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Original article

Blood pressure measurement with the tail-cuff method in Wistar and spontaneously hypertensive rats: Influence of adrenergic- and nitric oxide-mediated vasomotion

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ABSTRACT

Introduction: Systolic blood pressure (SBP) is still measured in rats by the tail-cuff method, allowing readings when pulse/flow disappears during cuff inflation and reappears during deflation, separated by a compression interval. Although cuff deflation is habitually used to estimate SBP, we found cuff deflation–cuff inflation pressure to be usually negative, indicating that cuff deflation pressure < cuff inflation pressure. **Methods:** SBP was measured in 226 male Wistar and SHR utilizing compression intervals of different durations, and also pharmacological interventions intended to modulate the cuff deflation–cuff inflation cycle. Direct, simultaneous intravascular measurements were also performed in some animals. **Results and discussion:** With compression interval ≅ 15 s, cuff deflation–cuff inflation was − 6 ± 0.6 mmHg in 73 Wistar and − 16 ± 1.4 mmHg in 51 SHR. Lengthening compression interval up to 4 min increased cuff deflation–cuff inflation pressure significantly to − 27 ± 3 mmHg in Wistar and to − 31 ± 5 mmHg in SHR, suggesting accumulation of a vasodilating mediator. This increase of cuff deflation–cuff inflation pressure was prevented by papaverine (totally in Wistar, partially in SHR), indicating its dependence on vasodilatory capacity. Adrenergic blockade decreased cuff deflation–cuff inflation pressure to − 13 ± 5 mmHg ($P < 0.05$) in SHR, but had no effect in Wistar rats. Injection of L-NAME decreased cuff deflation–cuff inflation pressure to − 5 ± 2 mmHg ($P < 0.05$) in Wistar rats but was ineffective in SHR. Simultaneous measurements by tail-cuff method and carotid cannulation revealed that the cuff inflation most accurately estimated the intravascular SBP. **Conclusions:** 1) Cuff inflation measurements should be considered representative of SBP, as cuff deflation can underestimate SBP depending on compression interval duration, 2) nitric oxide accumulation due to flow deprivation is the main cause of SBP underestimation by cuff deflation in Wistar, and 3) in SHR, nitric oxide effects were minimal, and sympathetic activation plus physical factors seemed to predominate in the determining the outcome of measurements.

1. Introduction

The tail-cuff method is still widely used for measuring systolic blood pressure (SBP) in rodents, principally when the screening of large populations of animals and/or the follow-up of SBP over long time periods are involved (Irvine, White, & Chan, 1997; Van Vliet, Chafe, Antic, Schnyder-Candrian, & Montani, 2000). Several methods of flow/pulse detection have been described in addition to the original water plethysmograph (Byrom & Wilson 1938) or its modifications (Dodson & Mackaness 1957; Lucas 1971; Martinelli, Beraldo, Campos, da Costa, & Silva, 1985; Okamoto & Aoki 1963; Sobin 1946): mercury-in-rubber (Maistrello & Matscher 1969) or strain gauge (Dowd & Jones 1968; Olmsted, Corcoran, & Page, 1951) detectors, Doppler effect (Buñag 1973, 1974, 1975; Newman & Looker 1972; Reichle 1971; Rowberg, Franklin, & Van Citters, 1969), photoelectric (Hermansen 1970; Ikeda, Nara, & Yamori, 1991; Lee, Wang, Lin, Chou, & Chen, 2002; Palbøl & Henningsen, 1979; Swales & Tange 1970; Yamakoshi, Shimazu, & Togawa, 1979), impedance (Wen, Tremblay, Qu, & Webster, 1988), microphonic (Buñag 1971a, 1971b; Fregly 1963; Friedman & Freed 1949), and piezoelectric pulse detectors (Bazil, Krulan, & Webb, 1993; Chiueh & Kopin 1978; Jamieson et al., 1997; Kubota et al., 2006; Kusaka, Kishi, & Sokabe, 1987; Pfeffer, Pfeffer, & Frolich, 1971; Resurreccion & Caster 1978), this last being the one employed most frequently.

With most of these methods it is possible to detect two events associated with the SBP: 1) disappearance of the pulse/flow signal during cuff inflation, and 2) its reappearance during deflation. However, in the papers just mentioned, which are specifically related to methodology of BP measurement, pulse/flow reappearance was the value most frequently considered as representative of SBP, even in those which performed and reported both readings (Buñag, Mueting,

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& Riley, 1975; Dowd & Jones 1968; Swales & Tange 1970; Yamakoshi et al. 1979), but no reason was given for this election.

