Common features associated with spinal-anesthesia-induced hypotension: A retrospective study

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A retrospective study investigated features common to 85 documented cases of spinal-anesthesia-induced hypotension. Low preoperative systolic blood pressure and anemia were the most predictive features. Physical status was less important, with the exception of emergency surgeries. An association was found between preoperative medication—especially narcotics—and hypotension. Other variables found to have a high frequency among hypotensive patients were known preexisting pathologic conditions, increasing concentrations of anesthetic used at the time of surgery, and increasing levels of anesthesia achieved. The study is weighted toward obstetric/gynecologic cases.

(Key words: Anesthesia, regional anesthesia, hypotension, spinal anesthesia, narcotics, narcotic analgesics)

Spinal-anesthesia-induced hypotension resulting from an anesthetic's sympatholytic action after lumbar subarachnoid spinal anes-

thesia is well documented.¹⁻⁴ With comparatively low anesthetic doses, there are negligible direct organ system effects.⁵ Sympathetic blockade to peripheral arterioles, causing vasodilation, profoundly affects spinal-anesthesia-induced hypotension.^{1,3,6,7}

Additional interrelated mechanisms eliciting hypotension include the following: loss of venomotor tone, diminishing venous return to the right side of the heart; muscle flaccidity, paralyzing venous segment support; venous return reduction via intra-abdominal pressure alterations and lowered negative intrathoracic pressures, resulting from abdominal muscle relaxation and slowed ventilatory activity; lowered cardiac output; cardiac accelerator fiber inhibition; accentuated vagal tone; attenuated vasoconstrictor response; and decreased stroke volume and peripheral vascular resistance.^{1,2,4,5,8-10}

Reportedly, total sympathectomy is attained with spinal anesthesia at or above thoracic levels T-3 or T-4.^{4,8,11} Typically, the level of sympathectomy is two dermatomes above the sensory blockade but may extend as far up as six.^{2,8} The more spinal segments involved, the fewer compensatory areas of vasoconstriction, and the more significant the hypotension.^{3,11}

Some degree of blood pressure decrease occurs almost universally after spinal anesthesia, but significant symptomatic hypotension can have harmful consequences. The purpose of this study was to identify features that could be helpful in predicting high-risk cases.

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Figure 1. Distribution of preoperative systolic blood pressure values in patients having spinal-anesthesia-induced hypotension.

Materials and methods

In this retrospective study, we found that 85 (approximately 25%) of 366 patients undergoing spinal anesthesia had a significant hypotensive episode. Data from these 85 cases were examined for similarities. The criteria for selection were a drop in systolic blood pressure of 30 torr or more or a systolic pressure decline below 100 torr within 20 minutes of a spinal injection.

The anesthesia reports of all spinal injections performed at Michigan Health Center Hospital from July to December 1986 were examined. The 85 patients in the hypotensive group ranged in age from 17 to 91 years. This group consisted of 17 (20%) male and 68 (80%) female patients, including 57 (67.1%) obstetric patients carried to term. No fatalities occurred and patient confidentiality was maintained.

Appropriate standard technique was used, and dosages of all agents used were administered according to manufacturers' recommendations. A 22-

gauge Whitacre needle was used to anesthetize 73 patients; the remaining patients required a 22-gauge regular needle. The anesthetic was introduced into the L3-4 interspace in 83 patients, and into the L4-5 interspace in the other two. Right or left lateral recumbent positioning was required in 17 patients; the others tolerated induction of anesthesia while sitting upright.

Central neural blocking agents injected into the subarachnoid space included 1% solution of tetracaine hydrochloride (Abbott Spinal Kit No. 4805), 5% solution of lidocaine hydrochloride (Xylocaine, Kendall Spinal Anesthesia Tray No. 4732), and 0.75% solution of bupivacaine hydrochloride (Marcaine, Winthrop-Breon) for 57 patients (67.1%), 25 patients (29.4%), and 3 patients (3.5%), respectively. Morphine sulfate (Duramorph, Elkins-Sinn) was added to the conduction mixture in 15 cases. An Accutor, Datascope I, or Dinamap automatic oscillotonometric cycling device was used to monitor systemic blood pressure. Glycopyrrolate (Rob-

Figure 2. Distribution of hemoglobin values in 53 patients having spinal-anesthesia-induced hypotension who were classified as anemic preoperatively. (Anemia was defined as a hemoglobin level of 14 g/dL or less in male patients and 12 g/dL or less in female patients.)

inul, Robins), atropine sulfate (Inenex), meperidine hydrochloride (Demerol, Winthrop-Breon), fentanyl citrate (Sublimaze, Janssen; and Elkins-Sinn), hydroxyzine hydrochloride (Vistaril, Roerig), and midazolam hydrochloride (Versed, Roche) were used preoperatively—individually or in combination—in 18 patients.

Variables examined included preoperative systolic blood pressure, preoperative hemoglobin levels, anesthetic agent and concentration used, spinal level of anesthesia, physical status, preexisting pathologic conditions, preoperative medication, and type of surgery performed. Criteria for patient selection were based on recommendations from references 9 and 11 through 17 (ie, a precipitous reduction of systolic blood pressure > 30 torr or a decline > 100 torr within 20 minutes of introduction of the anesthesia).

Results

It is noteworthy that 80% of the patients had

preoperative systolic blood pressure values of less than or equal to 120 torr (Fig 1). Of the 85 patients, 53 (62%) were classified as anemic preoperatively (Fig 2). Anemia was defined as a hemoglobin level of 14 g/dL or less in men and 12 g/dL or less in women. Nine men were classified as anemic. Among the 44 women in the study, 37 were gravid. Elevated hemoglobin levels were found in a few patients with preexisting diseases such as chronic obstructive pulmonary disease (COPD).

There was a tendency toward a greater incidence of spinal-anesthesia-induced hypotension with increasing dosages of lidocaine (Fig 3). The greatest number of episodes involved patients given dosages of 100 mg. Approximately 80% of the patients having spinal-anesthesia-induced hypotension received 10 mg or more of tetracaine (Fig 4); a quarter of

Figure 3. Distribution of patients having spinal-anesthesia-induced hypotension, characterized by administration of various dosages of 5% solution of lidocaine.

