0.43 at the third (C.L. 45.7–47.4). BMI was similar in the three steps. Subjects had made on average 7.3 ± 0.4 donations at the first step (C.L. 6.6–8.1), 23 ± 0.6 at the second (C.L. 21.8–24.3), and 30.9 ± 0.7 at the last step (C.L. 29.5–32.3). From the first to the second blood donation, 9.6 ± 0.2 years had passed (C.L. 9.2–10), and 13 ± 0.2 years had lapsed from the first to the third (C.L. 12.6–13.5).

Crude systolic BP regularly increased ($F = 6.75$, $p < 0.001$) by 1.6% from the first phlebotomy to the second and by 2.3% from the first to third (Figure 2, left panel). Adjusted systolic BP, on the contrary, decreased ($F = 8.56$, $p < 0.00005$) by 2.1% and by 2.7%, respectively (Figure 3, left panel). The effect of age was as follows: $F = 222.30$, $p < 0.00005$.

Figure 2. Crude mean values $\pm$ SE of systolic (SBP, left panel) and diastolic (DBP, right panel) blood pressure at the first phlebotomy ($\square$), at the last one 13 ± 0.2 years after the first ($\blacksquare$) and at the median of the previous two 9.6 ± 0.2 years after the first ($\square$). ANOVA: $F = 6.75$, $p < 0.001$; post-hoc test: $**p < 0.01$, $***p < 0.0001$.

Figure 3. Age-adjusted mean values $\pm$ SE of systolic (left panel) and diastolic (right panel) blood pressure. Legend as in Figure 2. ANOVA: $F = 8.56$, $p < 0.00005$; post-hoc test $**p < 0.01$, $***p < 0.0001$.

Crude diastolic BP tended to increase insignificantly (Figure 2, right panel) while the adjusted one did not change at all (Figure 3, right panel) (effect of age: $F = 133.79$, $p < 0.00005$).

The increase of systolic BP from the first to second step directly correlated with the number of donations ($R = 0.135$, $p < 0.005$), and this also applied to the first and the third ($R = 0.115$, $p < 0.01$). When the increase in age was introduced in the multiple regression analysis, systolic BP rise from the first to third step showed an inverse correlation with the number of phlebotomies (multiple $R = 0.312$, coefficient -0.084 , $p < 0.05$; effect of age $p < 0.005$), while any correlation at the second step was no longer evident.

Control subjects: Age of control subjects was 40.8 ± 10.5 at the first step and 55.6 ± 10.5 at the last ($F = 458.81$, $p < 0.00005$).

Age-adjusted systolic BP was 135.2 ± 0.8 and 135.4 ± 0.7 mmHg, respectively (NS), and diastolic BP 82.2 ± 0.5 and 83.2 ± 0.3 mmHg, respectively (NS).

DISCUSSION

Phlebotomy is an interesting human model of experimental hemorrhage. It is generally accepted that acute blood loss is accompanied or immediately followed by systemic vasodilatation^{15,16)} and a decrease in systolic and (less frequently) diastolic BP.^{1,2,4-10,15,17)} This is also our experience,^{11,17,18)} but a stimulation of sympathetic discharge with an increase of systolic BP,¹⁹⁾ heart rate,^{1,19)} plasma renin activity, adosterone, ACTH and norepinephrine^{10,11,17,20)} has also been described by other investigators both in humans and in the animal. BP fall has generally been attributed to hypovolemia,^{1,5,20)} based on the fact that similar effects were also observed after circulatory depletion due to diuretic treatment²¹⁾ or plasmapheresis,²²⁾ that the greater the blood loss the higher the BP fall,²³⁾ and that blood replacement sometimes has reversed the pressor effects of blood loss.^{15,17,21)} Hemodilution *per se*²³⁾ and the phlebotomy-induced increase in the release of circulating substances such as bromocriptine²⁴⁾ could constitute additional hypotensive factors.

Sometimes the phlebotomy-induced BP fall lasts 24 hours or more^{2,11)} (even 4 weeks in the experience of Zidek et al,¹²⁾ who hypothesize that phlebotomy can be used in addition to drug treatment in resistant essential hypertension), sometimes it is transitory.^{4,11,25)}

The long-term effects of blood donation on BP are essentially unknown and the question of whether regular blood letting implies higher, lower or unchanged BP values in blood donors remains unanswered. In our experience, regularly repeated blood donation was accompanied by a reduction in systolic BP. In fact, age-adjusted systolic BP regularly and significantly decreased by increasing the number of phlebotomies, being at the third step 2.7% lower than at the first (Figure 2). Diastolic BP did not change at all. The possibility that the systolic BP decrement was simply due to a progressive adaptation to BP measurement was excluded by the comparison with the control cohort of non-donors (where no variation was observed in 15 years of observation) and by the inverse correlation between adjusted BP and number of blood donations.

The reasons for the systolic BP decrease are difficult to define, as is its meaning. Literature on this topic is surprisingly poor and no data have been shown in humans. Susic et al.²⁶⁾ found a statistically significant correlation between the hematocrit decrease and BP fall following repeated blood letting in rats (they concluded that there was a direct association between hematocrit and systemic hypertension), while other investigators found in rats, in similar experimental conditions, no influence on the physiological pattern.²⁷⁾ In our experience BP decline was statistically significant, but it was not thought to be significant clinically. In any case, apart from their interest from a physiological point of view, our

data render somewhat suspect the results of epidemiological investigations which included cohorts of blood donors,²⁸⁻³¹⁾ although these cohorts may be anagraphically representative of a general population, repeated phlebotomies could introduce a procedural bias leading to the detection of misleadingly low BP values in regular blood donors.

A prospective study on BP changes following regular, repeated blood donation is in order.

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