In our laboratory's experience the readings obtained during deflation are usually lower than the ones recorded during inflation, and careful inspection of the figures presented in some papers (Buñag 1973, 1975; Pfeffer et al., 1971; Rowberg et al., 1969) reveals the same fact. In spite of this evidence, we found only two papers discussing differences between inflation and deflation readings, one of them stating that both values were not statistically different (Buñag 1973). In the other, however, the authors reported that the inflation readings were on the average 11 mmHg higher than the deflation readings, and the difference was statistically significant (Martinelli et al., 1985). They also found that the inflation readings were in closer agreement with the intra-arterial measurements than were the deflation readings, but did not provide any hypothesis and/or pursue further experiments to explain the difference between both values (Martinelli et al., 1985).

This difference between inflation and deflation readings resembles the one we usually find in our own laboratory (Fritz & Rinaldi, 2007), and could lead to important errors when the animals are considered normotensive or hypertensive based systematically on one or the other of those readings. In addition, it would be also of interest to know if this discrepancy between inflation and deflation readings is also present in hypertensive rats.

In view of the scarce and/or contradictory information existing on this subject, we undertook experiments in normotensive rats and in SHR, a widely used model of hypertension (Okamoto & Aoki 1963), wishing to explore: 1) if the inflation and deflation readings obtained with the tail-cuff method are coincident, and 2) if they are not, which of the values better represents the intra-arterial measurements, and the reason for the difference. Our hypothesis was that a vasodilator accumulated in the tail during the inflation–deflation interval could be responsible for the lower deflation readings.

2. Methods

2.1. Animals

A total of 226 male rats, aged 3 to 4 months, were used in the course of this study. Of this number, 132 were Wistar rats weighing 250–300 g and 94 were SHR weighing 220–270 g. The animals were bred and maintained in the central facility of the National University of La Plata School of Medicine, and all the experimental procedures were supervised and approved by the Ethics Committee if the Institution. The rats were housed in stainless steel cages with sterilized bedding (white pine wood shavings) which was changed every day. They had air conditioning and a 12 hour light–12 hour dark cycle, and free access to food and water. Tap water was provided in sterilized bottles with stainless steel nipples. Food was in the form of extruded chips (Purina nutrients) of the following composition (in %): humidity 10, proteins 24.6, lipids 7, ashes 6.4, raw fiber 4, hemicellulose 7.7, calcium 1.1, phosphorus 1.4, potassium 1.05, magnesium 0.2, sulphur 0.25, sodium 0.11, chloride 0.25, linoleic acid 2.25, linolenic acid 0.15, arginine 1.55, cysteine 0.42, glycine 1.4, histidine 0.59, isoleucine 0.97, leucine 2.25, lisine 1.2, methionine 0.4, phenylalanine 1.18, serine 0.09, treonine 0.9, valine 1.2, FDN 12, FDA 4.5, CNF 36, TDN 82.

2.2. BP measurement

For indirect SBP readings, the rats were placed in a chamber at 37 °C for 10 min, and then transferred to a standard setup with heating pad and acrylic restrainer, tail cuff and pulse sensor (Narco Biosystems, Houston, TX). The tail cuff was connected to a cylinder of compressed air through an arrangement of inlet and outlet valves that permitted inflation and deflation of the cuff at a constant rate. The tail-cuff pressure was continuously recorded with a solid state pressure sensor (Sensym, Honeywell Sensing & Control, Inc.). The signals from the pulse and pressure sensors were conveniently amplified and then digitized with an analog–digital board (DT16EZ, Data Translation, Inc., Marlboro, MA) mounted in a desktop computer. On-line display for controlling the procedure, and files for later processing, were obtained with an appropriate software (Labtech Notebook Pro, Laboratory Technology Corp., Wilmington, MA). For each indirect BP determination the inflation and deflation readings were always recorded, as well as the compression interval. The indirect measurements were all performed by the same person, who was kept blind about the purpose of the study. The animals quickly became familiar with the procedure and remained calm within the restrainer, and without the need for using the plastic door. In the rare cases when signs of discomfort were present the procedure was interrupted.

