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Experimental Research

Protective Effect of Posterior Cerebral Circulation on Carotid Body Ischemia

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Summary

Background and Purpose. Carotid Bodies (CB) are fed mainly by External Carotid Artery (ECA) and rarely by Internal Carotid Artery (ICA). We aimed to investigate the effect of Bilateral Common Carotid Artery ligation and BCCAL plus bilateral external carotid artery ligation on CB.

Methods. This study has been conducted on 30 hybrid male rabbits. Normal CB analyses were made in six of these animals and others divided into two groups. BCCAL has been applied to the 1st group, and the 2nd group has undergone bilateral ECA ligation in addition to BCCAL. After sacrificing the animals, both sides CB were histopathologically observed. Normal and ischemic cells were counted.

Findings. Bilateral Common Carotid Artery ligation did not cause total atrophy in CB. Partial reversible atrophy of CB was seen in group I, but that atrophy was found to be irreversible and all animals died within one week after ligation in group II.

Interpretation. Retrograde blood flow mechanisms and collateral circulation impede the oligemic CB atrophy after BCCAL. But bilateral ECA ligation, in addition to BCCAL, causes both sides irreversible CB atrophy and death of animals within one week of ligation.

Abstract. The CB are parasympathetic paraganglia. They are chemoreceptors and located at the bifurcation zone of common carotid arteries. They are fed mainly by ECA or by its branches and rarely by ICA. As a consequence of this, BCCAL and/or ligation of external branches of common carotid artery may lead to an ischemic impairment of CB. In order to analyse the effect of carotid stenosis on CB, CB were directly examined in 6 of 30 hybrid rabbits. BCCAL was applied to twelve rabbits (group I) with ligation of both ECA in addition to BCCAL were made to the others (group II). Animals were followed up four months in group I; but all of the animals in group II died within one week. From both sides the CB were taken including the carotid bifurcation and histopathological changes were evaluated. As a result, it has been observed that incomplete ischemic lesions have developed in the CB because of retrograde blood flow from posterior circulation to the ECA providing blood for the CB. But in the second group these changes were irreversible and on both sides CB complete atrophy developed in those whose ECA were also ligated bilaterally.

Keywords: Carotid body ischemia; common carotid occlusion; atrophy.

Introduction

CB are located behind or between the carotid bifurcation and are embedded in a fatty tissue in the carotid adventitia [2]. CB are the most vascularised structures in the body in terms of amount of blood supply/per tissue volume. CB are chemoreceptors which are quite sensitive to pH changes. When the O_2 difference in the arteriovenous blood is less than 1%, these bodies are stimulated [3]. CB are supplied mainly by glomus arteries coming from ECA and by occipital arteries or the ascending pharyngeal artery to a small extent (2.5%) and rarely by ICA [4, 7, 8].

Bilateral Common Carotid Artery Ligation can cause ischemic lesions on the cranio-cervical compartments for a certain period. BCCAL activates vertebro-basilar counter-flow mechanisms and collateral circulation. But such a disturbed circulation can return to normal to a great extent by blood flowing from the vertebro-basilar system to the carotid system via the posterior cerebral arteries. As a result of this mechanism, blood is supplied to ECA and its branches. This phemenon becomes apparent angiographically 7 days after ligation and prominent within two months. The whole carotid system can be seen by counter-flow, collateral circulation and angiogenesis mechanisms at the end of four months [6]. The ligation of arteries of CB results in necrosis in glomus and sustentacular cells of the CB within twelve hours. On both sides total CB atrophy was seen in one to four weeks after ligation of CB arteries [1]. Up to date we could not find any study dealing with the effect of BCCAL and bilateral ECA ligation on CB in the literature. Therefore, in this study, we aimed to investigate the effect of BCCAL

and/or ECA ligation on oligemia of CB and to emphasize the significance of the protective effect of retrograde blood-flow mechanisms on oligemic CB necrosis.

