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Effect of Blood on Arachnoiditis from Aqueous Myelographic Contrast Media

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Bloody cerebrospinal fluid is thought to increase the risk of arachnoiditis from myelography with iophendylate, but not with aqueous media. An experimental study was undertaken of the effects of metrizamide, iocarmate, and blood, independently and in mixtures, on the production of arachnoid fibrosis. Monkeys exposed to a mixture of iocarmate or metrizamide and blood developed no more significant arachnoid fibrosis than animals exposed to the contrast medium alone. Lumbar puncture with bloody cerebrospinal fluid, although a possible cause of adverse effects, is not a contraindication to proceeding with metrizamide myelography.

Bloody cerebrospinal fluid is not considered a contraindication to metrizamide myelography by radiologists [1], but is listed as a warning by the manufacturer in the package insert. To date, no clinical observations and only a few experimental data have been reported [2] on the effect of bloody cerebrospinal fluid on complications from metrizamide myelography, although a synergistic effect of intrathecal blood and oily contrast media has been demonstrated previously [3, 4]. Therefore, we studied the effect of small amounts of blood in the cerebrospinal fluid on arachnoiditis from meglumine iocarmate or metrizamide myelography.

Materials and Methods

Thirty bonnet, macaque, or nemestrina monkeys weighing 5–7 kg were used for these studies. All animals had successfully passed a 40 day quarantine and mycobacterial and intestinal parasite testing. For the intrathecal injections or myelography, each animal was fasted overnight and premedicated with atropine and phencyclidine hydrochloride. After its back was shaved and prepared in routine manner, the animal was placed prone on a myelographic table tilted 15° head-end up. The subarachnoid space was punctured at the L3–4 interspace with a disposable 22 gauge needle, and the contrast medium and/or blood was injected into the subarachnoid space. The substances injected are listed in table 1. Autologous blood was obtained by a venipuncture immediately before the injection. When blood and contrast medium were injected, they were mixed together in the same syringe before injection. Radiographs were obtained at 1 min after intrathecal injection to confirm that the contrast medium was subarachnoid. After the injection, the animal was placed in sitting position in a primate restraint chair overnight. The animals were sacrificed 12 weeks later, and the lumbar sac was removed, fixed, stained, and embedded in routine manner. Transverse histologic sections at L5, L6, and L7 were examined by light microscopy and scored for severity of arachnoiditis according to the following grading system: At each of three levels, the arachnoid membrane was scored on a scale of 0–4. For no abnormality, 0 scored; for a questionable thickening, 1 was scored; for a slightly abnormal amount of collagen in the arachnoid, 2; for moderate fibrosis, 3; and for severe thickening, 4. Infiltration of the adjacent subarachnoid and subdural space with fibroblasts and collagen was similarly scored 0–4. Thus, the minimal and maximal myelographic scores were 0 and 36, respectively.

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TABLE 1: **Arachnoiditis from Blood and Aqueous Myelographic Contrast Media**

Group No.: Substance Injected	Contrast Medium Volume (ml), Concentration (mg I/ml)	No. Animals	Arachnoiditis Scores	
			Range	Average
1: Metrizamide	2.4, 300	4	9–11	10.0
2: Metrizamide + blood*	1.9, 380	4	6–12	7.8
3: Iocarmate	1.2, 282	8	10–27	19.3
4: Iocarmate	0.7, 282	5	2–6	3.4
5: Iocarmate + blood*	0.7, 282	9	2–19	7.4

*0.5 ml.

Results

The animals tolerated myelography without seizures or other acute serious reactions. The results of the grading for arachnoiditis are shown in table 1.

The four animals in group 1 receiving 2.4 ml of metrizamide alone (300 mg I/ml) had very mild arachnoid thickening on histologic examination. The scores were 9–11. The four animals receiving 2.4 ml of a mixture of blood and metrizamide with a resulting concentration of 300 mg I/ml also showed very mild thickening of the arachnoid. The scores were 6–12 (average, 7.8). The difference between group 1 and group 2 animals was not statistically significant (Wilcoxan Rank Sum Test).

All eight animals in group 3 that received 1.2 ml of iocarmate alone had evidence of mild, moderate, or severe arachnoid fibrosis. The scores were 10–27 (average, 19.3).

Five animals receiving 0.7 ml of iocarmate (group 4) had essentially no evidence of arachnoid fibrosis. The scores were 2–6 (average, 3.4).

The animals in group 5 that received iocarmate (0.7 ml) and blood had evidence of minimal to moderate arachnoid fibrosis. The scores were 2–19 (average, 7.4). Group 4 and 5 scores were significantly different from group 3 ($p < 0.05$, Wilcoxan Rank Sum Test) but not from each other.

Discussion

The primate model for measuring postmyelographic arachnoiditis has been described and its value in identifying the factors causing postmyelographic arachnoiditis has been demonstrated [2, 5].

A possible synergistic effect of blood and aqueous contrast media on the arachnoid could be studied by injecting the blood either before or together with the contrast medium into the subarachnoid space. Although the former may reflect the clinical situation more accurately, the possibility that the contrast medium could displace blood from the caudal sac could not be excluded. Therefore, we selected the latter technique to ensure that the arachnoid was uniformly exposed to both contrast medium and blood. The second experimental choice was to compare a blood-contrast medium mixture with an equal volume or weight or concentration of the contrast medium alone. We performed each type of comparison. Since it was distributed as a solution, we used iocarmate in one concentration (282 mg I/ml), but in different volumes (0.7 or 1.2); since it is distributed as a lyophilized powder, we used metrizamide in different concentrations. We chose to reconstitute it to a concentration of 380 mg I/ml (in excess of the manufacturer's recommendation) so that when mixed with blood it had a concentration of 300 mg I/ml. The 300 mg I/ml concentration produces arachnoiditis in monkeys, if the animals are dehydrated overnight and kept in a sitting position in a primate restraint chair after the myelogram [2].

In the present study, the metrizamide-blood mixture containing 300 mg I/ml produced less arachnoiditis than metrizamide alone containing 300 mg I/ml. In another study, the mixture of metrizamide (380 mg I/ml) plus blood produced less arachnoiditis than metrizamide (380 mg I/ml) alone [6]. Also in a previous study, a metrizamide-blood mixture containing 220 mg I/ml was no more harmful than metrizamide alone containing 220 mg I/ml [2].

Iocarmate is no longer marketed in the United States. We used it in these studies because arachnoiditis is more easily detected following its intrathecal use. The mixture of iocarmate and blood produced significantly less arachnoiditis than an equal volume of iocarmate alone (group 3) and not significantly more arachnoiditis than an equal weight of iocarmate alone (group 4). These data show that diluting iocarmate with blood decreases its risk of causing arachnoiditis, just as does diluting it with water [7].

In these studies, blood did not increase the risk of arachnoiditis from aqueous myelographic contrast media. However, blood alone can produce arachnoiditis and acute toxicity [2]. We conclude, therefore, that bloody cerebrospinal fluid, although producing some adverse effects, is not a contraindication to aqueous myelography or an indication to postpone aqueous myelography. If blood is found in the cerebrospinal fluid before myelography, aqueous media are preferable to Pantopaque, since experimental evidence suggests Pantopaque and blood are synergistic in producing arachnoiditis [3, 4].

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