For direct BP measurements, the rats were anesthetized with sodium pentobarbital (50 mg/kg I.P.) and placed on a heating pad. The left carotid artery was exposed and cannulated with a short microbore teflon tubing 0.75 mm O.D. (Small Parts, Inc, Miami Lakes, FL) connected with a low-volume displacement pressure transducer (P23Gb, Gould Inc., Cleveland, OH). When the intra-arterial tracing was stable, the tail cuff and pulse sensor were placed on the tail, and the indirect BP was measured at the same time. All the signals were sent to the same acquisition system (see above) so that both the indirect and direct BP tracings could be superimposed (see also Fig. 2).

2.3. Drugs

Papaverine, propranolol, phenoxybenzamine, L-NAME and other analytical chemicals were purchased from SIGMA (St. Louis, MO).

2.4. Statistics

The results were expressed as mean ± 1 S.E.M., and the differences between means were evaluated using a statistical package (Sigmastat 2.0, Jandel Scientific Software, San Rafael, CA). When only two groups were involved the Student's t test (paired or unpaired) was used, while for multiple groups comparisons the one-way ANOVA was employed. The particular modifications of these tests as dictated by the circumstances are indicated in Methods for each specific protocol. The correlation between variables was studied with linear regression. A value of $P < 0.05$ was considered significant.

3. Results

Fig. 1 depicts on the left panel the SBP measured by the tail-cuff method in 73 Wistar and 51 SHR, showing that the deflation reading was slightly, yet significantly, lower than the cuff inflation. The average difference between them (deflation–inflation) was − 6 ± 0.6 mmHg in Wistar and − 16 ± 1.4 mmHg in SHR ($P < 0.05$, paired t test). The right panel shows the dependence of this difference on the prevailing SBP, and it can be seen that in only 1 SHR and 9 Wistar the deflation reading was equal to, or greater than, the inflation reading. Considering all the rats, there was a significant correlation between the inflation reading and the deflation–inflation difference as shown in Fig. 2. There was also a significant correlation if both groups were processed separately (Wistar: $r = -0.29$, $P < 0.05$; SHR: $r = -0.34$, $P < 0.05$; Pearson product moment correlation was used to calculate all correlations). These were routine measurements of SBP in which the compression interval had been less than 30 s.

In 13 additional experiments in Wistar (Fig. 2) we performed simultaneous measurement of BP by the tail-cuff method and by direct carotid cannulation, obtaining similar values for the direct SBP and the inflation reading (NS, Wilcoxon Signed Rank Test). However, the deflation reading was slightly but significantly lower that the directly measured SBP ($P < 0.006$, paired t test). Since these were the

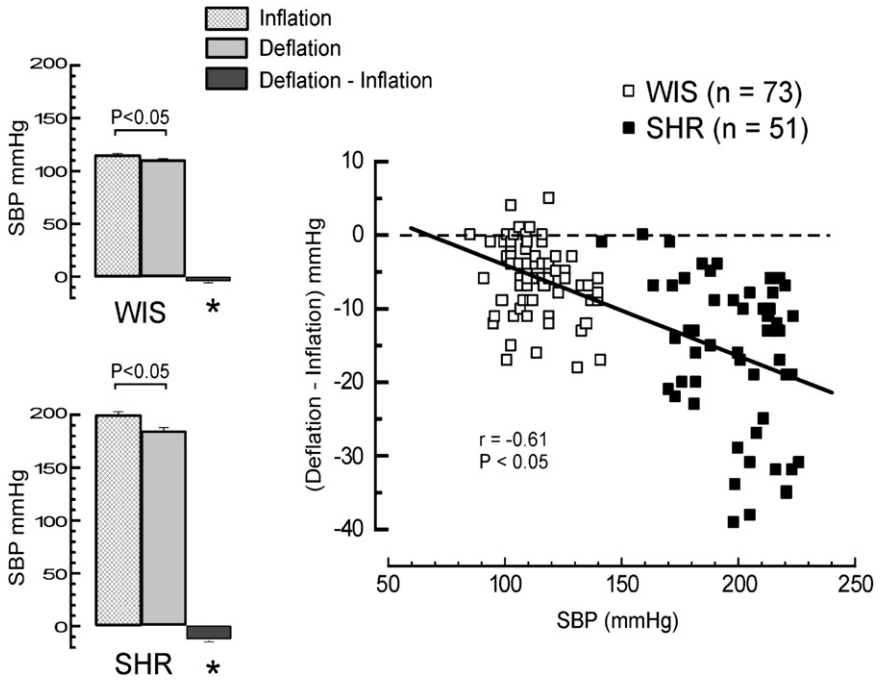

Fig. 1. Inflation and deflation readings of SBP measured by the tail-cuff method in 73 normotensive Wistar rats (WIS) and 51 SHR. The left panel shows the average values for inflation and deflation readings, and their difference. The right panel plots the difference as a function of the SBP for all the rats, showing a significant correlation between both variables. The asterisk (*) denotes $P<0.05$ with respect to zero.

only experiments performed with anesthesia, we compared the indirect BP values with the ones obtained in the same rats before surgery, and we found no significant differences between them (conscious rats: 115 ± 2 mmHg, anesthetized rats: 116 ± 4 mmHg, n = 13, NS with the paired t test) (data not illustrated).

