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Comparative Advantages of Small- and Large-Dose Metrizamide Myelography

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A series of myelographies performed with a smaller than customary dose (3.75 g) of metrizamide was compared with a series using the larger customary dose. While little decrease in the incidence of headache and vomiting resulted from the decreased dose, there was a heartening drop in the incidence of psychoneurologic side effects. Little difference in diagnostic quality between the two series resulted when the contrast agent was injected close to the site of main interest, but total spinal canal myelography performed with the low dose is often inadequate.

Metrizamide has become the contrast agent of choice for lumbar myelography because it is simple to use, provides superior anatomic definition, may be used in conjunction with computed tomography (CT), and does not cause arachnoiditis [1–5]. However, many are reluctant to use metrizamide for cervical or total myelography because of justifiable concern over acute toxic effects, such as headache, vomiting, mental and neurologic disorders, and seizures. Since a correlation between complications and the total dose of metrizamide has been established [1, 6], we have been interested in determining if the side effects of metrizamide myelography can be significantly reduced by using dosages below those customarily employed without sacrificing diagnostic information.

Subjects, Methods, and Results

Metrizamide, as distributed in North America, is packaged in two dosages. The larger package, hereafter called the *large dose*, is intended to be used for myelography and contains 6.75 g metrizamide (3.26 g I). When reconstituted, this yields 10.9 ml (at 300 mg I/ml) to 19.2 ml (at 170 mg I/ml) of contrast medium. The smaller package, which we will call the *small dose*, is intended to be used primarily for metrizamide CT examination, and contains 3.75 g metrizamide (1.81 g I). The volume of contrast medium available after reconstitution of this small dose varies from 6 ml (300 mg I/ml) to 10.6 ml (170 mg I/ml). In this study, myelography was performed using either the small dose, in which case all was generally used, or the large dose, in which case at least three-fourths of the total available dose was used. Of the 290 cervical and/or lumbar myelograms included in this study, 137 were obtained with the large dose and 153 with the small dose.

Assignment of patients to the two groups was not arbitrary, since we did not wish to compromise the quality of studies. The large dose was generally selected when patients were large, obese, and had unfavorable spinal curvatures or suspected large spinal canals, and when total spinal myelography was needed. The small dose was selected for small patients, children, and for those in whom only one region of the spinal canal was of clinical interest. As the study progressed, it became apparent that the small dose was adequate for most patients other than large persons needing total spinal myelography, and the relative use of the two dosages shifted. All myelographies termed *lumbar* were performed by lumbar injection, and the contrast material was not run above the thoracic region. Most small-dose cervical studies performed by lateral Cl–C2 punctures, while over half of the large-dose cervical studies were performed by a lumbar injection of the metrizamide. Typical concentrations and volumes of metrizamide used for the low-dose studies were 190 mg I/ml (9.5

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TABLE 1: **Incidence of Postmyelographic Headache, Vomiting, and Psychoneurologic Symptoms**

Level: Dose	No. Studies	Incidence (%) of Side Effects		
		Headache	Vomiting	Psychoneurologic
Cervical:				
Large	92	48	35	26
Small	87	37	18	7
Lumbar:				
Large	45	27	11	11
Small	66	15	9	0

TABLE 2: **Psychoneurologic Sequelae of Myelography**

Symptoms (All Transient)	No. Sequelae by Level and Size of Dose			
	Cervical		Lumbar	
	Large (n = 92)	Small (n = 87)	Large (n = 45)	Small (n = 66)
Dizziness	9	2	3	0
Agitation	11	3	3	0
Disorientation	6	1	1	0
Leg spasms	2	0	1	0
Facial tic	1	0	0	0
Temporary deafness	1	0	0	0
Decreased vision	1	0	0	0
Facial numbness	1	0	0	0
Diplopia	1	0	0	0
Nystagmus	1	0	0	0
Expressive aphasia	1	0	0	0
Anisocoria	1	0	0	0

TABLE 3: **Quality of Myelograms by Area and Contrast Dose**

Level: Dose	Quality of Myelograms (%)		
	Good	Adequate	Poor
Lumbar:			
Small	88	9	3
Large	93	4	2
Cervical (lumbar injection):			
Small	30	42	28
Large	63	33	4
Cervical (cervical injection):			
Small	80	16	4
Large	80	20	0

ml) for the usual lumbar myelogram and 220 mg I/ml (8.2 ml) for the usual cervical study.

Patients were checked for 48 hr after myelography, and all symptoms and neurologic signs were recorded (tables 1 and 2). Table 2 lists the numbers of patients in whom each specific symptom or sign occurred. Since more than one sign or symptom occurred in some of the patents, the total number of patients having side effects was not the same as the sum of the columns of individual side effects. The percentage of patients having mental or neurologic side effects in each group is noted in table 1.