Figure 4. Distribution of patients experiencing spinal-anesthesia-induced hypotension, characterized by administration of various dosages of 1% solution of tetracaine. *NS = not specified.

(continued on page 1201)

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Zinacef® (sterile cefuroxime sodium, Glaxo)

Zinacef® (cefuroxime sodium injection)

BRIEF SUMMARY

The following is a brief summary only. Before prescribing, see complete prescribing information in Zinacef® (sterile cefuroxime sodium/cefuroxime sodium injection) product labeling.

INDICATIONS AND USAGE: Zinacef® is indicated for the treatment of patients with infections caused by susceptible strains of the designated organisms in the following diseases:

1. **Lower Respiratory Tract Infections**, including pneumonia, caused by *Streptococcus pneumoniae* (formerly *Diplococcus pneumoniae*), *Haemophilus influenzae* (including ampicillin-resistant strains), *Klebsiella* spp., *Staphylococcus aureus* (penicillinase- and non-penicillinase-producing), *Streptococcus pyogenes*, and *Escherichia coli*.
2. **Urinary Tract Infections** caused by *Escherichia coli* and *Klebsiella* spp.
3. **Skin and Skin Structure Infections** caused by *Staphylococcus aureus* (penicillinase- and non-penicillinase-producing), *Streptococcus pyogenes*, *Escherichia coli*, *Klebsiella* spp., and *Enterobacter* spp.
4. **Septicemia** caused by *Staphylococcus aureus* (penicillinase- and non-penicillinase-producing), *Streptococcus pneumoniae*, *Escherichia coli*, *Haemophilus influenzae* (including ampicillin-resistant strains), and *Klebsiella* spp.
5. **Meningitis** caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* (including ampicillin-resistant strains), *Neisseria meningitidis*, and *Staphylococcus aureus* (penicillinase- and non-penicillinase-producing).
6. **Gonorrhea**: Uncomplicated and disseminated gonococcal infections due to *Neisseria gonorrhoeae* (penicillinase- and non-penicillinase-producing strains) in both males and females.
7. **Bone and Joint Infections** caused by *Staphylococcus aureus* (including penicillinase- and non-penicillinase-producing strains).

Clinical microbiological studies in skin and skin structure infections frequently reveal the growth of susceptible strains of both aerobic and anaerobic organisms. Zinacef has been used successfully in these mixed infections in which several organisms have been isolated. Appropriate cultures and susceptibility studies should be performed to determine the susceptibility of the causative organisms to Zinacef.

Therapy may be started while awaiting the results of these studies; however, once these results become available, the antibiotic treatment should be adjusted accordingly. In certain cases of confirmed or suspected gram-positive or gram-negative sepsis or in patients with other serious infections in which the causative organism has not been identified, Zinacef may be used concomitantly with an aminoglycoside (see PRECAUTIONS). The recommended doses of both antibiotics may be given depending on the severity of the infection and the patient's condition.

Prevention: The prophylactic administration of Zinacef may prevent the growth of susceptible disease-causing bacteria and thereby may reduce the incidence of certain postoperative infections in patients undergoing surgical procedures (e.g., vaginal hysterectomy) that are classified as clean-contaminated or potentially contaminated procedures. Effective prophylactic use of antibiotics in surgery depends on the time of administration. Zinacef should usually be given one-half to 1 hour before the operation to allow sufficient time to achieve effective antibiotic concentrations in the wound tissues during the procedure. The dose should be repeated intraoperatively if the surgical procedure is lengthy.

Prophylactic administration is usually not required after the surgical procedure ends and should be stopped within 24 hours. In the majority of surgical procedures, continuing prophylactic administration of any antibiotic does not reduce the incidence of subsequent infections but will increase the possibility of adverse reactions and the development of bacterial resistance.

The perioperative use of Zinacef has also been effective during open heart surgery for surgical patients in whom infections at the operative site would present a serious risk. For these patients it is recommended that Zinacef therapy be continued for at least 48 hours after the surgical procedure ends. If an infection is present, specimens for culture should be obtained for the identification of the causative organism, and appropriate antimicrobial therapy should be instituted.

CONTRAINDICATIONS: Zinacef is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

WARNINGS: BEFORE THERAPY WITH ZINACEF® IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. IF AN ALLERGIC REACTION TO ZINACEF OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad-spectrum antibiotics); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

Treatment with broad-spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis.

Cholestyramine and colestipol resins have been shown to bind the toxin *in vitro*.

Mild cases of colitis may respond to drug discontinuation alone. Moderate to severe cases should be managed with fluid, electrolyte, and protein supplementation as indicated.

When the colitis is not relieved by drug discontinuation or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *Clostridium difficile*. Other causes of colitis should also be considered.

PRECAUTIONS: Although Zinacef® rarely produces alterations in kidney function, evaluation of renal status during therapy is recommended, especially in seriously ill patients receiving the maximum doses. Cephalosporins should be given with caution to patients receiving concurrent treatment with potent diuretics as these regimens are suspected of adversely affecting renal function.

The total daily dose of Zinacef should be reduced in patients with transient or persistent renal insufficiency (see DOSAGE AND ADMINISTRATION), because high and prolonged serum antibiotic concentrations can occur in such individuals from usual doses.

As with other antibiotics, prolonged use of Zinacef may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken. Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Nephrotoxicity has been reported following concomitant administration of aminoglycoside antibiotics and cephalosporins. As with other therapeutic regimens used in the treatment of meningitis, mild-to-moderate hearing loss has been reported in a few pediatric patients treated with cefuroxime sodium. Persistence of positive CSF (cerebrospinal fluid) cultures at 18 to 36 hours has also been noted with cefuroxime sodium injection, as well as with other antibiotic therapies; however, the clinical relevance of this is unknown.