Materials and Methods

This study has been conducted on 30 hybrid male rabbits of 3 kg. Normal CB were analysed in 6 control rabbits. The remaining rabbits were divided into two groups. They were left hungry 6 hrs before surgical intervention. A balanced injectable anesthesia was used for reducing pain and mortality. Anesthesia was administered in two phases: 20 mg/kg of sodium penthobarbital was injected intraperitoneally for preoperative preparation. Thereafter, 0.2 mL/kg of the anesthetic combination (Ketamine HCL, 150 mg/1.5 mL; Xylazine HCL, 30 mg/1.5 mL; and distilled water, 1 mL) was subcutaneously injected before surgery. During the operation, 0.1 mL/kg anaesthetic combination was used when required. In the first group, both common carotid arteries were exposed, separated from their sheaths, nerves, and ligated with 4.0 silk sutures. The 2nd group has undergone bilateral external carotid artery ligation in addition to BCCAL, but all of the animals died within one week after ligation in group II. In the same group, Carotid Bodies together with the carotid bifurcation were removed after one week on both sides. Moreover, animals were followed up four months in group I, and four months later in the same group, both Carotid Bodies together with the carotid bifurcation were removed. The specimens, after being kept in 10% formaline solution for 7 days, were taken into paraffin blockage. Sections of 1 μm were obtained and stained with H§E and analysed under light microscopy. Ten fields have been taken into consideration from each CB and all the cells have been counted in the low power microscopic field (LPMF) and average values were obtained.

Results

Haemodynamic activities in the carotid bifurcation have been observed anatomically under the operation microscope in anesthetized rabbits. It was observed that the pulsation of the external carotid arteries continued in group I whereas it could not be observed in group II in which thrombus formation was observed in the post-ligational region of both the ECA. Upon histopathological analysis of CB in the 6 animals, it was observed that they had a dimension of 0.8–1.5 mm, were round or oval in shape and located at the carotid bifurcation (Fig. 1). A thin capsular structure surrounding them was identified as sending plenty of septa inside and dividing the body into subsections and that there were nerve endings and arterioles (Fig. 2). CB became small to some extent in size; cytoplasmic condensation, nuclear hyperchromasia, partial edema, cellular swelling with a significant decrease in the number of neurons as observed in Fig. 3. In group II; prominent neuronal hyperchromasia, neuronal angulation, cellular atrophy, neuronal loss and necrosis were seen

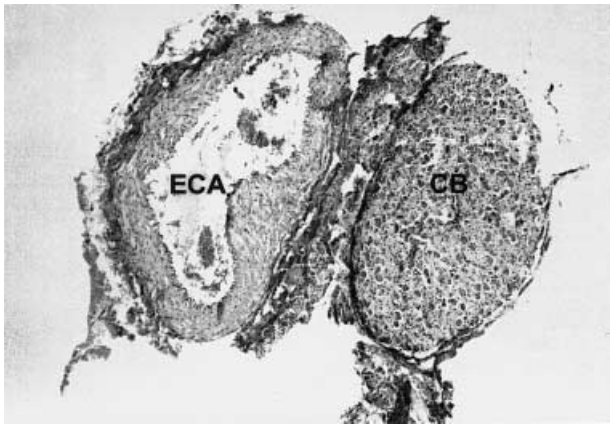

Fig. 1. CB in a normal subject. ECA and CB next to it (*LM* H§E, ×40)

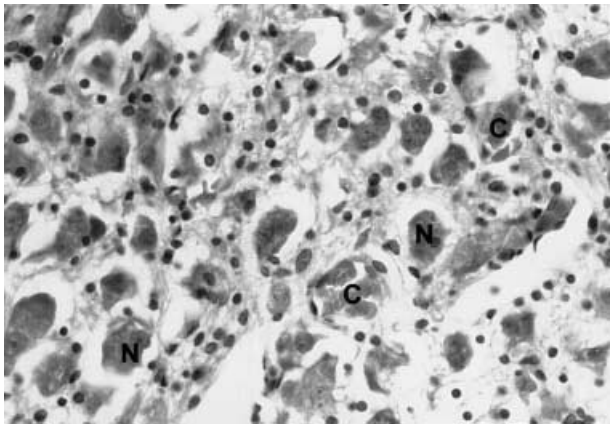

Fig. 2. Normal neurons (*N*), sections including the capillaries (*C*) can easily be seen (*LM* H§E, ×200)

