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Iopamidol and Metrizamide in Cervical Myelography: Side Effects, EEG, and CSF Changes

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Two nonionic contrast media, iopamidol and metrizamide (Amipaque), were used for cervical myelography (C1–C2 puncture) in 95 consecutive patients. Both contrast media gave excellent radiographic results. Headache and vagal symptoms were similar in both groups, whereas metrizamide produced more electroencephalographic changes and epileptic seizures. Meningeal irritation occurred in both groups and was severe in three cases. Cerebrospinal fluid showed protein and cellular changes of inflammatory type in both groups. Iopamidol is considered to be the more suitable contrast medium for cervical myelography despite its slight neurotoxicity.

Nonionic water-soluble contrast media are now commonly used to study the spinal cord as well as the subarachnoid spaces. Most of the early reports of these contrast media were extremely favorable; recently, reports of adverse and serious side effects have been published more and more frequently [1–5]. In order to evaluate the neurotoxicity of these contrast media more precisely, we have been studying iopamidol and metrizamide (Amipaque). In addition to side effects, we have observed the changes on the electroencephalogram (EEG) and of the cerebrospinal fluid (CSF) at 24 and 48 hr, respectively, after cervical myelography.

Subjects and Methods

The study, still in progress, involves 95 patients who underwent cervical myelography with C1–C2 puncture. Subjects were divided into three groups: 55 received injection of 10 ml iopamidol 300; 25 were given 10 ml of Amipaque with a concentration of 300 mg I/ml; and in the last 15 subjects the same quantity and concentration of Amipaque was aspirated into the syringe by microfilter 1 hr before the myelographic examination [6]. Fifty-six subjects were male, 39 female. The mean age of the subjects was 47 years (range, 27–71). The pathologies most frequently observed were disk prolapses (25%) and degenerative changes of the cervical spine (44%). In 22 cases no pathology was found. The iopamidol and Amipaque groups were comparable in gender distribution, mean age, and pathology, thus enabling statistical comparison to be made.

All subjects were premedicated with 5 mg Valium. No patients referred had histories of epileptic seizures or allergic reactions. The most important blood parameters (azotemia, glycemia, electrophoresis, etc.) were checked before the examination and 48 hr later. Blood pressure, heart rate, and respiratory rate were monitored during the procedure. Subjects were allowed no food or liquids the night before the examination. After the procedure 1,000–1,500 ml of isotonic solution was infused intravenously. After the examination all patients remained in a half-sitting position for 6 hr, then lay supine for up to 24 hr.

An EEG was obtained before and 24 hr after the examination in 89 subjects; CSF was collected during the examination at C1–C2 level and 48 hr after by the lumbar route in 65 subjects. Total proteins, protein electrophoresis, and the cellular content were evaluated.

Results

Quality of the Films

Over 90% of the myelograms were of excellent quality with both contrast media. The root sleeves in particular were very clearly shown on regular films, while the spinal cord was better demonstrated by sagittal tomography.

Clinical Controls

In agreement with investigators who have been using iopamidol in angiographies [7], we observed no significant changes in heart and respiratory functions or in blood parameters. Among the side effects (table 1), headache was the most frequent symptom [8, 9]; it had an early onset (about 6 hr after the examination), moderate intensity, and disappeared within 24 hr in most cases. Headache increased in over 50% of cases, with no gender differential, when functional tests were performed. Generalized seizures were observed in three subjects in the Amipaque group, beginning about 1 hr after the examination and disappearing after adequate therapy. All three subjects had a spondylotic stenosis of the cervical canal, which probably caused more contrast medium than usual to enter the cranial cavity. Among the other side effects, five cases (four with Amipaque and one with iopamidol) of temporospatial disorientation were observed; in these events also, there was early onset and rapid resolution without any particular therapy. Soon after the examination three subjects (two with iopamidol and one with Amipaque) experienced severe meningeal irritation with headache, neck pain, and hyperpyrexia; one had a temporary loss of consciousness. In all three cases the CSF sampled at the same time proved to be sterile but showed a noticeable increase of proteins and cells.

EEG Parameters

The measured EEG changes (table 2) were considered mild when a minimal disorganization of background activity was present; mod-

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TABLE 1: **Side Effects after Cervical Myelography with Iopamidol and Metrizamide (Amipaque)**

Side Effect	No. (%)	
	Iopamidol (n = 55)	Amipaque (n = 40)
Headache	21 (38.0)	16 (40.0)
Nausea/vomiting	5 (9.0)	7 (17.5)
Neck pain	2 (3.6)	1 (2.5)
Neurologic symptoms*	...	...
Epileptic seizures	...	3 (7.5)
Mental disorders	1 (1.8)	4 (10.0)
Meningeal irritation	2 (3.6)	1 (2.5)

* No neurologic symptoms were noted in either group.

