A NEW DEVICE FOR INDIRECT BLOOD PRESSURE MEASUREMENT IN RABBITS

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We evaluated the reliability of a new device for indirect measurement of systolic blood pressure in normal and hypertensive New Zealand White rabbits. This device consisted of an ear unit composed of an air chamber and sensitive photoelectric sensors, and was connected to an apparatus used for the tail-cuff method. Systolic blood pressure was determined by simultaneous recordings of pulse volume oscillations of the central ear artery and the chamber pressure. The blood pressure in 8 normal rabbits was $116 \pm 7/78 \pm 6$ mmHg (mean $\pm$ SEM) by direct measurement and 100 ± 6 mmHg by indirect measurement. In a one-kidney, one-clip hypertensive model, the new device showed that blood pressure increased from 100 ± 7 to 158 ± 7 mmHg over 4 weeks. After nicardipine was injected, blood pressure fell from $191 \pm 10/114 \pm 10$ to $117 \pm 7/72 \pm 8$ mmHg as measured by the direct method, and from 158 ± 7 to 92 ± 6 mmHg as measured by the new device. A strong correlation ($r=0.91$, $p<0.01$) was observed between direct and indirect measurements. Our findings indicate that this device provides rapid, easy and reliable measurement of blood pressure in rabbits. (*Jpn Circ J* 1994; **58**: 264–268)

ALTHOUGH indirect measurement of blood pressure is used in chronic hemodynamic studies, there are no devices available which can provide convenient serial measurements for rabbits. Indirect measurements were previously made in a central ear artery using the Grant-Rothschild capsule^{1–4} which consisted of an air chamber connected to a mercury manometer with a window to allow inspection of the central ear artery. With this device, the chamber pressure was increased above the systolic blood pressure and then decreased slowly. The mercury manometer indicated systolic blood pressure at the initiation of pulsations of the central ear artery. A major disadvantage of this old-

fashioned device was that simultaneous inspection of the height of the mercury and pulsations of the central ear artery required a great deal of skill, and sometimes resulted in unreliable readings. Subsequent devices were based on recording the electrical signals of arterial pulsation and the chamber pressure compressing the central ear artery^{5–7} which led to improved reliability.

Several convenient electrical devices are currently used to measure blood pressure by the tail-cuff method in rats. We analyzed the mechano-electrical principles of these devices and concluded that with minimal changes in design, some of these devices would be useful in rabbits. We developed an ear unit for use in rabbits that consisted of an air chamber for compressing the central ear artery and electrical sensors for detecting blood flow which corresponded to the tail-

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Fig.1. (A) Design of the ear unit. (B) Photograph of the ear unit.

cuff and sensor component of devices used in rats. In this study, we evaluated the validity of this ear unit when attached to a commercially available tail-cuff apparatus for indirect measurement of blood pressure in rabbits.

MATERIALS AND METHODS

Our design was based on a modification of the UR-1000 apparatus (Ueda, Tokyo, Japan), which is used for indirect measurement of blood pressure in rats. The original apparatus has a tail-cuff unit and a control unit. The tail-cuff unit consists of 2 pairs of light-emitting diodes (LEDs) and phototransistors placed on the opposite side of the cuff. The control unit consists of an air pump, a pressure transducer, a recorder, and a microcomputer that controls the entire apparatus.

We made no changes to the control unit. We substituted a custom-made ear unit for the tail-cuff unit. The ear unit, which combined a compression chamber and photoelectric sensors (Figs. 1a, 1b), was 35 mm in diameter, weighed 80 g, and was shaped to fit the rabbit ear. The lower part of the ear unit was an airtight chamber with a silicone rubber membrane in contact with the ear driven by the UR-1000 pump. Chamber pressure was recorded by the UR-1000 transducer. Light emitted by 2 LEDs (PS003E, Optrans, Tokyo, Japan) in the lower part of the unit was oscillated by pulsations of the central ear artery. These oscillations were detected by

the phototransistors (PS003D, Optrans, Tokyo, Japan) in the upper part of the unit. The UR-1000 recorded both chamber pressure and artery oscillations. LEDs were programmed to generate 1.5-kHz pulsed light to improve the signal/noise ratio to avoid noise interference from external sources of light.