Drug/Laboratory Test Interactions: A false-positive reaction for glucose in the urine may occur with copper reduction tests (Benedict's or Fehling's solution or with Clinistest® tablets) but not with enzyme-based tests for glycosuria (e.g., Tes-Tape®). As a false-negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase method be used to determine blood plasma glucose levels in patients receiving Zinacef.

Cefuroxime does not interfere with the assay of serum and urine creatinine by the alkaline picrate method.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Although no long-term studies in animals have been performed to evaluate carcinogenic potential, no mutagenic potential of cefuroxime was found in standard laboratory tests.

Reproduction studies revealed no impairment of fertility in animals.

Pregnancy, Teratogenic Effects, Pregnancy Category B: Reproduction studies have been performed in mice and rabbits at doses up to 50 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefuroxime. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: Since cefuroxime is excreted in human milk, caution should be exercised when Zinacef is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children below 3 months of age have not been established. Accumulation of other members of the cephalosporin class in newborn infants (with resulting prolongation of drug half-life) has been reported.

ADVERSE REACTIONS: Zinacef® is generally well tolerated. The most common adverse effects have been local reactions following IV administration. Other adverse reactions have been encountered only rarely.

Local Reactions: Thrombophlebitis has occurred with IV administration in 1 in 60 patients.

Gastrointestinal: Gastrointestinal symptoms occurred in 1 in 150 patients and included diarrhea (1 in 220 patients) and nausea (1 in 440 patients). Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment (see WARNINGS).

Hypersensitivity Reactions: Hypersensitivity reactions have been reported in fewer than 1% of the patients treated with Zinacef and include rash (1 in 125), pruritus, urticaria, and positive Coombs' test each occurred in fewer than 1 in 250 patients, and, as with other cephalosporins, rare cases of anaphylaxis, drug fever, erythema multiforme, toxic epidermal necrolysis, and Stevens-Johnson syndrome have occurred.

Blood: A decrease in hemoglobin and hematocrit has been observed in 1 in 10 patients and transient eosinophilia in 1 in 14 patients. Less common reactions seen were transient neutropenia (fewer than 1 in 100 patients) and leukopenia (1 in 750 patients). A similar pattern and incidence was seen with other cephalosporins used in controlled studies.

Hepatic: Transient rise in SGOT and SGPT (1 in 25 patients), alkaline phosphatase (1 in 200 patients), LDH (1 in 75 patients), and bilirubin (1 in 500 patients) levels has been noted.

Kidney: Elevations in serum creatinine and/or blood urea nitrogen and a decreased creatinine clearance have been observed, but their relationship to cefuroxime is unknown.

In addition to the adverse reactions listed above that have been observed in patients treated with cefuroxime, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics:

Adverse Reactions: Vomiting, abdominal pain, colitis, vaginitis including vaginal candidiasis, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemolytic anemia, hemorrhage.

Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced (see DOSAGE AND ADMINISTRATION). If seizures associated with drug therapy should occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

Altered Laboratory Tests: Prolonged prothrombin time, pancytopenia, agranulocytosis, thrombocytopenia.

DOSAGE AND ADMINISTRATION: (See complete prescribing information in Zinacef® product labeling.)

Impaired Renal Function: A reduced dosage must be employed when renal function is impaired. Dosage should be determined by the degree of renal impairment and the susceptibility of the causative organism (see Table 1 in product package insert).

HOW SUPPLIED: Zinacef® in the dry state should be stored between 15° and 30°C (59° and 86°F) and protected from light. Zinacef is a dry, white to off-white powder supplied in vials and infusion packs as follows:

NDC 0173-0352-31 750-mg* Vial (Tray of 25)
NDC 0173-0354-31 1.5-g* Vial (Tray of 10)
NDC 0173-0353-32 750-mg* Infusion Pack (Tray of 10)
NDC 0173-0356-32 1.5-g* Infusion Pack (Tray of 10)
NDC 0173-0400-07 5-g* Pharmacy Bulk Package (Tray of 6)

Zinacef frozen as a premixed solution of cefuroxime sodium should not be stored above -20°C. Zinacef is supplied frozen in 50-mL, single-dose, plastic containers as follows:
NDC 0173-0424-04 1.5-g* Plastic Container (Carton of 24)
NDC 0173-0425-00 1.5-g* Plastic Container (Carton of 24)

*Equivalent to cefuroxime.

Ceftin® (cefuroxime axetil) Tablets

BRIEF SUMMARY

The following is a brief summary only. Before prescribing, see complete prescribing information in Ceftin® (cefuroxime axetil) Tablets product labeling.

INDICATIONS AND USAGE: Ceftin® Tablets are indicated for the treatment of patients with infections caused by susceptible strains of the designated organisms in the following diseases:

1. **Pharyngitis and Tonsillitis** caused by *Streptococcus pyogenes* (group A beta-hemolytic streptococci). (Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. Ceftin Tablets are generally effective in the eradication of streptococci from the oropharynx. Ceftin Tablets are not indicated for the prophylaxis of subsequent rheumatic fever because data to support such use are not yet available.)
2. **Otitis Media** caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* (ampicillin-susceptible and ampicillin-resistant strains), *Moraxella catarrhalis* (ampicillin-susceptible strains), and *Streptococcus pyogenes* (group A beta-hemolytic streptococci).
3. **Lower Respiratory Tract Infections** (bronchitis) caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* (ampicillin-susceptible strains), and *Haemophilus parainfluenzae* (ampicillin-susceptible strains).
4. **Urinary Tract Infections** caused by *Escherichia coli* and *Klebsiella pneumoniae* in the absence of urological complications.
5. **Skin and Skin Structure Infections** caused by *Staphylococcus aureus* and *Streptococcus pyogenes* (group A beta-hemolytic streptococci).

Bacteriologic studies to determine the causative organism and its susceptibility to cefuroxime should be performed. Therapy may be started while awaiting the results of these studies. Once these results become available, antibiotic treatment should be adjusted accordingly.