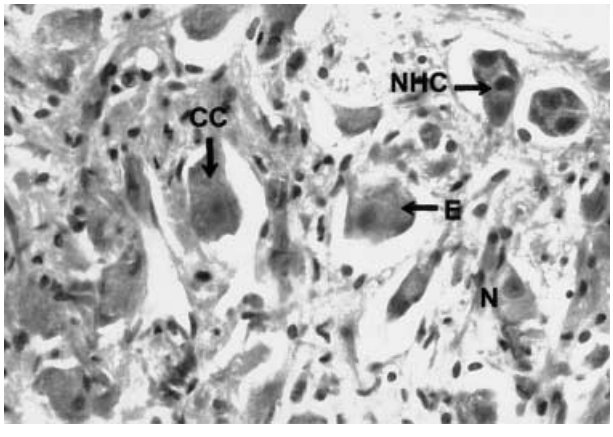

Fig. 3. CB pertaining to the 1st group. Decrease in arterioles, edema in neurons (*E*), cytoplasmic condensation (*CC*), neuronal hyperchromasia (*NHC*), and significant neuronal loss (*NL*) can be observed (*LM* H§E, ×200)

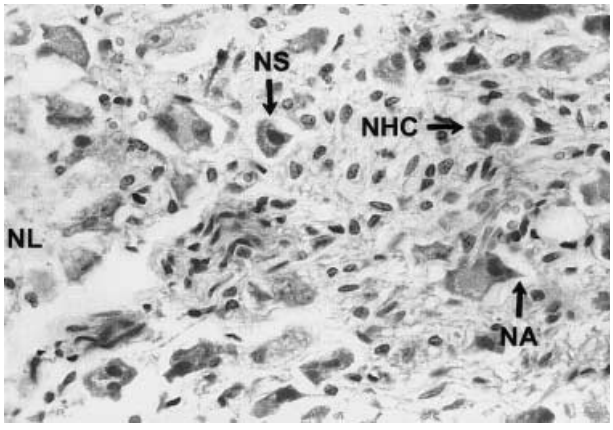

Fig. 4. CB pertaining to the 2nd group. Prominent neuronal hyperchromasia (*NHC*), neuronal shrinkage (*NS*), neuronal angulation (*NA*), neuronal loss (*NL*) and CB atrophy are seen (*LM* H§E, ×200)

in glomeral cells together with reduction in size of CB. No capillaries could be seen (Fig. 4). Mean numbers of normal and ischemic/necrotizing cells were 125 ± 15 and 2 ± 1 in the control group, 40 ± 10 and 30 ± 6/LPMF in group I, respectively. In group II, mean number of normal cells were 3 ± 1/LPMF, and the number of neuron loss was 100 ± 10/LPMF.

Discussion

Blood flow and perfusion of the CB may decrease in case of temporary or permanent carotid occlusions in thrombotic, atherosclerotic and tumoral diseases of CB, carotid endarterectomy, superior temporal artery-middle cerebral artery anastomosis, caroticocavernous fistula surgery. CB hyperplasia may develop in those who live at high altitudes (due to lack of O_2), and in those suffering from chronic obstructive lung disease, restrictive lung disease, cystic fibrosis and cyanotic heart disease [2]. The respiratory reflexes of subjects whose CB are removed is impaired [5]. This seems to be a baroreceptor function of the carotid bodies [4]. The organism cannot respond to the blood pressure changes as required, because afferent fibers of CB cannot convey the chemical stimulation to cardiorespiratory centers [1, 9]. Therefore, these are very important sequelae for the subjects with ischemic loss of both carotid bodies.

Interruption of the blood supply to the carotid body by ligating arteries of its vascular peduncle produces structural changes in parenchymal cells. Ischemia for two hours or longer produced irreversible functional damage and disappearance of glomus and sustentacular cells from the CB. Total CB atrophy was seen in one to four weeks after ligation of CB arteries [1]. BCCAL can cause ischemic lesions on cranio-cervical tissues by leading to impairment in cranio-cervical circulation for a certain period of time. BCCAL activates vertebro-basilar counter-flow and collateral circulation [6]. Eventually, blood supply to ECA and its branches is provided by these mechanisms. This situation becomes more appearent at 7th days after ligation, and in the 2nd month the whole carotid system can be seen angiographically [6]. Blood transfer reaches the ECA via counter-flow mechanisms. Consequently, recirculation occurs in group I and glomus arteries and ischemic impairment of CB can be reversed. Whereas bilateral ligation of ECA blocks the counter-flow pathway in group II. Thus blood flow to the ECA is prevented and both the carotid bodies atrophy inevitably.