Fig. 3 shows experiments designed to evaluate the relationship between the deflation–inflation difference and the duration of the compression interval in Wistar and SHR. The top panel shows the inflation and deflation readings obtained in four different SBP measurements in Wistar (n = 15) and SHR (n = 16) in which the compression interval was set at 15, 60, 180 or 240 s. In each rat the four measurements were performed on the same day, changing the compression interval at random, and allowing at least 1 h of rest between any two measurements. As can be seen, the initial deflation–inflation difference increased markedly as the compression interval changed from 15 to 240 s, which was the longest one that the animals

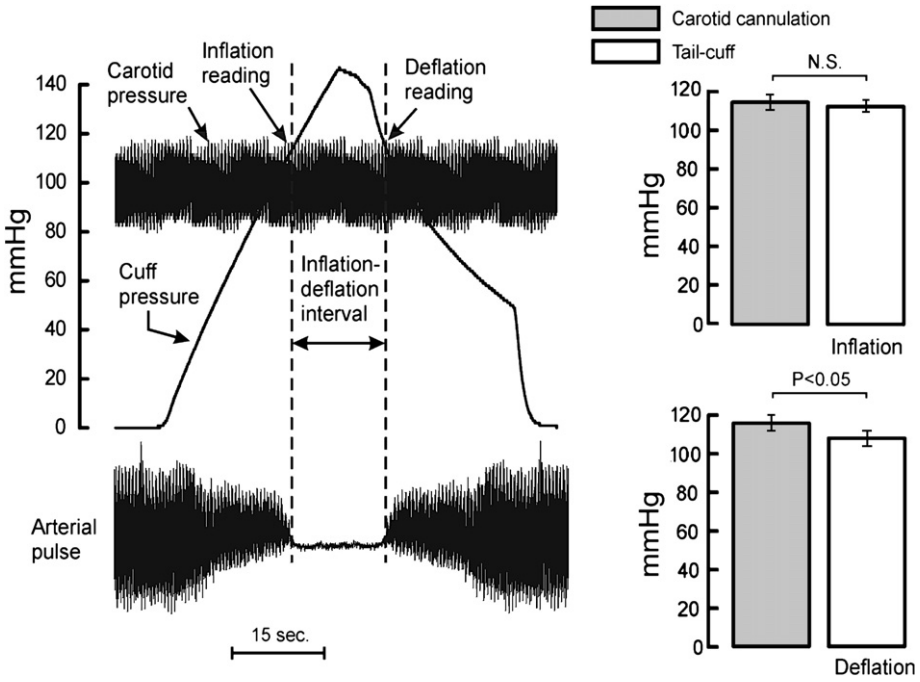

Fig. 2. The left panel shows the actual records of a blood pressure measurement by carotid cannulation and the tail-cuff method, with the inflation and deflation readings separated by a short interval (≈15 s). The right panel displays the average results of 13 similar experiments, showing that the deflation readings were significantly lower that the corresponding intra-arterial measurement; which in turn was not significantly different from the inflation readings.