CONTRAINDICATIONS: Ceftin® Tablets are contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

WARNINGS: BEFORE THERAPY WITH CEFTIN® TABLETS IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. IF AN ALLERGIC REACTION TO CEFTIN TABLETS OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

As with other cephalosporins (and other broad-spectrum antibiotics), pseudomembranous colitis has been reported with the use of Ceftin; therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

Treatment with broad-spectrum antibiotics alters normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind the toxin *in vitro*.

Mild cases of colitis may respond to drug discontinuation alone. Moderate to severe cases should be managed with fluid, electrolyte, and protein supplementation as indicated. Elderly patients may be susceptible to fluid losses and should be treated aggressively. Antiperistaltic agents such as opiates and diphenoxylate with atropine (e.g., Lomotil®) may prolong and/or worsen the condition and should be avoided if pseudomembranous colitis is suspected.

When the colitis is not relieved by drug discontinuation or when it is severe, metronidazole and oral vancomycin have been shown to be beneficial. Oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *Clostridium difficile*. Other causes of colitis should also be considered.

PRECAUTIONS: General: If an allergic reaction to Ceftin® Tablets occurs, the drug should be discontinued, and, if necessary, the patient should be treated with appropriate agents, e.g., antihistamines, pressor amines, or corticosteroids.

As with other antibiotics, prolonged use of Ceftin Tablets may result in overgrowth of nonsusceptible organisms. If superinfection occurs during therapy, appropriate measures should be taken.

Broad-spectrum antibiotics should be prescribed with caution for individuals with a history of colitis.

Information for Patients (Pediatric): Ceftin is only available in tablet form. During clinical trials, the tablet was well tolerated by children who could swallow the tablet whole. Children who cannot swallow the tablet whole may have the tablet crushed and mixed with food (e.g., applesauce, ice cream). However, it should be noted that the crushed tablet has a strong, persistent, bitter taste. Discontinuation of therapy due to the taste and/or problems of administering this drug occurred in 13% of children (range, 2% to 28% across centers). Thus, the physician and parents should ascertain, preferably while still in the physician's office, that the child can ingest Ceftin Tablets reliably. If not, alternative therapy should be considered.

Drug/Laboratory Test Interactions: A false-positive reaction for glucose in the urine may occur with copper reduction tests (Benedict's or Fehling's solution or with Clinistest® tablets) but not with enzyme-based tests for glycosuria (e.g., Clinistix®, Tes-Tape®). As a false-negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase method be used to determine blood plasma glucose levels in patients receiving Ceftin Tablets.

Cefuroxime does not interfere with the assay of serum and urine creatinine by the alkaline picrate method.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Although no long-term studies in animals have been performed to evaluate carcinogenic potential, no mutagenic potential of cefuroxime was found in standard laboratory tests.

Reproduction studies revealed no impairment of fertility in animals.

Pregnancy, Pregnancy Category B: Reproduction studies have been performed in rats and mice at doses up to 50 to 150 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefuroxime axetil. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: Since cefuroxime is excreted in human milk, consideration should be given to discontinuing nursing temporarily during treatment with Ceftin Tablets.

ADVERSE REACTIONS: The adverse reactions to Ceftin® Tablets are similar to reactions to other orally administered cephalosporins. Ceftin Tablets were usually well tolerated in controlled clinical trials. Pediatric patients taking crushed tablets during clinical trials complained of the bitter taste of Ceftin Tablets (see ADVERSE REACTIONS AND PRECAUTIONS: Information for Patients (Pediatric)). The majority of adverse events were mild, reversible in nature, and did not require discontinuation of the drug. The incidence of gastrointestinal adverse events increased with the higher recommended doses. Twenty-five (25) patients have received Ceftin Tablets 500 mg twice a day for one to 2.5 months with no increase in frequency or severity of adverse events.

The following adverse reactions have been reported.

Gastrointestinal: Nausea occurred in 2.4% of patients. Vomiting occurred in 2.0% of patients. Diarrhea occurred in 3.5% of patients. Loose stools occurred in 1.3% of patients. There have been reports of pseudomembranous colitis (see WARNINGS).

Crushed tablets have a bitter taste. In pediatric clinical studies conducted with crushed tablets, complaints due to taste ranged from 0/8 (0%) in one center to 47/71 (66%) in another center.

Hypersensitivity: Rash (0.6% of patients), pruritus (0.3% of patients), and urticaria (0.2% of patients) have been observed. One case of severe bronchospasm has been reported among the approximately 1,600 patients treated with Ceftin Tablets. Of the patients treated with Ceftin Tablets who reported a history of delayed hypersensitivity to a penicillin and not a cephalosporin, 2.9% of patients experienced a delayed hypersensitivity reaction to Ceftin Tablets.

As with other cephalosporins, hypersensitivity reactions including Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, drug fever, and anaphylaxis have been reported.

Central Nervous System: Headache occurred in less than 0.7% of patients, and dizziness occurred in less than 0.2% of patients.

Other: Vaginitis occurred in 1.9% of female patients.

Clinical Laboratory Tests: Transient elevations in AST (SGOT, 2.0% of patients), ALT (SGPT, 1.6% of patients), and LDH (1.4% of patients) have been observed. Eosinophilia (1.1% of patients) and positive Coombs' test (0.4% of patients) have been reported.

In addition to the adverse reactions listed above that have been observed in patients treated with Ceftin Tablets, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics:

Adverse Reactions: Allergic reactions including colitis, renal dysfunction, toxic nephropathy, hepatic dysfunction including cholestasis, abdominal pain, superinfection, aplastic anemia, hemolytic anemia, hemorrhage, and pain and/or paresthesia at the injection site.

Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy should occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

Altered Laboratory Tests: Increased prothrombin time, increased BUN, increased creatinine, false-positive test for urinary glucose, increased alkaline phosphatase, neutropenia, thrombocytopenia, leukopenia, elevated bilirubin, pancytopenia, and agranulocytosis.

