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Reduction of the Gastrointestinal Side Effects of Metrizamide Myelography with Oral Dexamethasone

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A prospective, double-blind study was undertaken to assess the effectiveness of oral dexamethasone premedication in reducing a variety of side effects associated with metrizamide myelography. We also examined the relationship between side effects and needle size, total metrizamide dose, radiographic findings, and personality. Patients were randomly assigned to either a placebo group (44 patients) or a dexamethasone group (38 patients). All patients completed a 24-item symptom checklist before and 24 hr after lumbar myelography. In addition, all patients completed the Minnesota Multiphasic Personality Inventory prior to myelography.

Analysis of variance demonstrated a statistically significant decrease in the frequency of gastrointestinal side effects (loss of appetite, nausea, vomiting) in the dexamethasone group. There were no significant differences between the two groups for the other 21 symptoms examined.

We concluded that premedication with oral dexamethasone significantly reduces the gastrointestinal side effects associated with metrizamide myelography. This reduction was especially important in older patients.

The introduction of nonionic metrizamide more than 10 years ago represented a significant advance in the field of myelography. In contrast to the dreaded side effect of arachnoiditis, reportedly associated in up to 67% of patients undergoing Pantopaque studies [1], arachnoiditis has not been reported in association with metrizamide in humans. In addition, the diagnostic quality of lumbar metrizamide myelograms is far superior to that of Pantopaque, making metrizamide the contrast agent of choice for lumbar myelography [2–5] prior to the recent introduction of the less toxic, water-soluble iohexol and iopamidol.

Despite the lack of arachnoiditis, intrathecal metrizamide is associated with a significant number of side effects. Although the symptoms seem to increase when higher levels of the spinal canal are examined, when one considers lumbar myelography alone, the incidence of transient side effects is still substantial: headache has been reported in 21–60% of patients [2–17], nausea in 3–33% [2–12, 14–16, 18], and vomiting in 7–24% [2–5, 7–9, 12, 14–16, 18]. Other, less common, transient side effects that have been reported in association with metrizamide lumbar myelography include dizziness [3, 4, 8, 9, 12, 14, 19], confusion/disorientation [9, 12, 20–27], aphasia [23, 25, 28–31], increased back and leg pain [3, 4, 8, 12, 13], hallucinations [4, 12, 24], asterixis [22, 23, 25, 27], visual defects and cortical blindness [23, 32], meningitis/ventriculitis [21, 33–36], burning paresthesias [9, 23], hearing loss [37], amnesia [9], and convulsions/seizures [28].

With the exception of headache, nausea, and vomiting, the majority of these side effects are uncommon. We, and several of our colleagues at other institutions, have noted that patients who were on steroid preparations at the time of myelography experienced fewer gastrointestinal side effects after their examinations. For this reason, we undertook a double-blind clinical study to assess the efficacy of oral dexamethasone in reducing headache and the gastrointestinal side effects associated with metrizamide lumbar myelography.

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Subjects and Methods

Adult patients with chronic low back and/or leg pain undergoing lumbar metrizamide myelography between January 1984 and February 1985 were solicited for participation in this study. After review of a subject information sheet, 82 patients gave informed consent to enter the study (Table 1). Each subject was assigned to a treatment group according to a random-numbers table by the pharmacist. A capsule containing dexamethasone (4 mg) or a placebo was administered to each subject at bedtime the evening before the myelogram, at 7 a.m. on the day of the myelogram, "on-call" to the radiology suite, and 1 hr after completion of the myelogram. The medication each participant received was recorded in the pharmacy and was unknown to subjects, investigators, and medical staff. Although patients fasted for 4 hr before the procedure, clear liquids were encouraged both before and after myelography to ensure adequate hydration.

The lumbar myelograms were performed by several radiologists who used similar techniques. Twenty-two- and occasionally 20-gauge spinal needles were used, and the total dose of metrizamide was kept between 2000 and 3000 mg/dl. The examination protocol required that the contrast material be kept below the midthoracic level at all times. The distal thoracic spinal cord and conus were examined only in the supine position. Most patients had CT examinations 4–6 hr after myelography. During transportation, the subject's head was elevated and the chin was kept in a hyperflexed position during scanning. The subjects rested in bed with their heads elevated at least 30° for 8 hr after myelography, and then they were placed in a horizontal position for another 16 hr.