Measurements were performed with the rabbits in a rectangular box to slightly restrict their movement. Xylene was applied to the tip of the ear to ensure sufficiently large pulse volume oscillations. After a few minutes, when the central ear artery was dilated, the artery was positioned properly between the LEDs and the phototransistors, and the air chamber was inflated to a pressure above systolic blood pressure, and then deflated slowly. The pressure recorded at the appearance of the oscillations was taken as the systolic blood pressure (Fig. 2). The average of three measurements was obtained to determine the systolic blood pressure.

We tested the validity of our instrument in male New Zealand White rabbits weighing 2.6 to 3.0 kg. A one-kidney, one-clip hypertensive model ($n=8$) was created by removing the right kidney and applying a silver 1.1 mm-diameter clip to the left renal artery under anesthesia with nitrous oxide and fluothane. Indirect measurements were made weekly for 4 weeks in these rabbits. After 4 weeks, simultaneous recordings of direct and indirect pressure measurements were made before and 15 min after an intravenous injection of nicardipine (0.5 mg/kg). Polyethylene tubing was inserted in

Fig.2. Recordings from a conscious rabbit. Upper tracing shows pressure in the air chamber; middle tracing shows pulse volume oscillations; lower tracing shows the aortic pressure. The reading (R) at the start of oscillation (S) indicates the systolic blood pressure of the ear.

Fig.3. Schematic illustration of the evaluation system.

TABLE I INDIRECT MEASUREMENTS OF SYSTOLIC BLOOD PRESSURES (SBP) IN ONE-KIDNEY, ONE-CLIP RABBITS

	week 0	week 1	week 2	week 3	week 4
SBP (mmHg)	100±7	118±8*	127±10*	127±10*	158±7*

The values are mean±SEM in 8 rabbits.

* $p < 0.05$ vs week 0.

the left femoral artery for direct measurement of blood pressure, and was connected to a P50 Statham transducer (Gould Inc.,

Oxnard, California, USA) which was placed at the level of the ear to eliminate the effects of hydrostatic pressure on pressure measurements. Signals from the transducer were amplified by an amplifier (LB810, Fukuda, Tokyo, Japan) and recorded by a multichannel recorder (WR3701-4L, Graphtec, Tokyo, Japan) together with signals from the UR-1000 (Fig. 3). In 8 normal rabbits, direct and indirect measurements were simultaneously made before and after an 800 ng/kg/min intravenous infusion of norepinephrine. All of the measurements were made in conscious rabbits. We followed our institution's guide for the care and use of laboratory animals

TABLE II DIRECT AND INDIRECT MEASUREMENTS OF BLOOD PRESSURE

	Direct SBP/DBP (mmHg)	Indirect SBP (mmHg)
normal rabbits (n=8)		
control	116±7 / 78±6	100±6
norepinephrine (800 ng/kg/min)	164±8 / 102±8	no signal
hypertensive rabbits (n=8)		
control	191±10/114±10	158±7
nicardipine (0.5 mg/kg)	117±7 / 72±8	92±6

The values are mean ± SEM.

SBP: mean systolic blood pressure; DBP: mean diastolic blood pressure.

Fig.4. Correlation between indirect and direct measurements of systolic blood pressure. Open squares are from normal rabbits; open circles are from hypertensive rabbits; closed circles are from hypertensive rabbits after nicardipine injection.

measurements were made in the 8 hypertensive rabbits. Blood pressure increased during the 4-week development of renal hypertension (Table I). Indirect blood pressure measurements were lower than direct measurements in both normal and hypertensive rabbits, but the difference was more apparent in the hypertensive rabbits (Table II). After nicardipine injection in the hypertensive rabbits, the ear unit appropriately detected the fall in blood pressure, although the values were lower than those obtained by direct measurement. There was an excellent correlation between the indirect and direct measurements ($r=0.91$, $p<0.01$, Fig. 4). In normal rabbits, the direct method recorded an increase in blood pressure from $116\pm7/78\pm6$ to $164\pm8/102\pm8$ after infusion of norepinephrine. In contrast, no oscillation signals were detected by the phototransistors in the indirect method after norepinephrine infusion (Table II).

through the experiment.

All data are expressed as the mean ± standard error of the mean (SEM). Statistical comparisons between indirect measurements in the hypertensive model were made using Student's *t* test. The correlation between indirect and direct measurements was assessed by least-squares regression analysis. A *p* value of less than 0.05 was considered statistically significant.