The studies were graded as to quality. The *good* studies were those in which all anatomic details, including spinal cord, nerve roots, and nerve root sleeves were clearly visible. *Adequate* studies were those in which some small anatomic details were not clear, but pathology was not likely to be obscured. *Poor* studies were those in which the concentration of contrast medium was so low that significant pathology could not be ruled out. There was little difference between the quality of large- and small-dose studies when only the cervical or lumbar region was studied by injection of metrizamide into that region, but large-dose studies were clearly superior to small when the site of injection was remote from the site of interest (table 3). The large-dose studies were generally more esthetically pleasing because larger segments of the spinal canal would be filled at one time and the concentrations were often higher, but closer inspection generally revealed that the same anatomic details were present in both. The small dose of contrast medium was generally adequate to fill the cervical spinal canal, so that filming techniques for large- and small-dose cervical studies were similar (fig. 1). For the lumbar studies, the smaller portion of the lumbar canal filled by the low-dose volume increased the importance of using horizontal-beam oblique filming to demonstrate nerve root sleeve filling (fig. 2).

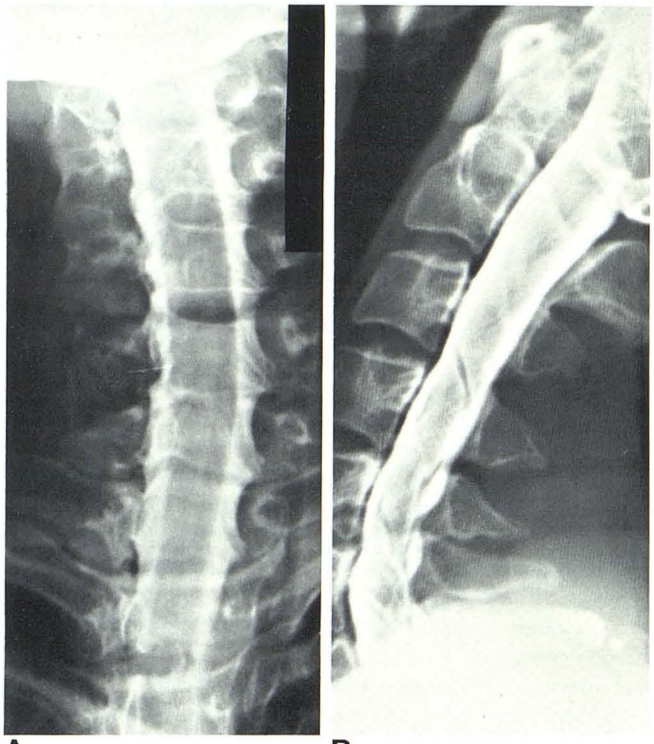

Fig. 1.—Cervical myelogram using 8.2 ml of 220 mg I/ml metrizamide. Lateral (**A**) and oblique (**B**) views show typically adequate filling obtained from small dose injected at C1–C2.

Discussion

It has been interesting to observe the wide variety of techniques proposed for metrizamide myelography and the varied experiences with postmyelographic complications. Early Scandinavian investigators used conservative techniques, keeping both the total dose and concentration low and avoiding unnecessary bathing of the spinal cord with metrizamide. They were no doubt influenced by their prior experiences with more toxic water-soluble myelographic

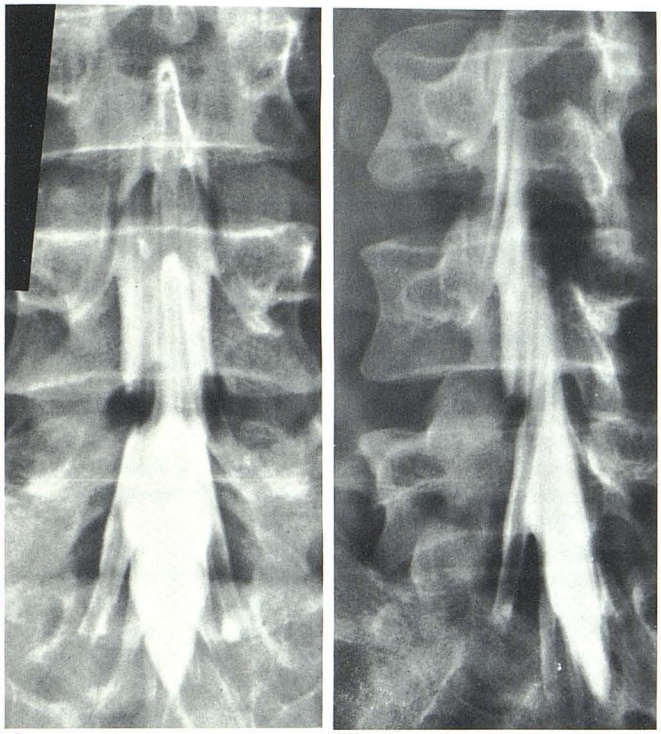

Fig. 2.—Lumbar myelogram using 8.2 ml of 220 mg I/ml metrizamide. **A,** Upright film. Only two disk spaces are adequately demonstrated. **B,** Horizontal-beam oblique view shows more reliable filling of larger number of nerve root sleeves.