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Zinacef® (sterile cefuroxime sodium): Glaxo Pharmaceuticals, Research Triangle Park, NC 27709

Zinacef® (cefuroxime sodium injection): Manufactured for Glaxo Specialties Inc., Research Triangle Park, NC 27709 by Baxter Healthcare Corporation, Deerfield, IL 60015

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Figure 5. Distribution of patients having spinal-anesthesia-induced hypotension, based on the highest level of anesthesia achieved in the thoracic or lumbar dermatomes. *NS = not specified.

them received 12 mg or more of tetracaine.

Of the 85 patients having hypotension, 52 had their highest level of anesthesia recorded (Fig 5). Thirteen (25%) of these attained anesthesia to dermatome T-4 or higher; 30 patients (58%) registered anesthesia at T-6 or above. One "high-block" occurred.

The patients all had physical status (PS) determined preoperatively, and expressed as a number from 1 to 5, according to the severity of the preexisting medical condition. The more severe the condition, the higher the number, according to the following classification:⁶

Class 1 (PS 1): Absence of organic physical mental dysfunction. Examples: elective herniorrhaphy, hysterectomy, or cesarean section in a healthy patient.

Class 2 (PS 2): Mild-to-moderate disturbance, such as controlled diabetes mellitus, hypertension, anemia, or obesity.

Class 3 (PS 3): Severe systemic disturbance or disease, such as debilitating organic heart disease, uncontrolled diabetes mellitus with neurovascular sequelae, severe chronic obstructive pulmonary disease, or a healed myocardial infarct.

Class 2-3 (PS 2-3): Moderate to severe disturbance having mixed features of PS 2 and

PS 3. An obese, diet-controlled diabetic patient experiencing reactive airways from COPD would be a representation of this difficult-to-classify, subjectively assigned group.

Class 4 (PS 4): Severe, life-threatening systemic disorders, such as organic heart disease accompanied by congestive heart failure; persistent symptomatic angina; or advanced pulmonary, hepatic, renal, or endocrine deficiency.

Class 5 (PS 5): Diseases typical of critically ill, moribund patients who have a negligible chance for survival, but who are subjected to surgery in desperation. Examples are patients with a ruptured aneurysm with profound shock, intracerebral bleeding after trauma, or a massive pulmonary embolism.

Emergency operation (E): "E" is added to any of the previous PS classes when the operation is performed on an emergency basis. Such patients are considered to be in poorer physical condition than their PS classification would otherwise indicate. Examples include an asymptomatic, uncomplicated hernia scheduled for elective herniorrhaphy that incarcerates and subsequently strangulates a portion of bowel, becoming symptomatic; a term pregnancy requiring an emergency cesarean section after

Table 1
Distribution of Patients Having
Spinal-Anesthesia-Induced Hypotension,
According to Physical Status

Physical status numeric classification*	No. of patients	% of total (N = 85)
1 (Healthy)	3	3.5
2 (Mild to moderate systemic disturbance)	55	64.7
2-3 (Moderate to severe systemic disturbances)	8	9.4
3 (Severe systemic disturbance)	18	21.2
4 (Severe life-threatening disturbance)	1	1.2
5 (Critical/moribund)	0	0
Total	85	100.0
E (emergency procedures)†	25‡	

*See text for explanation of physical status classification.
†The designation "E" is assigned to physical status when the scheduling of surgery is dictated by an unforeseen emergency; it suggests a downgraded condition.
‡All were in patients who underwent cesarean section.

the fetus has been in distress (a large presence in this study).⁶

As shown in Table 1, approximately 70% of the 85 patients had a physical status rating of PS 1 or 2, which is considered benign. No patient was listed as PS 5, and only one was listed as PS 4.

Among the patients who had spinal-anesthesia-induced hypotension, 18 (21%) had preexisting diseases (Table 2). Three of these 18 patients had carcinoma; 5 had diabetes. A similar number had a vascular disease; 6 had respiratory problems; and 9 had multiple, interdependent pathologic conditions.

Only 18 of the hypotensive patients received preoperative medication (Table 3). Narcotics—with meperidine the preferred agent—were administered to 16 patients (89%). Fourteen patients (78%) received a narcotic/anticholinergic mixture.

Regarding the various types of surgery performed on the hypotensive patients, the high-

Table 2
Conditions Preexisting in 18 Patients Having
Spinal-Anesthesia-Induced Hypotension

1. Atrial fibrillation
2. Adenocarcinoma of the prostate gland
3. Diabetes mellitus
4. Chronic obstructive pulmonary disease (COPD)
5. Cerebrovascular disease (CVD)
6. Arteriosclerotic heart disease (ASHD)/congestive heart failure (CHF)
7. Carcinoma of the endometrium
8. Intravenous drug abuse
9. Pneumonia
10. Upper respiratory tract infection
11. Cerebrovascular accident
12. ASHD/diabetes mellitus
13. ASHD/diabetes mellitus/CHF/COPD
14. ASHD/seizure disorder
15. COPD/CVD/hypertension
16. Diabetes mellitus/hypertension
17. Adenocarcinoma of the prostate/hypertension
18. COPD/hypertension/chronic anemia

est proportion were obstetric (Table 4). Urologic and vascular procedures figured prominently among the types of surgery performed.

Discussion

Certain features were common to the 85 patients who had spinal-anesthesia-induced hypotension. These features are listed in Table 5 in decreasing order of importance.

Low preoperative systolic blood pressure (120 torr or lower) was the most consistent common feature; it was found in 80% of the patients having hypotension. When systolic pressures of 124 torr and lower are included, the percentage of hypotensive patients increases to 85%. Approximately 13% of the patients had systolic pressures of 100 torr or less. Elevated pressures of 150 torr or more were discovered in three patients, all of whom had preexisting pathologic conditions; namely, chronic obstructive pulmonary disease, hypertension, and/or diabetes mellitus.

Preoperative anemia, defined as hemoglobin values of less than 14 g/dL in men and less than 12 g/dL in women,¹⁸ was also significant in the hypotensive patients. Forty-nine (58%) of the patients, irrespective of sex, had hemoglobin levels of less than 12 g/dL. Among the female patients, whose total number ac-

(continued on page 1205)

Do You Know Where Your Patients' NSAIDs Are?

