Implanted pulsatile balloon device for simulation of neurovascular compression syndromes in animals

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A self-contained neurovascular compression simulator (NCS) has been designed to function as an artificial artery that pulsates with the heart. When implanted in animals, this device simulates those naturally occurring situations in which there is compression of nervous elements in the region of the brain stem or other areas by aberrant, or ectatic branches of normal arteries. The NCS consists of an intra-aortic balloon, a smaller (cephalic) balloon, a connecting tube, and an injection port, all fabricated of polyurethane-silicone compounds. With each heart systole, the rise in intra-aortic pressure is transmitted to the smaller cephalic balloon in the form of a pulsation. Thus, part of the cardiac ejection energy is transferred to the desired nervous structures. The performance of each NCS is tested in vitro in a pulse duplicator system.

The NCS was chronically implanted for up to 2 years in four dogs and 10 baboons. The cephalic balloon was placed intracranially in the subarachnoid space on the ventrolateral medulla adjacent to the entry zone of the ninth and 10th cranial nerves on the left side of baboons and on the right side of dogs. The position of the balloons was checked by fluoroscopy. Following implantation, the NCS could be inflated or deflated at will using the injection port which served to restart or discontinue the pulsations. No occlusion of the aorta or reduction of blood flow to the lower limbs or trunk was detected. By means of the NCS, an experimental model of neurogenic hypertension was produced in baboons.

KEY WORDS - neurovascular compression - hypertension - medulla oblongata - nerve compression - animal model - cranial nerve disease

VASCULAR compression of cranial nerves has been identified as the causal factor in numerous clinical syndromes. Progressive loss of vision and paresis or palsy of the third cranial nerve may be caused by an intracranial aneurysm. Oculomotor nerve weakness can also be caused by an ectatic posterior communicating artery. Similarly, trigeminal neuralgia can be caused by compression of the fifth cranial nerve root entry zone by an ectatic superior cerebellar artery or another artery or vein, and is relieved by micrvascular decompression. Hemifacial spasm has been relieved by moving the vertebral, basilar, or the anterior inferior (AICA) or posterior inferior cerebellar arteries (PICA) so as to decompress the seventh cranial nerve entry zone. Improvement in hearing and decrease in tinnitus or vertigo were observed after decompression of the eighth cranial nerve involving moving a vascular loop compressing its cochlear or vestibular portions. Glossopharyngeal neuralgia has been similarly relieved by decompression of the nerve root entry zone on the brain stem, moving AICA, PICA, or vertebral artery loops. Finally, decompression of the ventrolateral medulla on the left side adjacent to the entry zone of the ninth and 10th cranial nerves has been correlated with relief from arterial hypertension. Despite these significant clinical data, no experimental evidence is available to demonstrate the physiological and structural effects of pulsatile vascular loop compression on the central nervous system.

A self-contained double-balloon device was designed to function as an artificial artery pulsating with the heart. This device simulates those naturally occurring situations in which there is compression of
neurovascular compression simulation

Fig. 1. Photograph of the neurovascular compression simulator. For a description see text.

nervous elements in the region of the brain stem or other areas by aberrant or ectatic branches of normal arteries.

Description of Device and Methods

The neurovascular compression simulator (NCS) consists of four parts: an intra-aortic balloon, a smaller balloon for placement in the cephalic subarachnoid space, connecting tubing, and an injection port (Fig. 1). The aortic balloon is an enclosed cylindrical bag, 5 mm in diameter and 8 cm long. The blood-contacting surface is composed of a complex band of polyurethane, silicone, and the copolymer of both (Cardiothane-51 copolymer).* The inner surface is made up of an ultra-pure polyether-based polyurethane (Cardiomat-610 polymer).* The elastic (Young) modulus of this material is relatively high. That is, the relative deformability in response to stress (or pressure) is low as compared with common balloon materials such as latex or silicone rubber. A perforated Cardiothane tube impregnated with barium runs the length of the interior of the large balloon. The small balloon, also composed of Cardiothane-51 and Cardiomat-610 polymer is 1 cm long and 2 mm in diameter, and is attached to the Cardiothane tubing only at the proximal aspect. The tube connecting the large balloon with the port is 18 cm long, and the tube connecting the small balloon is 12 cm long; both are 1 mm in outside diameter. The tubes meet in a T-port with a silicone rubber septum for inflation and monitoring purposes. The entire NCS can be sterilized with a cold cycle of ethylene.

* Cardiothane-51 copolymer and Cardiomat-610 polymer manufactured by Kontron Cardiovascular, Inc., 9 Plymouth St., Everett, Massachusetts.

The NCS was implanted into experimental animals (primates and dogs) in the following fashion. The large fluid-filled balloon was introduced into the intrathoracic aorta through a small incision in the axillary artery. The arteriotomy around the PVC tubing was closed with 6-0 silk in a purse-string fashion. The connecting tube, T-port, and small balloon were tunneled subcutaneously in a cephalad direction, with the T-port lying over the scapula. The small balloon was then placed intracranially in the desired anatomical position in the subarachnoid space via a retrosigmoid craniectomy. The position of the balloons was checked by fluoroscopy (Fig. 2).