Measures

All subjects completed a 24-item symptom checklist before and 24 hr after myelography. The presence or absence of the 24 symptoms and their severity were recorded both before and after the procedure on a Likert scale in the following manner: 0 = not at all; 1 = just a little; 2 = pretty much, 3 = very much; 4 = don't know. The 24 items related to headache; back and leg pain; and gastrointestinal, genitourinary, and CNS symptoms (Table 2). The subject's medical records were reviewed to determine needle size, volume and concentration of metrizamide used, and conventional and CT myelographic findings. Generally, low-back-pain patients undergoing a diagnostic workup also complete a Minnesota Multiphasic Personality Inventory (MMPI). When available, MMPI scores for hysteria, depression, and hypochondriasis were also recorded for each subject. Twenty subjects failed to complete the inventory, and scores for these subjects were, therefore, not available.

Methods of Analysis

Obviously, many patients undergoing myelography have preprocedure symptoms, such as backache, leg pain, and leg or foot numbness. For this reason, side effects of myelography were computed as the difference between the subject's pre- and postmyelography symptom scores. Thus, positive scores reflected worsened, negative scores reflected improved, and zero scores reflected unchanged symptoms. Many symptoms were either low-frequency occurrences or ambiguous (that is, no clear majority of subjects worsened or improved). Only symptoms with unequivocal worsening or improving were targeted for subsequent analysis. Worsening symptoms were defined as those in which the percentage of patients that worsened was at least 20% *and* was at least three times the percentage that improved. An improving symptom was defined as one in which the percentage of patients that improved was at least 20% *and* was at least three times the percentage that worsened. From the remaining unclassified (neither worsened nor improved) symptoms, a low-frequency symptom was defined as any symptom for which the total percentage (worsened plus improved) of subjects

TABLE 1: Descriptive Statistics for the Total Sample and by Treatment Group

Demographic Variable	Total	Treatment	
		Dexamethasone	Placebo
No. of subjects	82	38	44
Mean age (range)	45 (19–79)	48 (24–79)	42 (19–72)
Gender (%):			
Male	52.4	44.7	59.1
Female	47.6	55.3	40.9
Positive myelogram (%)	52.4	57.9	47.7
Positive CT scan (%)	52.4	57.9	47.7
Previous back surgery (%)	51.3	52.6	50.0
Needle size:			
No. of subjects	60	28	32
% 20 gauge	45	35.7	53.1
% 22 gauge	55	64.3	46.9
Contrast material:			
No. of subjects	75[a]	37	38[a]
Mean volume (range) in ml	13 (8–18)	13 (8–18)	13 (11–17)
Mean concentration (range) in mg/ml	214 (180–270)	214 (180–270)	215 (190–250)
Mean dosage (range) in g	2.8 (1.7–3.2)	2.7 (1.7–3.2)	2.8 (2.3–3.2)
MMPI personality scores:			
No. of subjects	62	25	37
Mean (range) for depression (D)	63 (46–94)	64 (47–94)	62 (46–80)
Mean (range) for hysteria (Hs)	65 (36–95)	67 (36–95)	63 (41–90)
Mean (range) for hypochondriasis (Hy)	66 (45–96)	67 (45–96)	65 (49–84)

Note.—MMPI = Minnesota Multiphasic Personality Inventory.

[a] No. of subjects should be 76 (total) and 39 (placebo) for concentration of contrast material.

TABLE 2: Summary of Patient Reports of Symptoms After Myelography

Symptom	No. of Reports	% Worsened	% Improved
01(w) Loss of appetite	82	26.8	8.5
02(w) Increased thirst	82	40.2	4.9
03(i) Backache	79	14.5	44.3
04(w) Nausea	81	44.4	6.2
05(l) Increased urination at night	80	16.2	15.0
06(i) Leg pain	81	6.2	54.3
07(l) Itchy or scratchy skin	82	4.9	12.2
08(w) Headache	82	62.2	11.0
09(i) Leg or foot numbness	80	3.7	45.0
10(w) Vomiting	82	20.7	0
11(l) Increased appetite	82	9.8	3.7
12(l) Rashes	82	0	6.1
13(i) Leg or foot weakness	80	3.7	48.7
14(l) Blurred vision/flashing lights	81	18.5	3.7
15(l) Difficulty urinating	80	17.5	2.5
16(w) Dizziness	80	33.7	5.0
17(l) Difficulty using hands	80	16.2	6.3
18(a) Hyperactivity	79	13.9	25.3
19(a) Tired/fatigued	80	22.5	25.0
20(a) Difficulty sleeping	81	30.9	24.7
21(l) Hallucinations	82	11.0	4.9
22(l) Confusion	81	12.3	11.1
23(l) Forgetfulness	80	13.7	12.5
24(l) Difficulty paying attention	81	16.0	7.4

