Anesthesiology
V 75, No 3A, Sep 1991

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TITLE: ELEVATED ENDOTHELIN-1 LEVEL IN CEREBROSPINAL FLUID OF PATIENTS WITH SUBARACHNOID HEMORRHAGE

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Introduction; The mechanism of cerebral vasospasm following subarachnoid hemorrhage (SAH) is not yet known. Endothelin(ET)-1, originally isolated from porcine aortic endothelial cells, elicits a strong and long-lasting contraction in cerebral vessels in vivo and in vitro (1). To investigate the clinical implication of ET in cerebral vasospasm after SAH, we measured the ET-1-like immunoreactivity (ET-1-LI) level in cerebrospinal fluid (CSF) of patients with SAH.

Subjects and Methods; CSF samples through cerebrocisternal catheter were obtained from patients with SAH (n=4). CSF samples from neurologically normal patients (n=23) were also obtained at the induction of spinal anesthesia to determine the normal level of ET-1-LI in CSF. The CSF ET-1-LI was measured by radioimmunoassay (2).

Results; The ET-1-LI levels in CSF of neurologically normal patients were 8.3±2.0(mean±SD)pg/ml. Fig. shows time courses of the CSF ET-1-LI levels in individual patients with SAH. The CSF ET-1-LI levels of patients with SAH were elevated 3 days after the onset and declined thereafter. In patient 1 and 2 (Grade III) the CSF ET-1-LI levels increased again a week after the attack, in association with the symptomatic vasospasm. In patient 3 (Grade I), a small increase of the CSF ET-1-LI level was observed again in association with weak symptomatic vasospasm. In patient 4 (Grade I), who had no symptomatic vasospasm, the CSF ET-1-LI level was within normal range.

Discussion; These observations suggest that ET is involved in SAH-related vasospasm. Although the mechanism of elevation of the ET-1-LI level in CSF is not clear at present, endothelial damage or hemorrhage-induced activation of coagulation system may stimulate the production of ET-1(3).

References;1)Biochem.Biophys.Res.Commun. 159;1345, 1989. 2)Biochem.Biophys.Res.Commun. 161;320,1989. 3)Biochem. Pharmacol. 38;1877,1989.

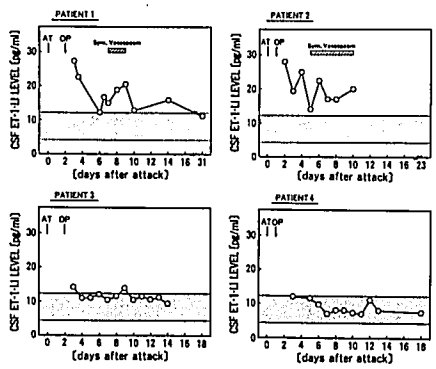

Fig.
CHANGES IN CSF ET-1-LI LEVELS OF PATIENTS WITH SAH
AT;attack of SAH. OP;clipping operation of cerebral aneurysm. Shaded area;normal ET-1-LI level.

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INDIRECT MEMORY DURING ANESTHESIA: EFFECT OF MIDAZOLAM

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INTRODUCTION: Studies suggesting indirect memory for events during anesthesia have not usually controlled for anesthetic depth or benzodiazepine usage.(1) This study was designed to test for indirect memory at stable anesthetic conditions with and without midazolam. We used 3 tasks: category generation, free association and homophone spelling.

METHOD: After approval by the Human Investigations Committee, informed consent was obtained from 48 unpremedicated patients, ASA I-III, 18-60 yr. Preoperatively, patients were randomly assigned to 2 groups, midazolam 2 mg IV or normal saline 2 ml/IV. Induction was with propofol (up to 2.5 mg/kg), then midazolam or normal saline (blinded) with fentanyl 3 μg/kg. Anesthesia was maintained with 1.3 MAC isoflurane in 70% nitrous oxide until incision and 1.0 MAC thereafter. Fentanyl in 50-100 μg increments was used for supplementation of anesthesia. During anesthesia a 50-minute tape was played to each patient on an auto-reverse cassette player. Playing time varied from 50 to 250 min. The three types of verbal material, homophones biased to the less common spelling, word pairs, and category examples, were recorded so that each stimulus was presented 21 times. The presentations were distributed throughout the 50 min. In recovery and 48 hours after surgery, patients were engaged in the three tasks by a blinded observer. Each task consisted of 50% material on the tape (primed) and 50% new material (non-primed). Task order, tape, drug condition, and delay, were counter-balanced. Statistical analysis was with ANOVA.

RESULT: The percent correct responses are given for each task in the table. Higher numbers in the primed than the non-primed condition would have provided evidence of priming by exposure to taped material. No significant main effect of priming or midazolam was observed in any of the tasks. There was a significant interaction between priming and midazolam ($F=9.62$, $p<0.01$) in the free association task and an interaction between priming, midazolam and delay ($F=4.21$, $p<0.05$) in the homophone task.

DISCUSSION: The lack of a main effect of priming in any of the 3 tasks is consistent with the conclusion that indirect memory was not demonstrated for events occurring during standard anesthetic conditions. Further, midazolam appeared to have no effect. However, two significant interactions involving priming were observed. These both appear to be due to inexplicable negative priming effects.

REFERENCE: 1. Memory and Awareness in Anesthesia, Eds. Bonke B, Fitch W, Millar K, Swets and Zeitlinger, 1990.

Table: Mean Responses % ± SD

	Recovery		48 hours	
Category	**prime**	**no prime**	**prime**	**no prime**
Midazolam	22.9±22.0	16.7±14.0	30.2±28.5	30.2±27.5
Placebo	16.7±19.0	14.6±20.7	30.2±24.4	20.8±20.4
Homophone				
Midazolam	28.3±21.2	24.2±16.7	19.2±15.0	31.6±22.8
Placebo	25.0±15.9	23.3±19.3	25.8±18.2	19.1±19.1
Free Association				
Midazolam	55.0±29.6	49.2±22.8	60.0±16.7	58.3±22.8
Placebo	53.3±24.7	60.0±22.1	51.7±22.7	55.8±27.0