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CLINICAL EXPERIENCE OF PENTOXIFYLLINE IN THE MICROSURGERY OF INTRACRANIAL ANEURYSMS

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Intracranial aneurysms were, not many years ago, classified as one of the uncommon conditions in Thailand. With ever increasing improvement ofdiagnostic means,the condition has become more and more recognised and requires urgent and delicate neurosurgical treatment. However, one stumbling block facing each neurosurgeon in such treatment is, what is the best way to prevent the second rupture of the aneurysm and yet not produce unduly long and perhaps permanent neurological deficits particularly with regard to the patient's consciousness. When an aneurysm ruptures for the first time every attempt is made by the patient's own mechanism to stop the bleeding. One of the most effective means is constriction or spasm of the mother artery in order to reduce or shut off the circulation into the aneurysmal sac and thus stop the bleeding. This in a way is unfortunate because the spasm also shuts off or reduces the circulation of the perforating arteries which supply the diencephalon and brain stem. As a result of that, the patient's consciousness is altered ranging from drowsiness to deep coma depending on the degree of ischaemia. In other words, when you are dealing with ruptured intracranial aneurysms you are dealing with two things — first, the ischaemia of the reticular formation in the diencephalon and brain stem and second, the threatening second haemorrhage from the already ruptured aneurysm. Too long a wait for the spasm to clear up may be too late to stop the second rupture which is almost always fatal. Too early surgical interference, on the other hand, may prevent further bleeding but intensify the ischaemia resulting in permanent unconsciousness or severe neurological deficit (Alcock and Drake, 1965; Connolly, 1976; Echlin, 1942; Gillingham, 1958; Robertson, 1974; Wilkins et al, 1968; Wilson et al, 1954).

Even with careful surgery under the operating microscope, the small delicate perforating arteries are most of the time disturbed. Thus, in the post-operative period one will usually expect more constriction of the perforating arteries as a result of the mechanical irritation, therefore resulting in deterioration of the patient's consciousness. In our series of studies, we tried to improve the circulation into the diencephalon and brain stem through these perforating arteries after surgery. In this way we achieved these two points. First of all, we prevented further haemorrhage and secondly we tried to improve the circulation. These two steps must done hand in hand. Pentoxifylline in the past, has been shown to improve micro-circulation into the brain (Ehrly and Kohler, 1976; Robertson, 1974; Stormer et al, 1977), and we think that at the same time it may improve circulation into the diencephalon and for that reason we embarked on this study.

MATERIAL AND METHOD

Over the past two years we have operated on twenty-six patients who came to us with spontaneous subarachnoid haemorrhage. Three of the patients who were of grade 4 and 5 of the Botterelle scale died shortly after surgery. They were excluded from this present study as the clipping of the neck of the aneurysm wasn't satisfactory and we could not ensure complete isolation of the aneurysmal sac. The other 23 patients were operated on under the operating microscope and the necks of the aneurysms were clipped satisfactorily. They were divided at random into 2 groups — the control group consisted of 8 patients one of whom had 3 aneurysms and all of them were clipped at one sitting (Table 1). The other group consisted of 15 patients, 2 of whom had 2 aneurysms each, which were again operated on at one sitting (Table 2). All of the patients in this group received 300mg. of pentoxifylline per day by mouth or nasogastric tube, as the case may be, immediately after surgery. The administration of pentoxifylline was terminated at the time of the patient's discharge.

Table 1: Control group, post-operative (2 years — 1979)

No.	Sex	Age	Side of aneurysm	Grade pre-op.	Date of Surgery	Days of stay post-op.	Duration of Follow-up months
1	F	58	Rt. P. Com./Lt. Com/ Lt. M	III	2.1.77	14	24
2	F	26	Rt. M.	III	20.12.77	14	14
3	F	50	Rt. A. Com.	IV	28.2.78	15	12
4	F	53	Rt. M.	III	18.4.78	15	10
5	F	57	Rt. P. Com.	III	11.7.78	9	7
6	F	30	Rt. M. Com.	II	1.9.78	9	5
7	F	45	Rt. P. Com.	I	19.10.78	9	4
8	F	60	Rt. M. Com.	I	8.11.78	12	3
Mean		47.37		2.5		12.12	

Table 2: Pentoxifylline trial, post-operative (2 years, 1979)

No	Sex	Age	Site of aneurysm	Grade (Botterelle Scale) Pre-op.	Date of Surgery	Days of stay post-op.	Duration of follow-up months
1	M	60	A. Com.	IV	11.3.77.	12	23
2	F	30	Lt. vertebral/Basilar	III	13.5.77	12	21
3	M	55	Rt. P. Com.	II	8.7.77	7	19
4	M	40	Rt. P. Com.	III	2.9.77	7	17
5	M	45	Lt. A. Cerebral	III	17.1.78	7	13
6	M	54	A. Com.	I	24.1.78	11	13
7	M	51	A. Com.	I	2.2.78	6	12
8	F	42	Rt. P. Com.	II	7.4.78	7	10
9	M	58	Lt. P. Com.	III	25.7.78	8	7
10	F	50	Lt. P. Com.	I	3.8.78	7	6
11	M	65	A. Com.	II	10.8.78	7	6
12	M	54	Rt. P. Com.	III	20.9.78	7	5
13	F	72	Rt. P. Com./Lt. P. Com.	IV	10.10.78	6	4
14	M	61	Rt. P. Com./Lt. P. Com.	III	12.10.78	6	4
15	M	51	A. Com.	I	19.1.79	6	1
Mean		52.53		2.4		7.7	

RESULT

In the group that pentoxifylline was given, there seemed to be rapid improvement of the patient's conscious level post-operatively. These patients became ambulatory quicker than the other group and the average duration of stay in hospital was shorter (Table 3). Post-operative intracranial haemorrhage was not found in both groups.

Table 3: Comparison of Treated and Control Groups

	Age	Pre-op. grade	Days of stay, post-op.
Pentoxifylline	52.53	2.4	7.7
Control	47.37	2.5	12.12

DISCUSSION

It seems to us that pentoxifylline given to the patient at the dosage of 300mg/day is safe, even in the immediate post-operative period. The appreciable improvement in the patients' conscious level may be explained by the improved microcirculation into the reticular formation in the diencephalon. There is no evidence, however, that pentoxifylline has any effect on the spasm of the cerebral arteries. The clinical improvement which was observed in this series is similar to that in cerebral thrombosis which we have also treated by pentoxifylline.

SUMMARY

26 patients of intracranial aneurysms have been operated on during the past 2 years. 14 patients were given pentoxifylline during the post-operative period, in order to improve the cerebral blood flow to the diencephalon which to a certain extent always suffers from ischaemia as a result of spasm of perforating arteries during the initial rupture of the aneurysms and during the surgical intereference.

The author has experienced no risk of intracranial haemorrhage during the post-operative period with pentoxifylline, provided the necks of the aneurysms were successfully and satisfactorily clipped. With the administration of the drug in the immediate post-operative period the author feels that there is improvement in the patients' level of consciousness. The patients' stay in hospital is also shortened.

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