Note.—A patient was considered worsened if his/her postmyelogram symptom was more severe than his/her premyelogram symptom. Conversely, a patient was considered improved if his/her postmyelogram symptom was less severe than his/her premyelogram symptom. (w) = worsening symptom—reported by at least 20% of patients and was at least three times the percentage that improved; (i) = improving symptom—reported by at least 20% of patients and was at least three times the percentage that worsened; (l) = low-frequency symptom—could not be classified as worsened or improved and was reported by less than 35% of total patients; (a) = ambiguous symptom—could not be classified as worsened or improved and was reported by more than 35% of total patients.

reacting was *less* than 35%, while an ambiguous symptom was defined as any symptom for which the total percentage of subjects reacting was more than 35%. Participants' symptoms and their severity are summarized in Table 2.

To determine treatment effects, treatment groups were compared according to the percentage of subjects with improved or worsened symptoms. Chi-square test of independence of treatment with type of reaction was performed on these comparisons. In some instances, the pattern of results indicated that overall comparisons of the two treatments and two symptoms were not statistically significant, although the results of one symptom (for example, worsening) appeared significantly different between treatment groups. When this pattern occurred, a post hoc one-tailed test of differences in two proportions was used to determine the significance of the difference in the frequency of symptom occurrence (Table 3).

Since the purpose of this study was to determine the efficacy of oral dexamethasone in reducing headache and the gastrointestinal side effects associated with metrizamide lumbar myelography, additional analysis was limited to investigation of the interactive effects of treatment on these side effects with individual differences among patients. Thus, Pearson rho correlation coefficients were determined for each treatment group between the symptom of interest (gastrointestinal and headache) and demographic variables (age and gender); medical record variables (needle size, total metrizamide dose, conventional and CT myelographic findings); and personality variables (hysteria, depression, and hypochondriasis MMPI scores). The results of this analysis with respect to nausea and vomiting are summarized in Table 4.

Results

As expected, three of the six worsening symptoms were gastrointestinal (Table 2). Vomiting was almost three times more likely to occur in the placebo group than in the dexamethasone group (29.6 and 10.5%, respectively; $p < .04$) (Table 3). Worsened (increased) loss of appetite and nausea were also more frequent in the placebo group. Although the overall comparisons for these two symptoms were not statistically significant, post hoc comparisons demonstrated a significant difference between treatment groups for loss of appetite. Loss of appetite worsened (increased) in 36.4% of the placebo group vs only 15.8% in the dexamethasone group ($p < .02$).

There was an overall significant positive correlation between age and severity of vomiting ($r = .23$, $p < .05$), such that older subjects tended to report more severe vomiting reactions. However, the correlation between age and vomiting was quite different between treatment groups (Table 4). Age was positively correlated with vomiting severity for the placebo group ($r = .44$; $p < .01$) but unrelated to vomiting severity for the dexamethasone group ($r = .05$; $p < .77$). Thus it would appear that dexamethasone protected older subjects from a severe vomiting reaction.

Gender was an important predictor of vomiting [$F(1, 78) = 6.11$, $p < .02$]. Examination of mean differences in the magnitude of the side effect revealed that women reported worse vomiting than men (.31 vs .12, respectively). Since age, gender, and treatment were all related to vomiting, all three variables were considered simultaneously with multiple regression techniques in an effort to more completely explain and describe these interrelations. Although this model accounts for more than 32% of the variability in vomiting severity, no additional interrelationships among the predictors were identified.