When the implanted NCS was inflated by a 1.1-ml injection of normal saline solution through the subcutaneously placed T-port, its action followed the following mechanism. With each heart systole, the increased intra-aortic pressure compresses the large balloon. The rise in pressure is transmitted via the connecting catheter to the smaller intracranial balloon in the form of an arterial pulsation with each heartbeat. Thus, the device serves to transfer part of the cardiac ejection energy to the desired nervous structures, so functioning as an artificial artery pulsating in synchrony with the heart.

Intraballoon pressure was monitored through a No. 26 needle penetrating the injection port and connected to a transducer. The physical properties of the NCS were tested both in vitro and in vivo. A pressure-volume study was carried out in order to characterize the performance of the NCS. A pulse duplicator system† was used for the in vitro test (Fig. 3). Both static and pulsatile pressures were applied.

† Pulsatile pump manufactured by Harvard Apparatus Co., Inc., Millis, Massachusetts.
Results

Originally the NCS was filled with air, but we found that the system rapidly deflated (in less than 3 days) due to the outward diffusion of air. When the system was filled with isotonic saline and kept immersed in an isotonic solution, there was no measurable loss of volume.

In Vitro Test

With the large balloon introduced into the test chamber, the pulse duplicator created a pulsatile cycle of pressure similar to the systolic-diastolic sequence. It was possible to regulate both the rate and the pressure in the NCS and also maintain a static pressure with the pulse duplicator deactivated. Static (30 torr) and mean dynamic (120 torr) pressure-volume correlating curves are shown in Fig. 4. When the pulse duplicator was activated, the cycle of systolic/diastolic pressure on the “aorta” was reproduced with reasonable fidelity in the interior of the NCS (Fig. 5). The correlation between the pressure inside the NCS and the lateral force exerted by the wall of the small balloon was measured by a linear strain gauge system and is plotted in Fig. 6. Volume displacement of the small balloon was recorded from the displacement scale (0.1 ml in 0.001 Pipete) of the plethysmograph. The pulse duplicator served as a convenient method for standardization of the NCS, performance characteristics, leak, and endurance testing.
Neurovascular compression simulation

**Fig. 5.** Simultaneous record of pulsatile pressure from the pulse duplicator and neurovascular compression simulator. Speed of recording: 25 mm/sec.

**Fig. 6.** Relationship between the mean aortic pressure and the lateral force exerted by the exteriorized cephalic balloon as measured by a strain gauge system in dogs. The rise in mean arterial pressure is induced by intravenous phenylephrine. The regression line is shown, and the high correlation coefficient (0.98) confirms the linear relationship.

**In Vivo Test**

The feasibility of the use of the NCS device under *in vivo* conditions has been tested on four dogs and 10 baboons. No signs indicating decrease in blood flow to the trunk or lower limbs were detected in the animals implanted with the NCS for up to 2 years. No aortic thrombosis was found at autopsy. In three baboons, a fine catheter was inserted alongside the large balloon catheter and was used intraoperatively to ascertain that there was not an excessive pressure drop across the aortic balloon when placed in its final position. No significant pressure gradient was found.

The pressure-volume curves recorded *in vivo* were identical to those recorded *in vitro* when the NCS was functioning properly, and could be used to assess its functional status after implantation. The presence of leaks was indicated by reduction in the internal fluid volume, and kinking of the NCS was indicated by loss of compliance.

**Preliminary Results**

Arterial hypertension developed in five baboons when the NCS was implanted on the left ventrolateral aspect of the medulla. Five control baboons underwent similar experimental manipulations, but the NCS was implanted deflated (not pulsating) and no changes in blood pressure or heart rate were detected. These findings will be described in a separate report.

In preliminary studies in dogs, cardiac arrhythmias occurred in four dogs with pulsatile pressure on the lateral medulla oblongata and 10th cranial nerve entry zone on the right side.

**Discussion**

The use of a Fogarty catheter with a balloon juxtaposed to the entry zone of the ninth and 10th cranial nerves in contact with the left ventrolateral medulla was described in earlier reports from this laboratory. This balloon was activated by an external mechanical pump in an acute model in anesthetized cats. We found it difficult to maintain the connection between the external pump and the experimental
animal for extended periods of time. We also realized that such a system is subject to mechanical failure, such as problems with the pump power. We considered the fact that naturally occurring vascular compression involves pulsations in phase with the cardiac action and that it would be difficult (although not impossible) to synchronize pulsations using an external pump. A final problem was that that model required total restraint of the animal.

In consideration of the foregoing, the present neurovascular compression simulator (NCS) has been developed. It has the advantage of permitting chronic studies in the more physiological setting of unrestrained animals. It also prevents the problem of infection created by a chronic transcutaneous bridge to the subarachnoid space. The device has been chronically implanted in dogs and baboons without causing occlusion of the aorta. Changes on the position of the NCS components may be checked by radiography. Recording of pressure-volume curves by percutaneous access to the filling port makes it possible to check on the proper function of the NCS. The pulsations may be discontinued and reinitiated at will by simply deflating and reinflating the NCS.

The use of the NCS makes it possible to investigate the effect of vascular loop compression of cranial nerves and brain structures in laboratory models. The effects of chronic pulsatile pressure on different nerve structures can thus be studied in terms of the natural history of the development of the “disease” and the electrophysiological, biochemical, and morphological changes elucidated. Results of experiments with a neurogenic hypertensive baboon model have demonstrated the usefulness of this device.

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