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As with other NSAIDs, GI-related side effects may occur in some patients; these include ulceration, bleeding, and perforation.

Brief Summary

FELDENE[®] (piroxicam) Capsules

CONTRAINDICATIONS: FELDENE (piroxicam) should not be used in patients who have previously exhibited hypersensitivity to it, or in individuals with the syndrome comprised of bronchospasm, nasal polyps and angioedema precipitated by aspirin or other nonsteroidal anti-inflammatory drugs.

WARNINGS: Peptic ulceration, perforation, and GI bleeding—sometimes severe, and, in some instances fatal—have been reported with patients receiving FELDENE. If FELDENE must be given to patients with a history of upper gastrointestinal tract disease, the patient should be under close supervision (see ADVERSE REACTIONS). Physicians should remain alert for ulceration and bleeding in patients treated chronically with NSAIDs even in the absence of previous GI tract symptoms.

PRECAUTIONS: Renal Effects: As with other nonsteroidal anti-inflammatory drugs, long-term administration of piroxicam to animals has resulted in renal papillary necrosis and other abnormal renal pathology. In humans, there have been reports of acute interstitial nephritis with hematuria, proteinuria, and occasionally, nephrotic syndrome.

A second form of renal toxicity has been seen in patients with prerenal conditions leading to a reduction in renal blood flow or blood volume, where the renal prostaglandins have a supportive role in the maintenance of renal perfusion. In these patients administration of an NSAID may cause a dose-dependent reduction in prostaglandin formation and may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics, and the elderly.

Because of extensive renal excretion of piroxicam and its biotransformation products (less than 5% of the daily dose excreted unchanged), lower doses of piroxicam should be anticipated in patients with impaired renal function, and they should be carefully monitored.

Although other nonsteroidal anti-inflammatory drugs do not have the same direct effect on platelets that aspirin does, all drugs inhibiting prostaglandin biosynthesis do interfere with platelet function to some degree.

Because of reports of adverse eye findings with nonsteroidal anti-inflammatory agents, it is recommended that patients who develop visual complaints during treatment with FELDENE have ophthalmic evaluation.

As with other nonsteroidal anti-inflammatory drugs, borderline elevations of one or more liver tests may occur in up to 15% of patients. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom abnormal liver tests have occurred, should be evaluated for evidence of the development of more severe hepatic reaction while on therapy with FELDENE.

Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with FELDENE. Although such reactions are rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), FELDENE should be discontinued. (See also ADVERSE REACTIONS.)

Although at the recommended dose of 20 mg/day of FELDENE increased fecal blood loss due to gastrointestinal irritation did not occur, in about 4% of the patients treated with FELDENE alone or concomitantly with aspirin, reductions in hemoglobin and hematocrit values were observed.

Peripheral edema has been observed in approximately 2% of the patients treated with FELDENE. Therefore, FELDENE should be used with caution in patients with heart failure, hypertension or other conditions predisposing to fluid retention.

A combination of dermatological and/or allergic signs and symptoms suggestive of serum sickness have occasionally occurred in conjunction with the use of FELDENE. These include arthralgia, pruritus, fever, fatigue, and rash including vesiculo-bullous reactions and exfoliative dermatitis.

DRUG INTERACTIONS: Interactions with coumarin-type anticoagulants have been reported with FELDENE since marketing. Therefore, physicians should closely monitor patients for a change in dosage requirements when administering FELDENE to patients on coumarin-type anticoagulants and other highly protein-bound drugs.

Plasma levels of piroxicam are depressed to approximately 80% of their normal values when FELDENE is administered in conjunction with aspirin (3900 mg/day), but concomitant administration of antacids has no effect on piroxicam plasma levels.

Nonsteroidal anti-inflammatory agents, including FELDENE, have been reported to increase steady state plasma lithium levels. It is recommended that plasma lithium levels be monitored when initiating, adjusting and discontinuing FELDENE.

Carcinogenesis, Chronic Animal Toxicity and Impairment of Fertility: Subacute and chronic toxicity studies have been carried out in rats, mice, dogs, and monkeys.

The pathology most often seen was that characteristically associated with the animal toxicology of anti-inflammatory agents: renal papillary necrosis (see PRECAUTIONS) and gastrointestinal lesions.

In classical studies in laboratory animals, piroxicam did not show any teratogenic potential.

Reproductive studies revealed no impairment of fertility in animals.

Pregnancy and Nursing Mothers: Like other drugs which inhibit the synthesis and release of prostaglandins, piroxicam administration continued late into pregnancy increased the incidence of dystocia and delayed parturition in animals. Gastrointestinal tract toxicity was increased in pregnant females in the last trimester of pregnancy compared to non-pregnant females or females in earlier trimesters of pregnancy.

FELDENE (piroxicam) is not recommended for use in nursing mothers or in pregnant women because of the animal findings and since safety for such use has not been established in humans.

Use in Children: Dosage recommendations and indications for use in children have not been established.

ADVERSE REACTIONS: Gastrointestinal symptoms are the most prominent side effects, occurring in approximately 20% of the patients, which in most instances did not interfere with the course of therapy. Of the patients experiencing gastrointestinal side effects, approximately 5% discontinued therapy with an overall incidence of peptic ulceration of about 1%.

Adverse reactions are listed below by body system for all patients in clinical trials with FELDENE at doses of 20 mg/day.

Incidence Greater Than 1%: The following adverse reactions occurred more frequently than 1 in 100.

Gastrointestinal: stomatitis, anorexia, epigastric distress, nausea, constipation, abdominal discomfort, flatulence, diarrhea, abdominal pain, indigestion

Hematological: decreases in hemoglobin* and hematocrit* (see PRECAUTIONS), anemia, leucopenia, eosinophilia

Dermatologic: pruritus, rash

Central Nervous System: dizziness, somnolence, vertigo

Urogenital: BUN and creatinine elevations (see PRECAUTIONS)

Body as a Whole: headache, malaise

Special Senses: tinnitus

Cardiovascular/Respiratory: edema (see PRECAUTIONS)

* Reactions occurring in 3% to 9% of patients treated with FELDENE. Reactions occurring in 1% to 3% of patients are unmarked.