There was a significant interaction between treatment and MMPI hysteria scores in predicting nausea ($p < .03$) (Table 4). There was a trend for hysteria to be positively related to nausea for patients in the dexamethasone group ($r = .29$, $p < .16$) and for hysteria to be negatively related to nausea for patients in the placebo group ($r = -.26$, $p < .12$). Thus, the traditional pattern, in which patients who are more hysterical report more severe symptomatology, held true for the dexamethasone group. A trend suggesting a reversal of this pattern, in which the hysterical patients actually report less severe symptomatology, was evidenced in the placebo group.

Headache worsened in 51 (62%) of all 82 subjects. However, only 22 (27%) of 81 reported severe headache. A severe headache was considered to be present if the postmyelography headache score was at least two scale points worse than the premyelography headache score. Headache was not significantly related to the variables of treatment, demographics, medical record, or personality.

TABLE 3: Assessment of Treatment Effects on Frequency of Worsening and Improving Symptoms After Myelography

Type: Reaction	Treatment		Test 1[a]			Test 2[b]	
	Dexamethasone	Placebo	df	χ^2	*p*	Z	*p*
Worsened:							
Loss of appetite	*n* = 38	*n* = 44	2	4.44	.108	–	–
% Improving	10.5	6.8	–	–	–	–	–
% Worsening	15.8	36.4	–	–	–	2.07	.020
Increased thirst	*n* = 38	*n* = 44	2	1.15	.562	–	–
% Improving	2.6	6.8	–	–	–	–	–
% Worsening	44.7	36.4	–	–	–	–	–
Nausea	*n* = 37	*n* = 44	2	1.38	.501	–	–
% Improving	8.1	4.5	–	–	–	–	–
% Worsening	37.8	50.0	–	–	–	–	–
Vomiting	*n* = 38	*n* = 44	1	4.48	.034	–	–
% Improving	0	0	–	–	–	–	–
% Worsening	10.5	29.6	–	–	–	2.09	.019
Headache	*n* = 38	*n* = 44	2	0.74	.690	–	–
% Improving	7.9	13.6	–	–	–	–	–
% Worsening	63.1	61.4	–	–	–	–	–
Dizziness	*n* = 37	*n* = 43	2	1.54	.462	–	–
% Improving	5.4	4.7	–	–	–	–	–
% Worsening	40.5	27.9	–	–	–	–	–
Improved:							
Backache	*n* = 38	*n* = 41	2	3.98	.137	–	–
% Improving	55.3	34.2	–	–	–	1.86	.032
% Worsening	15.8	17.1	–	–	–	–	–
Leg pain	*n* = 38	*n* = 43	2	4.71	.095	–	–
% Improving	57.9	51.2	–	–	–	–	–
% Worsening	0	11.6	–	–	–	2.17	.016
Leg or foot numbness	*n* = 37	*n* = 43	2	5.64	.059	–	–
% Improving	51.4	39.5	–	–	–	–	–
% Worsening	8.1	0	–	–	–	1.88	.031
Leg or foot weakness	*n* = 37	*n* = 43	2	2.70	.260	–	–
% Improving	51.4	46.5	–	–	–	–	–
% Worsening	0	7.0	–	–	–	–	–

[a] Test 1 is a chi-square (χ^2) test of independence between symptoms and treatment. In the chi-square test, degrees of freedom (df) are defined by the numbers of rows (R) and columns (C) involved in the cross classification such that df = (R − 1) × (C − 1). The *p* value is interpreted as the probability that the two variables are independent. In this table, the number of rows corresponds to the symptom classifications (no change, % improving, % worsening) and the number of columns corresponds to the treatments (dexamethasone and placebo). For brevity, the "no change" category is not reported in the table, but these values were considered in computing the chi-square statistic (See Appendix 1).

[b] Test 2 is a post hoc one-tailed test of the differences in two proportions. The difference in the two proportions is scaled by the standard deviation of the difference in two proportions to yield a value on the normal distribution, labeled as Z. The *p* value is interpreted as the probability that the two proportions are equal. (See Appendix 2).

