HAEMODYNAMIC EFFECT ON THE GROWTH OF EXPERIMENTALLY INDUCED SACCULAR ANEURYSMS IN RATS

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OBJECTIVE
Haemodynamic stress has been considered to be an important factor in aneurysm formation and growth. The aim of this study was to reveal the effect of salt induced hypertension on the experimental saccular aneurysm model.

MATERIALS AND METHODS
Forty Sprague-Dawley rats of both sexes in equal number were used in this study. Under general anesthesia with ketamine hydrochloride (Ketalar, Parke-Davis, England), a linear arteriotomy of the right carotid artery was performed in all rats. Transluminally a tunica intima and media defect at the arterial bifurcation was made under the microscope and the wound was closed after arteriotomy. They were divided into four groups according to type and duration of diet. After the sacrifice of each rat, the carotid bifurcation with aneurysm was fixed in 10% formalin and embedded in paraffin. Each aneurysm section was examined in detail and the height of aneurysmal sac was measured using an ocular micrometer in the section in which the aneurysm was observed to be largest.

RESULTS
The mean size of each group was compared using the single-sided variance analysis technique and among the 4 groups of rats, the mean size of aneurysmal sac of 4th group found greater than the others (P< 0.05).

CONCLUSION
The present study indicates that haemodynamic stress plays a very important role in the growth of saccular aneurysms.

INTRODUCTION:
Many factors that influence the formation and growth of saccular aneurysms have been studied in detail. Haemodynamic factors, such as persistent hypertension or unilateral common carotid ligation, have been
considered to be very important [2,19] it has been found a relationship between the enlargement or rupture of saccular aneurysms and temporary physical stress in patients [12].

In our previous study we described an experimental saccular aneurysm in the rat [3]. This animal model was used to test the effect of haemodynamic stress on the growth of experimental saccular aneurysms.

MATERIAL AND METHODS

Forty Sprague-Dawley rats of both sexes in equal number were used in this study. They were 6 months old and weighted 220-250 g. Under general anesthesia with ketamine hydrochloride (Ketalar, Parke-Davis, England), a linear arteriotomy of the right carotid artery was performed in all rats. Transluminally a tunica intima and media defect at the arterial bifurcation was made under the microscope and the wound was closed after arteriotomy. After closing the incision, an experimental saccular aneurysm developed in all rats immediately and the rats were fed with two different diets after the operation. They divided into four groups according to type and duration of diet.

Group I, which consisted of ten rats, was fed a standard diet and water without drugs before and after the operation. They were sacrificed 7 days postoperatively. Group II, consisting of another the rats, was fed a standard diet and water replacing by 2% NaCl solution after the operation. They were sacrificed 14 days postoperatively. Group III, consisting of ten rats, was fed a standard diet and water replacing by 2% NaCl solution after the operation. They were sacrificed 7 days postoperatively. Group IV, consisting of ten rats, was fed a standard diet and water replacing by 2% NaCl solution after the operation. They were sacrificed 14 days postoperatively.

After the sacrifice of each rat, the carotid bifurcation with aneurysm was fixed in 10% formalin and embedded in paraffin. The specimen was cut into 6 um sections perpendicularly to the site of aneurysm and stained with haematoxylin-eosin (H&E). The pathological examination of specimens was made in the department of pathology. Each aneurysm section was examined in detail and the height of aneurysmal sac was measured using ocular micrometer in section in which the aneurysm was observed largest.

RESULTS

All rats survived without neurological disturbance during the entire experimental period. All aneurysms were still of the saccular type and located at the apex of the bifurcation of the common carotid artery. No aneurysms bulge was found after incision. The experimental aneurysms were neither thrombosed nor ruptured during the study.