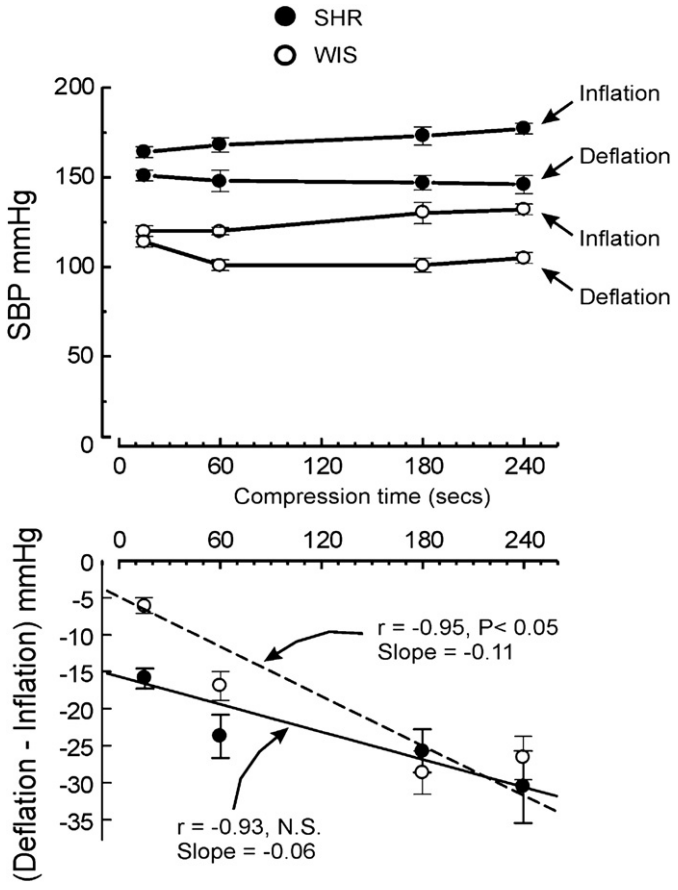

Fig. 3. The top panel shows inflation and deflation readings of SBP measured by the tail-cuff method in 15 normotensive Wistar rats (WIS) and 16 SHR. In each rat the SBP was measured 4 times employing compression intervals of 15, 60, 180 and 240 s. The bottom panel shows that the difference between readings increased as a function of the compression time.

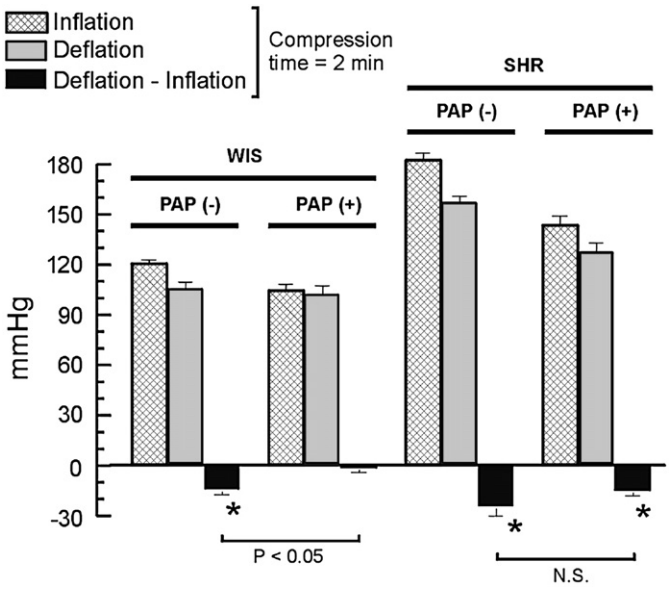

Fig. 4. Inflation and deflation readings of SBP measured by the tail-cuff method in 12 normotensive Wistar rats (WIS) and 7 SHR before and after injection of papaverine 75 mg/kg I.P. The compression interval was kept at 2 min to obtain a large inflation–deflation difference. The papaverine abolished the difference in WIS, but only diminished it non-significantly in SHR. The asterisk (*) denotes $P<0.05$ with respect to zero. PAP = papaverine.

tolerated without experiencing discomfort. The deflation–inflation difference increased from − 15 ± 1.8 mmHg to − 31 ± 5 mmHg in SHR ($P < 0.05$, one-way ANOVA and Tukey test) and from − 6 ± 0.8 mmHg to − 27 ± 3 mmHg in Wistar ($P < 0.05$, Kruskal–Wallis One Way Analysis of Variance on Ranks and Dunn's method). Expressing the increase of deflation–inflation difference with respect to the 15 sec values, it was more pronounced in the Wistar (≈ a fourfold increase) than in the SHR (≈ a twofold increase). It also has to be noted that the increase of the deflation–inflation difference was caused not only by decrease of the deflation readings but also by elevation of the inflation readings, which was significant in both groups: from 120 ± 3 mmHg to 132 ± 3 mmHg in Wistar and from 164 ± 3 mmHg to 177 ± 3 mmHg in SHR ($P < 0.05$, Kruskal–Wallis One Way Analysis of Variance on Ranks and Dunn's method). The bottom panel depicts the negative correlation existing between the compression interval and the deflation–inflation difference, which was significant only in the Wistar rats (Pearson product moment correlation).