TABLE 4: Correlations Between Symptoms of Gastrointestinal Worsening and Patient Descriptive Variables According to Type of Treatment

Symptom, Descriptive Variable	Statistic	Treatment		
		Dexamethasone	Placebo	*p*[a]
Nausea, MMPI hysteria	r	.29	−.26	.03
	p	<.16	<.12	–
	n	26	37	–
Vomiting, age	r	.05	.44	.02
	p	<.77	<.01	–
	n	38	44	–

Note.—Positive correlations indicate a direct relationship between the magnitude of the descriptive variable and the magnitude of reaction worsening. Negative correlations indicate a direct relationship between the magnitude of the descriptive variable and the magnitude of reaction improvement. Statistics are Pearson correlation (r), the *p* value associated with the test of the null hypothesis that r is equal to 0, and *n*, the number of patients involved in computing r.

[a] *p* value for the null hypothesis that the two r values associated with the treatment groups are equal.

The remaining two worsening symptoms, dizziness and increased thirst, were more common in the dexamethasone than in the placebo group, although the differences in frequency were not significant. These symptoms were not significantly related to demographic, medical record, or personality variables.

The subjects in the dexamethasone group were more likely to report improvement than the subjects in the placebo group for the symptoms of backache, leg pain, leg or foot numbness, and leg or foot weakness. Significant post hoc comparisons were found for three of these symptoms. There was significantly more improvement (lessening) of backache in the dexamethasone-treated group (55.3 vs 34.2%, $p < .032$). There was a significant improvement in leg pain and leg or foot numbness symptoms for all subjects. However, considering only those subjects with worsened leg pain, there were no reports of worsening among subjects in the dexamethasone group vs 11.6% worsening in the placebo group ($p < .016$). On the other hand, considering only those subjects with worsened leg or foot numbness, there was no worsening for

subjects in the placebo group compared with worsening in 8.1% of subjects in the dexamethasone group ($p < .031$).

Discussion

Since the present investigation was prompted by empiric observation that patients on steroid preparations at the time of metrizamide myelography experienced fewer gastrointestinal side effects, we expected and found a statistically significant decrease in these symptoms in our controlled double-blind study. Although the administration of dexamethasone did not completely eliminate these gastrointestinal side effects in any patient population, the protective effects in reducing the severity of vomiting were greatest in older patients.

Since our study has been completed, Food and Drug Administration approval for intrathecal administration of both iopamidol and iohexol has been granted. A number of comparison studies evaluating these contrast agents have been published. Although the incidence of the common side effects of headache, nausea, and vomiting is reportedly lower with iopamidol and iohexol than with metrizamide, a certain percentage of patients still experience these side effects. Concerning lumbar myelography with iopamidol, headache has been reported in 17–58% of patients [6, 7, 17, 18, 23, 38], nausea in 0–23% [7, 18, 23, 38], and vomiting in 0–23% [7, 23, 38]. Lumbar myelography with iohexol seems to be somewhat better tolerated, with the incidence of headache reported as 1–24% [9–11, 15, 39–41], nausea as 1–10% [9–11, 15, 39–41], and vomiting as 0–4% [9–11, 15, 39, 41]. Since we changed over to these newer contrast agents 5 months ago, three patients have experienced severe, prolonged vomiting.

Although we cannot directly extend our results with metrizamide to include iopamidol and iohexol, we believe that, because of the chemical similarities among these drugs, the overall incidence of common gastrointestinal side effects may be further reduced with oral dexamethasone. Premedication with dexamethasone would be most beneficial for persons undergoing metrizamide myelography, all elderly patients, and those patients with a history of severe, prolonged vomiting reactions after myelography with any contrast agent.

Another issue that must be addressed is that of steroid psychosis and dosage of dexamethasone. The exact dose at which steroid psychosis can be expected to be produced is not known. In a study comparing the antiemetic effects of dexamethasone with prochlorperazine in patients undergoing cancer chemotherapy, Markman et al. [42] reported no significant side effects among 42 patients given 20 mg of IV dexamethasone 30 min before chemotherapy, followed by 10 mg orally every 6 hr for 24 hr. Our total dexamethasone dose of 16 mg during a 24-hr period is far below the 24-hr total of 60 mg used by Markman et al. [42], and we would not anticipate side effects related to our dosage among the majority of the population.

Although the mechanism of steroid activity as an antiemetic is not known, it has been suggested that inhibition of prostaglandin synthesis by corticosteroids may play an important role [43], but this has not to our knowledge been demonstrated experimentally. Suggested mechanisms of metrizamide toxicity include osmolality difference from CSF and less than optimal solubility in water [44]. The hypothesis that has received the most consideration is related to brain glucose metabolism.