The mean sizes of experimental saccular aneurysms were summarized in Table I. The mean size of each group was compared using the single-sided variance analysis technique and among the 4 groups of rats, the mean size of aneurysmal sac of 4th group was found to be greater than the others (P< 0.05).
Haemodynamic Effect on Aneurysm

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Aneurysm size</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0.535 mm</td>
</tr>
<tr>
<td>II</td>
<td>0.667 mm</td>
</tr>
<tr>
<td>III</td>
<td>0.616 mm</td>
</tr>
<tr>
<td>IV</td>
<td>0.894 mm</td>
</tr>
</tbody>
</table>

Table I: the mean size of the saccular experimental aneurysms

DISCUSSION:

Several factors are considered to be of importance in the pathogenesis and pathophysiology of saccular aneurysms. These include congenital defects in the tunica media, degenerative changes of the internal elastic lamina and haemodynamic factors [4,16]. Degenerative changes of the elastic lamina play a very important role in the development of saccular aneurysms. But, it might be thought that augmented haemodynamic stress is related to diffuse degenerative changes of the internal elastic lamina, and that experimental aneurysms are induced rapidly and frequently in the presence of the degenerated elastic lamina and a defect of the medial muscle layer [10,11]. High blood pressure has also some influence on the development of cerebral saccular aneurysms [14]. During the last few decades, the importance of haemodynamic factors in the formation and growth of saccular aneurysms has been widely studied both clinically and experimentally. Experimental and clinical evidence has suggested that haemodynamic stress may be a casual factor in the formation, growth and, rupture of intracranial saccular aneurysms [6,20].

The pathogenesis, expansion, and rupture of aneurysms has been associated clinically with hypertension [5,17]. It may be assumed that, because hypertension increases haemodynamic stress and accelerates atherosclerosis, a persistently hypertensive subject is more likely to develop a saccular aneurysm from an arterial wall defect. Once the aneurysm is formed, it is more likely to enlarge and rupture [4,9,18]. Our experimental study showed that hypertension increased the size of aneurysms.

The aim of these experimental studies was to determine the factors that cause the development of aneurysms, elucidate the likelihood pathophysiology of aneurysms and to define the affect of such factors on the size of aneurysm. Most of the experimental aneurysms were induced by damaging the arterial walls [11]. In the present study, we developed saccular aneurysms in the rat carotid artery using such a method and obtained saccular aneurysms in all animals. Then, we fed the rats with two different diet, including a standard diet with water without salt and standard diet with water and salt. After 7 and 14 days, we sacrificed the rats and measured the size of each aneurysm after the histopathological examination. The size of the aneurysms in group IV was larger than in the others.

Gadowski and Andijar showed that experimental abdominal aortic aneurysms in hypertensive animals grew larger than those in normotensive rats [8]. It seems to follow that simple treatment of the high blood pressure would result in a decrease in aneurysm size.

Andrew and Spiegel compared more than 200 aneurysm patient with an age and sex matched populations and found
that the systolic blood pressure was significantly higher in women with aneurysms in the age range 18-45 years. In both men and women under the age of 55, persistent hypertension was twice as likely to occur in aneurysm patients as in the normal population [1].

Some aneurysms were discovered due to the appearance sudden neurological signs. This was because of an abrupt change in volume that may result in a lobular formation or an enlargement of the original shape. In either case, concomitant pressure on one of the cranial nerves may result in typical the signs of visual blurring, visual field loss, or dropping of one eyelid. Another feature of aneurysms is that some tend to bleed [2,7].

Austin et al have showed that the danger of either a high pulse rate or suddenly increased pressure which can give rise to critical pressure jump phenomena and increased turbulence of flow within an aneurysm. These pressure jump phenomena tend to cause sudden enlargement or rupture of a aneurysms [2].

On the other hand, in all clinical studies, there are always many aneurysm patients without persistent hypertension, and many environmental events, such as lifting and bending, emotional strain and coitus all of which are observed to be factors that induce acute enlargement and rupture of aneurysms [2,13]. Research has proved that these events can temporarily and repeatedly elevate venous and arterial pressure [15,21].

In conclusion, it is suggested that aneurysm growth can be linked to acute blood pressure changes and thickening of the wall with increasing aneurysm diameter. The present study indicates that haemodynamic stress plays a very important role in the growth of saccular aneurysms.

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Commentary
This experimental study describes a successful technique for the production of aneurysms at the carotid bifurcation. The use of saline almost doubled the size of the aneurysms. The importance of the study is in relation to producing a reliable model of arterial aneurysms for future use and also in relation to modelling of size and blood pressure. It is a pity that the authors didn’t report blood pressure values because the use of saline would probably have elevated the prevailing blood pressure. It would be good to see more studies using this model.

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