Incidence Less Than 1% (Causal Relationship Probable): The following adverse reactions occurred less frequently than 1 in 100. The probability exists that there is a causal relationship between FELDENE and these reactions.

Gastrointestinal: liver function abnormalities, jaundice, hepatitis (see PRECAUTIONS), vomiting, hematemesis, melena, gastrointestinal bleeding, perforation and ulceration (see WARNINGS), dry mouth

Hematological: thrombocytopenia, petechial rash, ecchymosis, bone marrow depression including aplastic anemia, epistaxis

Dermatologic: sweating, erythema, bruising, desquamation, exfoliative dermatitis, erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson syndrome, vesiculo bullous reactions, photoallergic skin reactions

Central Nervous System: depression, insomnia, nervousness

Urogenital: hematuria, proteinuria, interstitial nephritis, renal failure, hyperkalemia, glomerulitis, papillary necrosis, nephrotic syndrome (see PRECAUTIONS)

Body as a Whole: pain (colic), fever, flu-like syndrome (see PRECAUTIONS)

Special Senses: swollen eyes, blurred vision, eye irritations

Cardiovascular/Respiratory: hypertension, worsening of congestive heart failure (see PRECAUTIONS), exacerbation of angina

Metabolic: hypoglycemia, hyperglycemia, weight increase, weight decrease

Hypersensitivity: anaphylaxis, bronchospasm, urticaria/angioedema, vasculitis, "serum sickness" (see PRECAUTIONS)

Incidence Less Than 1% (Causal Relationship Unknown): Other adverse reactions were reported with a frequency of less than 1 in 100, but a causal relationship between FELDENE and the reaction could not be determined.

Gastrointestinal: pancreatitis

Dermatologic: onycholysis, loss of hair

Central Nervous System: akathisia, hallucinations, mood alterations, dream abnormalities, mental confusion, paresthesias

Urogenital System: dysuria

Body as a Whole: weakness

Cardiovascular/Respiratory: palpitations, dyspnea

Hypersensitivity: positive ANA

Special Senses: transient hearing loss

Hematological: hemolytic anemia

OVERDOSAGE: In the event treatment for overdosage is required, the long plasma half-life of piroxicam should be considered. The absence of experience with acute overdosage precludes characterization of sequelae and recommendations of specific antidotal efficacy at this time. It is reasonable to assume that the standard measures of gastric evacuation and general supportive therapy would apply. In addition to supportive measures, the use of activated charcoal may effectively reduce the absorption and reabsorption of piroxicam. Experiments in dogs have demonstrated that the use of multiple-dose treatments with activated charcoal could reduce the half-life of piroxicam elimination from 27 hours (without charcoal) to 11 hours and reduce the systemic bioavailability of piroxicam by as much as 37% when activated charcoal is given as late as 6 hours after administration of piroxicam.

ADMINISTRATION AND DOSAGE: Rheumatoid arthritis, Osteoarthritis: It is recommended that FELDENE therapy be initiated and maintained at a single daily dose of 20 mg. If desired, the daily dose may be divided.

Dosage recommendations and indications for use in children have not been established.

More detailed professional information available on request.

Revised October 1988

Pfizer Labs

Table 3
Distribution of Patients Having Spinal-Anesthesia-Induced Hypotension, After Administration of Preoperative Medications

Agents	No. of patients	% of total
• Meperidine hydrochloride/glycopyrrolate/hydroxyzine hydrochloride	4	22.2
• Fentanyl citrate*/hydroxyzine hydrochloride	5	27.7
• Meperidine hydrochloride/hydroxyzine hydrochloride/atropine sulfate	2	11.1
• Meperidine hydrochloride	2	11.1
• Atropine sulfate/fentanyl citrate†	2	11.1
• Meperidine hydrochloride/atropine sulfate	1	5.6
• Atropine sulfate	1	5.6
• Midazolam hydrochloride	1	5.6
Total	18	100.0

*As Sublimaze (Janssen).
†Fentanyl citrate (Elkins-Sinn).

counted for 80% of the patient population, about two thirds were considered anemic. From a physiologic standpoint, anemia is expected to be associated with hypotension.

Just as some patients had elevated blood pressure, a few (6) patients had elevated hemoglobin levels (> 14.9 g/dL). These patients also had underlying preexisting pathologic conditions, including COPD, hypertension, leukocytosis, vesical outlet obstruction, or pneumonia.

The results suggest a relation between increased lidocaine concentrations and increased rates of hypotension. This relation was maximally observed at a dosage of 100 mg. Only three patients received 15 mg of 0.75% solution of bupivacaine and consequently cannot be evaluated in terms of dosage. However, the fact that all of the three patients receiving bupivacaine had hypotension may be of importance.

Increasing dosages of tetracaine showed a less linear relationship to the incidences of hypotension compared with lidocaine, but that drug also tended to be associated with higher

incidences of hypotension at higher concentrations. The peak incidence of hypotension occurred at 10 mg of 1% solution of tetracaine.

Although the highest level of spinal anesthesia attained was discovered after the anesthetic was administered, this information may be a predictive factor. Conclusions based on this value are less significant because only 61% of the patients had the spinal level dermatome reported. Total sympatholysis reportedly occurs at about dermatome T-4 or above. This level is represented by a quarter of those patients whose dermatome levels were recorded.

Considering individual responses to anesthesia and the variable nature of sympatholysis, it can be inferred that dermatome T-6 or above would approximate total sympathetic inhibition. Such an assumption covers 49 (58%) of the study's hypotensive patients.

Physical status, a necessary preoperative determination, was evaluated and found to be disappointingly related to spinal-anesthesia-induced hypotension.