The CNS uses D-glucose as its primary source of energy [45]. D-glucose is transported across membranes into the CNS cells by means of a facilitated membrane carrier. This carrier can be competitively inhibited by structural analogues such as D-glucosamine or 2-deoxy-D-glucose. Metrizamide is composed of a 2-deoxy-D-glucose bound to metrizoate with an amide linkage. This compound is known to inhibit glucose metabolism in neural tissues, and there is competitive inhibition between D-glucose and 2-deoxy-D-glucose for the specific membrane carrier [46]. Metrizamide has been shown to produce significant depression of glucose metabolism in the rat hippocampus [45]. Bertoni et al. [27, 47] have demonstrated competitive inhibition of glucose metabolism in vitro with metrizamide by using a purified, commercially available microbial hexokinase. The inhibitory effects of metrizamide on hexokinase and glucose metabolism are dependent on brain glucose concentration, which in turn is dependent on blood glucose concentration. Therefore, conditions that produce hypoglycemic states, such as fasting, would be expected to potentiate the competitive inhibition [47]. It has been suggested that glucose, administered IV, or preferably intrathecally, might offset metrizamide's interference with glucose metabolism, thereby reducing its toxic side effects [47]. However, in a double-blind study with dextrose (30 m*M*) in solution with metrizamide injected intrathecally in dogs, Northington et al. [48] found the addition of dextrose offered no significant protective effects against seizures.

It is doubtful that dexamethasone has any direct central action on either the thirst or emetic centers of the brain. A much more likely explanation is that dexamethasone acts peripherally, suppressing the release of insulin, inducing a hyperglycemic state. An increase in blood glucose would increase the amount of glucose available to the brain and thereby lessen the magnitude of metrizamide's hexokinase inhibition. Increased thirst experienced by subjects in the dexamethasone group may also be explained on the basis of hyperglycemia, since it is a known side effect of glucocorticoid excess. Reduction of toxic metrizamide effects in the presence of systemic hyperglycemia would add additional support to previous reports attributing metrizamide's toxicity to interference with brain glucose metabolism.

The incidence of headache of any severity in our series was quite high, 62.2%. Severe headache, however, was reported by only 27% of all subjects. This percentage is in keeping with the incidence of 35% reported by Tourtellotte et al. [49] in association with simple lumbar puncture performed with a 22-gauge spinal needle. We found no significant increase in headache among women, as has been reported by others [8, 49, 50], nor was there a difference in headache between treatment groups. The cause of postmyelography headache is commonly considered to be the result of lumbar puncture with persistent leakage of CSF. In a classic study, Tourtellotte et al. [49] reported a decreased incidence of headache when lumbar puncture was performed with a 26-gauge, vs a 22-gauge, needle. Deisenhammer and Hammer

[51] believed increased leakage of CSF and the resulting low CSF pressure was the cause of postmyelography meningeal irritation symptoms, especially headache. Recently, however, Dieterich and Brandt [50] reported a higher incidence of post-lumbar-puncture headache when studies were performed with a 22-gauge needle vs a 20-gauge needle. Sykes et al. [52] reported a significantly decreased incidence of headache when patients were allowed to ambulate after myelography. They concluded that the irritant effects of metrizamide on the CNS were more important in the production of postmyelography headache than was leakage of CSF. The findings of Robertson et al. [53], however, were just the opposite. They reported no difference in the frequency of headache with respect to patient positioning after myelography. If postmyelography headaches were primarily the result of metrizamide's irritant effects, then we would expect to have seen a decrease in postmyelography headache in our dexamethasone subjects. This was not the case. The fact that no significant difference in headache was present between treatment groups supports the contention that lumbar puncture is more responsible for their production than is metrizamide toxicity.

Although there were no significant differences between genders in our study for the majority of side effects, we did find that women reported more severe vomiting than did men. The same tendency for a higher frequency of a variety of side effects (headache, nausea, vomiting, dizziness) in women has been reported by others [3, 4, 8, 49, 50].