The influence of a nonspecific smooth muscle dilator, papaverine, was evaluated in 7 SHR and 12 Wistar (Fig. 4). In this protocol two consecutive SBP determinations were performed, both with a compression interval of 2 min to obtain a considerable deflation–inflation difference The first determination was performed as a control, and the second was carried out 20 min after the administration of 75 mg/kg I.P. of papaverine. As can be seen on Fig. 4 the increase of the deflation–inflation difference was prevented by papaverine in Wistar, and its value did not differ from zero ($P = 0.69$, paired t test). In the SHR, however, the increase of the deflation–inflation difference could not be totally prevented, with a portion significantly different from zero still remaining ($P < 0.05$, paired t test).

In a last set of experiments (Fig. 5) we evaluated the participation of two important routes of vascular smooth muscle control, i.e. the sympathetic innervation and the NO pathway, on the increase of the deflation–inflation difference. As in the papaverine protocol, two consecutive SBP determinations were performed, both with a compression interval of 2 min to obtain an enlarged deflation–inflation

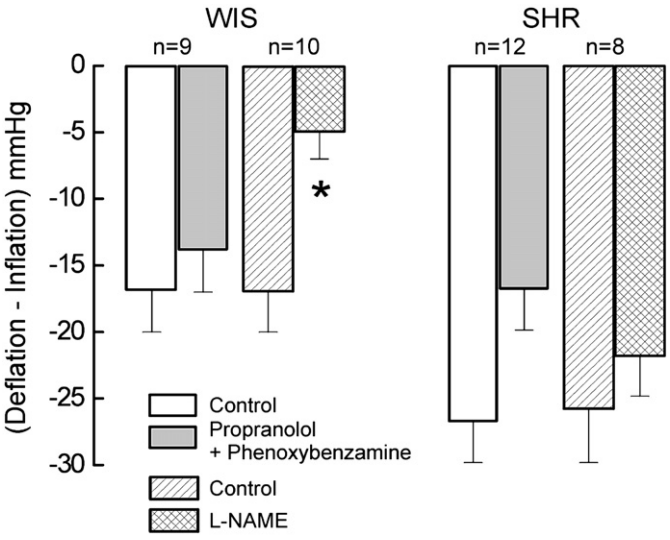

Fig. 5. Difference between inflation and deflation readings of systolic blood pressure measured by the tail-cuff method in 19 normotensive Wistar rats (WIS) and 13 spontaneously hypertensive rats (SHR). In the WIS animals (left four bars) the injection of phenoxybenzamine (4 mg/kg i.p.) and propranolol (10 mg/kg i.p.) did not modify the inflation–deflation difference but injection of L-NAME (100 mg/kg i.p.) reduced it significantly. In the SHR (right four bars) the injection of the same doses of phenoxybenzamine and propranolol reduced the inflation–deflation difference significantly, but injection of L-NAME had no effect. The asterisk (*) denotes $P<0.05$ with respect to the control experiments.

difference. The first measurement was used as a control, and the second was performed after the administration of: a) phenoxybenzamine (4 mg/kg i.p.) and propranolol (10 mg/kg i.p.), or b) L-NAME (100 mg/kg i.p.). In the Wistar rats (n = 19), the adrenergic blockade (n = 9) was effective as could be ascertained by the fall in blood pressure from 103 ± 2 mmHg to 75 ± 2 mmHg (cuff inflation); however, the deflation cycle under adrenergic blockade produced a still lower deflation reading of 62 ± 3 mmHg. The deflation–inflation difference of − 14 ± 2 mmHg was similar to the one obtained in absence of adrenergic blockade (− 17 ± 2 mmHg). On the contrary, treatment with L-NAME (n = 10) did reduce the deflation–inflation difference from − 17 ± 2 mmHg to − 5 ± 2 mmHg ($P < 0.05$, paired t test). The effectiveness of NO synthesis blockade was demonstrated by an increase in BP from 111 ± 3 mmHg to 123 ± 3 mmHg after its injection.

In the SHR (n = 13) the adrenergic blockade (n = 6) produced a significant decrease of the SBP from 168 ± 2 mmHg to 126 ± 2 mmHg ($P < 0.05$, paired t test); and it also reduced the deflation–inflation difference which varied from − 27 ± 4 mmHg to − 13 ± 5 mmHg ($P < 0.05$, paired t test). Injection of L-NAME (n = 7) did not change the SBP (165 ± 2 mmHg to 168 ± 3 mmHg (NS, paired t test); and also failed to reduce the deflation–inflation difference, which varied from − 26 ± 4 mmHg to − 22 ± 3 mmHg (NS, paired t test).