No patient had a physical status rating of PS 5—a rating assigned to patients with a neg-

Table 4
Distribution by Type of Surgery Performed in Patients Having Spinal-Anesthesia-Induced Hypotension (N = 85)

Type of surgery	No. of patients	% of group
Obstetric/gynecologic (n = 59)		
• Cesarean section	55	93.0
• Vaginal delivery	2	3.0
• Dilation and curettage	1	2.0
• Postpartum cervical laceration repair	1	2.0
Urologic (n = 8)		
• Transurethral resection of prostate	5	62.5
• Urethrocystoscopy	2	25.0
• Unilateral orchiectomy	1	12.5
Abdominal/perianal (n = 6)		
• Herniorrhaphy (includes 2 orchiectomies)	4	66.0
• Hemorrhoidectomy	1	17.0
• Perirectal fistulectomy	1	17.0
Vascular (n = 4)		
• Femoral-popliteal bypass	3	75.0
• Above-knee amputation	1	25.0
Orthopedic (n = 4)		
• Open reduction/fixation of hip fracture	3	75.0
• Right total hip replacement	1	25.0
Integumental (n = 4)		
• Ulcer debridement	3	75.0
• Skin graft to right ankle	1	25.0

ligible chance of survival. Only one patient was graded PS 4. Most patients (approximately 70%) were graded PS 1 or 2.

This high percentage of benign presentations can be accounted for by the large number of healthy, young obstetric patients, the absence of any substantial number of life-threatening conditions, and the number of elective surgical procedures. Significant here is the fact that about 30% of the surgeries were performed on patients graded as PS 2 to 3 through PS 4. Emergency surgery is a separate category in the physical status grading system. In this group of patients, cesarean sections accounted for all 25 emergency surgical procedures.

Documented preexisting conditions were re-

Table 5
Features Common to Patients Having Spinal-Anesthesia-Induced Hypotension, in Decreasing Order of Importance

- Low preoperative systolic blood pressure (≤ 120 torr)
- Anemia, specifically hemoglobin level ≤ 12 g/dL, irrespective of sex; ≤ 14 g/dL in male patients
- Increasing dosages of anesthetic
- Spinal dermatomes at T-6 or above
- Physical status class 3 or greater; emergent surgery
- Preexisting conditions
- Narcotic/anticholinergic premedication
- Type of surgery

ported in approximately a fifth of those patients having spinal-anesthesia-induced hypotension. Respiratory complaints led the list, accounting for 6 of the 18 affected patients. The remaining pathologic conditions, listed in decreasing order of prevalence, were diabetes and vascular conditions (including cerebrovascular disease and arteriosclerotic heart disease), 5 (27.8%); hypertension, 4 (22.2%); carcinoma, 3 (16.7%); congestive heart failure, 2 (11.1%); and chronic anemia, 1 (5.6%). More importantly, half of the patients with documented preoperative conditions had multiple, interdependent diseases.

About a fifth of the patients receiving documented preoperative medication had a hypotensive episode. Narcotic premedication was a common feature shared by 16 patients; a narcotic/anticholinergic mixture was the next most common regimen, administered to 14 patients.

Type of surgery was the final variable evaluated. Because Michigan Health Center Hospital is one of the few local hospitals providing obstetric services, cesarean section surgeries are not unusual. This relatively high number of obstetric/gynecologic patients experiencing hypotension was also observed by Kang and associates.¹⁹

Urologic and abdominal/perirectal surgical

(continued on page 1208)

MEDICAL DIRECTOR'S PAGE

Bruce H. Medd, M.D., Associate Vice President and Director,
Professional Services

Managing the Benzodiazepine-Dependent Patient

Since their introduction almost three decades ago, the benzodiazepines have become one of the most widely prescribed group of drugs in the history of medicine. Despite periodic trends to criticize the broad use of the benzodiazepines, their popularity seems to be well deserved, when one considers the many thousands of references in the worldwide medical literature that clearly reflect the significant benefits realized with these agents. In addition to their more familiar applications in anxiety, insomnia and preoperative sedation, administration of the benzodiazepines extends to certain life-saving uses as well (i.e., control of the muscle spasms of tetanus and other conditions often seen in certain Third World countries).

The potential for abuse and the occurrence of dependence during benzodiazepine therapy has prompted numerous studies and reports. Although physiologic dependence can develop in some patients, available evidence does not appear to support the wide occurrence of abuse in the general population.¹ However, it is critically important that health care professionals be able to recognize and treat benzodiazepine dependence when it occurs. To assist physicians in this effort, a workshop was held in Basle, Switzerland, in September of 1987. Experts gathered there to evaluate their experiences and establish guidelines for managing benzodiazepine-dependent patients.²

These experts agreed that:²

- the physician must evaluate a number of behavioral and clinical features and their time course to distinguish benzodiazepine-dependent patients from those patients with chronic anxiety who may be suffering from a return of their symptoms.
- some patients should not be withdrawn from therapy even if they show signs of dependence. Careful evaluation of the patient should always precede any attempt at withdrawal.
- while there are many methods available for the safe and effective withdrawal of the benzodiazepine-dependent patient, gradual reductions in dosage in an outpatient setting is preferred in uncomplicated cases.
- continued management of the patient withdrawn successfully is essential to reduce the patient's risk of relapsing into drug dependency. Of course, the importance of support from the patient's family and friends during and after the withdrawal period cannot be stressed enough.

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If you would like more information on the management of benzodiazepine-dependent patients, ask your Roche representative or write to me: Bruce H. Medd, M.D., Associate Vice President and Director, Professional Services, Roche Laboratories, a division of Hoffmann-La Roche Inc., Nutley, New Jersey 07110.

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procedures were the next most common among the hypotensive patients; they were performed in eight (9%) and six (7%) of the patients, respectively. Vascular, orthopedic, and superficial surgical procedures accounted for four cases (5%). The last three surgical procedure types suggest the presence of renal/cardiovascular pathologic conditions that are related to the feature of preexisting conditions listed previously.

Conclusion

Certain factors have been found to be associated with spinal-anesthesia-induced hypotension. These factors can help to predict which patients may have significant perioperative hypotension. Anticipation of such occurrences can shorten response time.

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