It is of interest that hysterical patients in the dexamethasone group tended to report more severe nausea after myelography, but that this tendency was not present in the placebo group. The nature of the hysterical personality is to magnify complaints. One explanation for the discrepancy between the two groups may be that metrizamide toxicity and hysterical personality are two interwoven variables related to nausea. Assuming that the metrizamide toxicity variable controls more of the variance related to the report of nausea than does personality, then the relationship between hysteria and the report of nausea would not be found when a significant degree of toxicity is present. However, if the toxicity were reduced by the administration of dexamethasone, then personality could control more of the variance related to the report of nausea, and the relationship between hysteria and the report of nausea could be found.

Among the less common side effects reported in association with lumbar metrizamide myelography are increased back and leg pain [3, 4, 8, 12, 13]. It should be noted that, in many of the studies reporting these side effects, patients were only questioned as to the presence and severity of symptoms after myelography. Patients undergoing lumbar myelography almost invariably have back and/or leg pain as part of their presenting symptom complex. To only question patients about these symptoms after myelography and to then attribute positive responses as secondary to the procedure seems unreasonable. We found significant improvement in leg pain and leg or foot numbness for all subjects. In addition, there was significantly more improvement (lessening) of backache for subjects in the dexamethasone group. There are a number of possible explanations for our findings: (1) The patients rested in bed after their procedures; (2) the patients may have slightly restructured their pain scale after myelography (what was considered as moderate to severe pain before myelography may have been considered as only mild to moderate pain after the procedure); and (3) the known antiinflammatory effects of dexamethasone may have been partially responsible for the significant lessening of back pain noted in the dexamethasone treatment group. Since patients undergoing lumbar myelography commonly have symptoms before the study that are similar to those ascribed to side effects after the study, we suggest that future studies of this type measure pre- as well as postprocedure symptoms.

Appendix 1: Detailed Explanation and Example of Chi-Square Test

The chi-square test of independence is based on the frequencies generated by cross-classifying two categorical variables, such as loss of appetite—coded as worsened, unchanged, or improved—and treatment—coded as dexamethasone or placebo. In such a 3×2 cross classification six cells result with some observed frequency (f_o) of patients ranging from 0 to n, the total number of subjects, residing within each of the six cells. The chi-square test (1) computes the expected cell frequency (f_e) from the marginal row and column totals under the hypothesis of independence (no cell is expected to contain more counts than marginal totals would indicate); (2) compares each of these values with the actual or observed cell frequency and squares this difference $(f_o - f_e)^2$; and (3) adjusts this squared difference by the expected cell frequency, $(f_o - f_e)^2/f_e$. The sum of these adjusted squared differences across all cells is distributed as chi-square with $(R - 1) \times (C - 1)$ degrees of freedom (df), where R = number of categories in the row variable and C is the number of categories in the column variable in the cross classification. In the example above, R = 3 and C = 2 and, therefore, Df = 2.

Appendix 2: Detailed Explanation and Example of Test of Difference in Two Proportions

The difference in two proportions or percentages is computed by taking the difference in the two proportions (P1/N1 − P2/N2) and computing the standard error, SE, of this difference, P = (P1 + P2)/(N1 + N2) = SE = $\{[P(1 - P)/N1 - 1] + [P(1 - P)/N2 - 1]\}^{1/2}$. Scaling the difference in the proportions by SE to create a Z statistic, $N(0,1)$ (distributed as a normal variate with mean = 0 and SD = 1), Z = (P1/N1 − P2/N2)/SE.

Example

Suppose a total of 100 candidates from a field of 200 applicants were to be accepted into a program. Group 1 screened the candidates and selected 70 females and 30 males. Group 2 screened the candidates and selected 55 females and 45 males. Is there a significant difference between the two groups in their propensity to choose female over male applicants?

Group 1: P1/N1 = 70/100 = 0.70.
Group 2: P2/N2 = 55/100 = 0.55.
Group 3: P = (P1 + P2)/N1 + N2) = (70 + 55)/200 = 0.625.

SE = $\{2 \times [0.625(1 - 0.625)]/99\}^{1/2}$ = 0.069; Z = (0.70 − 0.55)/0.069 = 2.17, where $p < .015$ (one-tailed) and $p < .030$ (two-tailed). Group 1, which selected 70% female applicants, had a significantly larger portion of females that group 2 did, in which 55% of the selected applicants were female. Thus, the two groups did differ in their propensity to select female applicants.

Note. Although unrelated to this example, the above situation does not necessarily indicate bias on the part of either selection group.

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