TABLE 2: **Electroencephalographic (EEG) Changes after Cervical Myelography with Iopamidol and Metrizamide (Amipaque)**

EEG Change	No. (%)	
	Iopamidol (n = 49)	Amipaque (n = 39)
Mild	7 (14.2)	10 (25.6)
Moderate	...	6 (15.3)
Severe	2 (4.0)	9* (23.0)
Totals	9 (18.2)	25* (63.9)

* Three subjects had generalized seizures.

TABLE 3: **Mean Total Protein and Cell Count in Cerebrospinal Fluid before and after Cervical Myelography with Iopamidol and Metrizamide (Amipaque)**

	Iopamidol (n = 39)	Amipaque (n = 26)
Total proteins (mg/dl):		
Before contrast administration	28.08	32.04
After contrast administration	40.83	50.72
No. cells/mm^3:		
Before contrast administration	0.20	0.45
After contrast administration	3.47	6.66

erate when theta or slow theta activity was present and organized as runs or discharges; and severe when spikes and sharp waves were diffuse or present as discharges or when slow delta activity was present. EEG activity showed alterations in 18.2% of cases in the iopamidol group and in 63.9% of cases in the Amipaque group. Severe changes in particular were more frequent in the Amipaque group than in the iopamidol group. EEGs with serious hemispheric or irritative alterations were observed only in patients with partial stenosis of the cervical canal. The EEG showed mild alterations only in 13% of the 22 cases with negative myelography. In general, alterations occurred most frequently about 6 hr after the examination and tended to normalize after 24 hr.

CSF Analyses

Analyses of CSF samples obtained from 26 Amipaque subjects and 39 iopamidol subjects (table 3) showed that if total protein and cellular variations are considered together, using the Hotelling t-square test, no statistically significant changes were observed. In both groups, proteins and cells increased in the postmyelographic samples. The mean total amount of proteins in the second sample for both groups was at the upper limit of normal or slightly pathologic. The electrophoresis showed a minimal variation of the single fractions with a slight increase in gamma globulins. The increase in the mean number of cells was not statistically significant because in both groups values were rather scattered. Nevertheless, in the Amipaque group the mean count of 6.66/mm^3 was the result of single values that were undoubtedly pathologic. The statistical analysis does not include the data from the three subjects (two iopamidol, one Amipaque) who had severe meningeal irritation; these subjects showed a marked CSF protein increase, and the number of cells varied from 700 to 2,480 mm^3.

Discussion

Both nonionic water-soluble contrast media tested enabled us to obtain cervical myelograms of excellent quality. Our study dealt with the cervical spinal region because this is one of the most critical areas in which contrast media are used. We could not prevent part of the contrast material from entering the cranial cavity; we agree with other investigators [1, 10] who believe that this is the primary cause of EEG changes and of most of the adverse side effects. The relatively high frequency of side effects and EEG changes observed may be attributable to the site of the injection and the total amount of contrast medium administered (3,000 mg I), the latter possibly approaching the upper limits of safety. The direct action of the contrast medium on the brain also explains the increase in headaches and EEG changes observed when dynamic tests were carried out or in cases of obstruction of the cervical canal; in 22 subjects with negative myelography we noted only slight EEG changes in a small percentage of cases.

The CSF changes observed are attributable to a moderate meningeal irritation as has been reported with other water-soluble and gaseous contrast agents [8, 11]. In the cases of severe mengineal irritation a direct effect of the contrast material should be regarded as the main cause, since a bacterial etiology could be excluded. Our work has reconfirmed that metrizamide may cause epileptic seizures. Considering that in two of three cases of generalized seizures the contrast medium had been aspirated into the syringe with a microfilter, we are doubtful about the real effectiveness of the latter device, which is designed to ensure a more complete dilution and homogeneous solution of the contrast agent.

In conclusion, we believe that nonionic water-soluble contrast media are extremely valuable for studying the spinal canal, but an ideal contrast agent without neurotoxic properties is not yet available. Of the nonionic contrast media available, iopamidol is clearly among the least toxic. In order to reduce the number of side effects, it is advisable to decrease the total amount of contrast medium injected. This may be achieved by using an image intensifier to carefully monitor the procedure during the injection.

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