4. Discussion

In routine measurements of SBP by the tail-cuff method we noticed that the deflation readings consistently produced lower values than the inflation readings, a fact rarely mentioned in the literature (Buñag 1973, 1975; Pfeffer et al., 1971; Rowberg et al., 1969; Martinelli et al., 1985). In analyzing the causes for this phenomenon, the simplest explanation could lie in the procedure's own definition: if in the inflation cycle the cuff pressure *has to be* higher than the intravascular BP for the pulse to disappear, and the contrary holds true for the deflation cycle, this in itself implies a lower estimation during deflation if the intravascular BP is stable. However, the difference is likely to be too small to be detected with the current methods, and more so if the inevitable oscillations in BP over time are taken into account.

A physical explanation could be based on the different velocities of blood flow during the inflation and deflation cycles. On cuff constriction flow velocity progressively decreases to zero; but on deflation the arterial lumen is initially narrower than normal, and flow velocity is high. According to Bernoulli's theorem, if the fluid flows horizontally so that no change in gravitational potential energy occurs, then an increase in fluid velocity is associated with a decrease in lateral fluid pressure and vice versa (i.e. the Venturi effect) that could produce a lower deflation reading (Cameron and Skofronick, 1978). This explanation would be compatible with our finding that the inflation–deflation difference was significantly correlated with the prevailing BP, being greatest in SHR. In addition, if the inflation–deflation difference for each of the SHR of Fig. 1 is calculated using the linear regression equation of the Wistar rats, a value of − 13.9 ± 0.3 mmHg results, which is not significantly different from the − 16 ± 1.4 mmHg obtained experimentally. In other words, and when the compression time is short, the increased inflation–deflation difference of the SHR could be explained solely as a result of their higher SBP.

Also in support of a purely physical explanation is the fact that in collapsible-tube analogues of the brachial artery (Bertram & Butcher 1992) it has been demonstrated that when an external pressure suppresses the oscillations, the cessation (as pressure increases) occurs at a higher value than the onset (as pressure decreases), and this phenomenon is flow-dependent.

However, the foregoing explanations consider the tail artery as an entirely passive conduit, which is not the case. When during deflation the cuff pressure no longer counteracts the intravascular BP, the state of constriction of vascular smooth muscle constitutes the principal remaining resistance to flow, and it must be overcome for the arterial pulse to reappear. By decreasing smooth muscle tone during deflation, the readings obtained could appear lower than the ones obtained during inflation. This lowered smooth muscle tone could be provoked by a vasodilator accumulated during the compression interval, when the tail is rendered ischemic. Three pieces of our experimental findings support this possibility.

Firstly, the experiments in which we extended the compression interval (and thus the ischemic period) up to 4 min and obtained a corresponding increase in the inflation–deflation difference. In addition, if the increase is calculated on the basis of the corresponding regression equations of Fig. 1, the expected length of the inflation–deflation difference at the end of the 4-minute compression should have been − 7.3 ± 0.3 mmHg in Wistar and − 11.2 ± 0.6 mmHg in SHR. Instead, the increase obtained was nearly three times as great in SHR and more than four times as great in WKY. This indicates that although the influence of the inflation reading increase cannot be neglected, the lengthening of the inflation–deflation difference was due in its greatest proportion to the prolonged compression, of which the accumulation of a vasodilator is a likely consequence.

Secondly, the fact that the relative increase of the inflation–deflation difference was different in Wistar and in SHR in spite of a similar compression time could indicate a different vasodilator capacity in both strains. Moreover, the increase of the inflation–deflation difference was greater in the Wistar where the SBP was lowest, and smaller in the SHR in spite of showing the highest SBP. This dissociation from the prevailing SBP clearly indicates the participation of a local factor in addition to the mere variation and/or magnitude of SBP.

Thirdly, in the experiments with the nonspecific smooth muscle relaxant papaverine the smooth muscle was placed in a state of relaxation beforehand, and this prevented the action of the hypothesized vasodilator and the lengthening of the inflation–deflation difference in the Wistar, while only attenuated this lengthening in the SHR.