RESULTS

Indirect blood pressure measurements using the ear unit and UR-1000 were completed in less than 5 min. Successive weekly

DISCUSSION

The UR-1000, a device that measures blood pressure by detecting pulsations of the tail artery, has been shown to be sufficiently accurate in rats⁸. We adapted this system for rabbits by using the same principle to detect blood pressure of the central ear artery. When a custom-made ear unit was attached to the UR-1000, all of the components, including the air compressor, the transducer for detecting air pressure, the LED controller, and the phototransistors, worked well.

Indirect blood pressure measurements were completed within 5 min after xylene was applied to dilate the central ear artery,

which allowed us to make repeated blood pressure measurements in many rabbits without the need for invasive maneuvers. We were able to trace the development of hypertension over 4 weeks in 8 rabbits. It should be possible to monitor a larger number of rabbits over a longer period with this system. The device was able to detect a rapid decrease in blood pressure in hypertensive rabbits after injection of nicardipine, but did not detect an increase in blood pressure during norepinephrine infusion in normal rabbits. However, this lack of validity in normal rabbits should not affect the usefulness of this device for investigation of antihypertensive agents in hypertensive models.

Direct measurements correlated well with indirect measurements ($r=0.91$, $p<0.01$). Values obtained by the indirect method were consistently 20 to 40 mmHg lower than those obtained by direct measurements. Although we placed the catheter for direct measurements in a femoral artery approximately 20 cm below the central ear arteries, the pressure transducer used for direct measurements was placed level with the ear to eliminate the effects of hydrostatic pressure. Therefore, differences in hydrostatic pressure between the 2 sites were not responsible for the differences in blood pressure values. Studies have found that measurements of systolic blood pressure obtained at the central aorta or carotid artery are more than 10 mmHg above measurements at the central ear artery, when both values are determined by a direct method^{7,9} which suggests that arterial pressure is intrinsically lower at the central ear artery than at the aorta. Thus, despite the differences between direct and indirect measurements, our device appears to be sufficiently accurate.

The UR-1000 accurately determines mean arterial pressure when used in rats⁸. Oscillation signals from the central ear artery of rabbits in our study were similar to those

from the rat tail artery in a previous study⁸, which suggests that the new device determines the mean arterial pressure at the central ear artery in rabbits.

In conclusion, the modified UR-1000 measured blood pressure rapidly, conveniently, and reliably in conscious rabbits.

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REFERENCES

1. ANDERSON HC: Demonstration of an instrument for taking repeated blood pressures in rabbits, with report of some experiments. *Proc Soc Exp Biol Med* 1922-23; **20**: 295-297
2. KURAYA T: A new nonsurgical method for blood pressure measurement of a rabbit, with special reference to the blood pressure in pericarditis. *Acta Sch Med Univ Imp Kyoto* 1924; **6**: 373-388
3. WATSON EM: A method for estimating blood pressure in rabbits. *J Lab Clin Med* 1926-27; **12**: 706-707
4. GRANT RT, ROTHSCCHILD P: A device for estimating blood pressure in the rabbit. *J Physiol* 1934; **81**: 265-269
5. LANDIS EM, MONTGOMERY H, SPARKMAN D: The effects of pressor drugs and of saline kidney extracts on blood pressure and skin temperature. *J Clin Invest* 1938; **17**: 189-206
6. FRANGIPANE G, APORTI F: Improved indirect method for the measurement of systolic blood pressure in the rabbit. *Arch Sci Biol* 1970; **54**: 121-128
7. MORIZONO T, JOHNSTONE BM, LULICH C: Alternative method for measurement of arterial pressure in the rabbit. *J Appl Physiol* 1975; **39**: 312-314
8. SAKAMAKI T, TAJIMA Y, ICHIKAWA S, MURATA K: Measurement of mean arterial pressure in rats by a tail-cuff method with sensitive photoelectric sensors. *Exp Anim* 1987; **36**: 409-414
9. WILSON DM, ROMERO JC, STRONG CG, LEE KE, SCHRYVER SM: Indirect blood pressure measurements in the rabbit: correlations with direct aortic and ear pressures. *J Lab Clin Med* 1975; **86**: 1032-1039