The external system can be seen angiographically on the 1st day and it completely returns to normal on the 7th day [6]. In our study, we have formed CB ischemia by BCCAL until counter-flow mechanisms are activated. In the histopathological analysis of CB, we have identified that the ischemic impairment was less in the group I and even a repair phase had started. However, in the group II, there was a complete ischemic necrosis of CB on both sides. The counter-flow pathway, which was described by Oldendorf, is established by means of Willis' polygon from posterior circulation to ICA and ECA [6].

In one study, Oldendorf performed BCCAL and described the counter flow pathway in which blood is transferred to the carotid system from vertebrobasilar arteries. In the present study, we performed bilateral ECA ligation in addition to BCCAL as in the Oldendorf study and observed that blood supply to CB was interrupted and finally atrophy of the CB was observed bilaterally. In conclusion, ischemic lesions which develop in CB due to BCCAL can be reversed by way of transferring blood from the posterior cerebral circulation to the ECA. Whereas this retroflow pathway can be blocked by the ligation of both ECA plus BCCAL, and this condition could result in complete CB atrophy bilaterally.

References

1. Bloch LM, Stensaas LJ, Eyzaguirre C (1983) Effect of ischemia on the function and structure of the cat carotid body. Brain Research 270: 63–76
2. Fitch R, Smith P, Heath D (1985) Nerve axon in the carotid body hyperplasia. Arch Pat Lab Med 109: 234–237
3. Gonzalez C (1994) Carotid body chemoreceptors from natural stimuli to sensory discharges. Physiol Rev 74: 829

4. Habeck JO, Honig A, Pfeiffer C, Schmidt M (1981) The carotid bodies in spontaneously hypertensive (SHR) and normotensive rats – a study concerning size, location and blood supply. Anat Anz 4: 374–384
5. Honda Y, Myojo S, Hasegawa S, Hasegawa T, Severinghaus JW (1979) Decreased exercise hyperpnea in patients with bilateral carotid chemoreceptor resection. J Apply Physiol Environ Exercise Physiol 150: 908–912
6. Oldendorf WH (1989) Trophic changes in the arteries at the base of the rat brain in response to bilateral common carotid artery ligation. J Neuropathol Experiment Neurol 48: 534–547
7. Seidl E (1976) On the variability of form and vascularization of the cat carotid body. Anat Embriyol 2: 78–86
8. Unur E, Aycan K (1999) Arteries of the carotid body in rats. Anat Histol Embriol 28: 167–169
9. Verna A (1970) Ultrastructure of the carotid body in the mammals. Int Rev Cyto 60: 271–330

Comment

The clinical significance relates to surgical interventions, e.g. in case of an endarterectomy of stenotic cervical arteries. Thereby, the adjacent carotid body seemingly depending on a high blood flow may be damaged. The objective of this study, thus, appears to be straightforward.

The experiments were carried out by studying male rabbits subjected to bilateral common carotid artery ligation with and without additional ligation of the external carotid artery. Study endpoint was the histological assessment of the carotid body of animals subjected to carotid artery ligation. The resulting changes were quite clear. Ligation of the carotid arteries alone was found to induce pathological changes of the carotid bodies, albeit less severe than, if combined with ligating the external carotid artery in addition. Accordingly, ligation of the common carotid artery alone led to shrinking of the Glomus, cytoplasmic condensation, and nuclear hyperchromasia with edema or cell swelling, respectively and loss of neuronal cells – all indicative of some irreversible damage. Damage of the carotid body, however, was apparently more pronounced in the experiments with ligation of both the common and external carotid arteries, as e.g. shown by the greater loss and necrosis of neuronal cells.

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