We then set out to investigate which vasodilator could participate in this phenomenon, focusing our attention on sympathetic innervation and on the nitric oxide (NO) system. For that purpose we used BP readings with a 2 min. interval between inflation and deflation cycles in order to turn the inflation–deflation difference well evident; the first measurement was performed in control conditions (no blockers) and the second after the specific blocker had been administered. When the sympathetic system was explored, alpha- and beta-blockade were produced simultaneously to make sure that the tail artery, usually richly innervated, did not receive any autonomic influence. Although the decrease in SBP indicated that the adrenergic blockade was successful, a significant inflation–deflation difference still persisted in the Wistar, indicating that the sympathetic system was not predominant in the production of this phenomenon. In the SHR, however, the sympathetic blockade did produce a significant reduction of the inflation–deflation difference, although its increase could not be totally prevented.

These results on adrenergic blockade are consistent with the studies showing that in the SHR the sympathetic nerves appear to be overly active. This hyperactivity could explain why the adrenergic blockade was at least partially effective in preventing the lengthening of the inflation–deflation difference in the SHR, while it was not so in the normotensive Wistar rats.

When the NO production was blocked by L-NAME the lengthening of the inflation–deflation difference was significantly diminished in the Wistar, indicating that NO accumulation during the occlusion period was relevant in its production. It has to be noted that the blockade of NO synthesis was even more effective than could appear at first sight because the prevailing SBP increased with the administration of L-NAME, and this by itself augments the inflation–deflation difference as discussed before. Had the SBP remained stable, the decrease could have been even greater. Contrary to these results, in the SHR the exposure to L-NAME could not prevent the lengthening

of the inflation–deflation difference brought about by the prolonged compression.

The foregoing results about NO blockade are consistent with recent experiments in normotensive rats performed in this laboratory (Fritz & Rinaldi, 2007), in which we demonstrated an increase of 28.5 ± 9.9 % of NOS activity in samples of tail arteries obtained after cuff compression and preserved under hypoxic conditions.

Further mechanisms of NO accumulation during the ischemic interval could be the following: 1) since there is a tonic production and release of NO by the endothelium (Moncada & Higgs 2006), and the cuff compression precludes either the arterial inflow and the venous outflow, NO is likely to accumulate and be responsible for the vasodilation during the deflation cycle; and 2) endothelial cell deformation is another cause of NO production (Moncada & Higgs 2006), but in this case it can probably be ruled out because during the ischemic interval there is no flow and consequently no shear stress. Upon restoration of flow there will be shear stress and NO release, but its effect would be evident later on, and not when the pulse reappears.

The lack of effect of L-NAME that we found in SHR is also compatible with the well-known depression of NO synthesis that is present in that model of hypertension, and also in essential hypertension in humans (Moncada & Higgs 2006; Schulman, Zhou, & Raji, 2006).

To our knowledge this is the first study looking for an explanation of the difference between inflation and deflation values obtained during tail-cuff measurement of SBP in normotensive and hypertensive rats, and establishing different roles for nitric oxide accumulation and sympathetic stimulation in the production of this phenomenon. These are novel results, because in our previous study on the same subject (Fritz & Rinaldi, 2007) only normotensive animals were studied.

The following conclusions may be drawn:

1) The inflation–deflation cycle usually involved in the tail-cuff methods produces a deflation reading that is significantly lower than the inflation reading. This phenomenon is proportional to the prevailing SBP, and can be demonstrated in artificial models of the circulation.
2) In addition to the physical factors, local production of vasodilators during compression of the tail originates differences between Wistar and SHR that cannot be explained solely on the basis of their different SBP before compression.
3) In the normotensive (Wistar) rats, prolonged compression leads to NO production, which in turn produces a lengthening of the inflation–deflation difference. Sympathetic innervation does not seem to play an important role in the production of this phenomenon in these animals.
4) In the hypertensive (SHR) rats, prolonged compression leads to vasodilation and this may partly explain the lengthening of the inflation–deflation pressure difference. However, the participation of NO production and sympathetic response is reversed: the NO production does not seem to play an important role, while the sympathetic system appears as mediating at least in part the increased inflation–deflation pressure difference. This predominance of the sympathetic system could be the result of its hyperactivity in hypertensive animals, and/or a compensatory reaction to the depressed NO synthesis known to be present in hypertension.

As a practical conclusion, the duration of suprasystolic compression by the tail cuff should be kept as short as possible, and the inflation value should be taken as representative of SBP. In the case of experienced operators SBP measurements will be fast and then the error inherent to the deflation reading would be small or even non-existent. However, if less-experienced persons and/or non-trained animals are involved, repeated attempts to measure BP will lead to prolonged tail compression and ischemia, and could produce deflation readings that do not estimate intravascular SBP accurately.

5. Conflict of interest

To our knowledge, there are no conflicts of interest emerging from this paper.

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