agents such as meglumine iothalamate (Conray), meglumine iocarmate (Dimer X), and methiodal sodium [4, 7, 8]. Using conservative methods, they experienced a low incidence of postmyelographic side effects. In a series of 4,568 lumbar myelographies reported to Nyegaard and Co. before 1976, the incidence of headaches was only 32%, only 7% of patients had vomited, and only one seizure had occurred, and that in a known epileptic [9]. The concentration of metrizamide used in most of these cases was only 170 mg I/ml, and the average dose was 1.87 g I, nearly the same as that used in the small-dose examinations in our study. At the same time, 1,232 cervical myelographies were reported [10]. Headache occurred in 37%, vomiting in 14%, and seizures in 0.6% (eight patients). Average dose for cervical studies was 2.5 g I. Similar low incidences of side effects were reported in other articles, with the side effects of cervical myelography [11] being greater than those of lumbar myelography [2, 7, 8]. Skalpe and Amundsen [11] encountered no seizures in their first thousand myelograms, and only 17 seizures were found among the first 40,000 examinations compiled by Nyegaard and Co. [12].

American users of metrizamide have reported more side effects. Using most or all of the large dose of metrizamide (2.5–3.2 g I), Sackett et al. [13] noted headaches in 57% and nausea in 39% of the patients. They attributed these higher incidences to the inclusion of many cervical and thoracic studies. Baker et al. [12] noted headaches in 62% and nausea and vomiting in 38% of their myelograms, and observed that they had used a higher mean dose (2.69 g I) of metrizamide than had been used in various Scandinavian series [12]. The incidence of seizures also increased in the reported American experience. Sackett et al. [13] had three seizures in 215 patients, and Kieffer et al. [14] noted seizures in two patients, each of whom received 4.2 g I, in a series of 117 myelograms. In a series from the Netherlands, cervical myelography, using very high doses of metrizamide (4.5–5.5 g I), resulted in one seizure in 16 patients [15].

Concern has recently developed over mental disorders related to the neurotoxicity of metrizamide. These disorders range from subtle psychoorganic syndromes consisting of impaired memory and depression to cases of psychosis. In a series of 18 lumbar myelograms obtained with a small dose of metrizamide (1.8 g I), Rickert et al. [16] found short-term memory deficits and depression in six patients. These findings were mild and probably would not have been detected without the extensive neurologic, psychiatric, and psychomotor testing they employed. In a series of 75 patients who had received various amounts of metrizamide for cervical, thoracic, or lumbar myelography, Schmidt [6] noted a profound organic psychosis in seven and visual hallucinations or illusions in three. The frequency of mental disorders was higher after cervical myelography, in older patients, and when larger amounts of metrizamide were used. Using still higher doses of metrizamide (4.5–5.5 g I), Gelmers [15] found 12 of 16 patients who had cervical myelograms experienced acute psychoorganic reactions, with clouding of consciousness, difficulty paying attention, disordered perceptions, and anxiety or panic states. These disorders lasted 3–5 days. Psychoorganic reactions did not follow lumbar or thoracic myelograms performed with small doses (1.8–3 g I) [15]. Hauge and Falkenberg [17], in their recently published series, reported the unusual finding of a higher incidence of postmyelographic cerebral side effects after lumbar (46%) than after cervical (25%) myelograms.

In our series, we found that dizziness, agitation, and disorientation occurred more often after large-dose cervical myelograms than after small, and more often after large-dose lumbar studies than after small-dose cervical studies (table 2). Objective neurologic signs were only found in the high-dose studies (table 3). This correlation of mental and neurologic disorders with dose levels was the most interesting finding in this series. While we had hoped for a significant reduction in the incidence of headache and vomiting using a smaller dose, the differences were not impressive (table 1). However, the comments of referring physicians regarding postmyelographic patient discomfort decreased significantly after adoption of lower-dose studies, perhaps reflecting a change in severity of the postmyelographic symptoms. No seizures occurred in these patients, and none had occurred in the metrizamide myelographic patients preceding them at the UCLA Medical Center. No premedication has been used in an attempt to prevent seizures.

When using relatively low doses of metrizamide for myelography, it is necessary to pay close attention to such details of radiographic technique as low kilovoltage, optimal film-screen combinations, small focal spots, and tight coning. As several authors have emphasized [1, 2, 18], horizon-

tal-beam filming is very important. This is particularly true in low-dose lumbar myelograms, for it enables one to fill multiple nerve root sleeves with a relatively low volume of contrast medium. Metrizamide must be injected slowly to avoid excessive dilution, and injection into the cervical region should be done in the prone position to promote pooling of contrast medium. Cervical myelography is generally performed by C1–C2 injections, as preferred by early investigators [11], since good studies may be obtained using less contrast agent than is needed for lumbar injection techniques [19, 20]. An exception is made in cases in which plain film findings and clinical evidence of myelopathy suggest the possibility of a cervical block, in which case metrizamide is injected first into the lumbar canal to avoid trapping contrast material in the high cervical region. After having tried most of the described methods for performing metrizamide myelography, we now generally use small-dose technique for routine lumbar or cervical myelography. When it is necessary to obtain good filling of the entire canal or both the cervical and lumbar regions, we generally use large doses except in small patients and children. Alternatively, a small dose may be used with the option of examining a region remote from the injection site with CT if the concentration of metrizamide proves to be too low for standard myelographic technique.

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