ARCHIVES OF INTERNAL MEDICINE

Magnesium Sulfate in Exacerbations of Chronic Obstructive Pulmonary Disease

Background: Acute exacerbations of chronic obstructive pulmonary disease are commonly seen and difficult to treat. We sought to determine the bronchodilator efficacy of magnesium sulfate in this situation, as this compound is helpful in acute asthma.
Methods: Subjects who came to either of two Veterans Affairs emergency departments were randomized in a double-blind fashion to receive either 1.2 g of magnesium sulfate or placebo over 20 minutes after they first received albuterol, 2.5 mg by nebulization. Peak expiratory flow, dyspnea scores, arterial hemoglobin oxygen saturation by pulse oximetry, maximal inspiratory and expiratory pressures, and vital signs were monitored for 45 minutes after the start of magnesium sulfate or placebo treatment.
Results: Seventy-two individuals were studied. The peak expiratory flow increased 16.6%±27.7% (mean±SD) in both groups after the initial albuterol treatment, from 121.2±55.7 L/min to 136.9±63.9 L/min. The peak expiratory flow increased from 136.7±69.7 L/min at the start of the infusion to 162.3±76.6 L/min at 30 minutes and 161.3±78.7 L/min at 45 minutes with magnesium sulfate treatment. The peak expiratory flow was 137.0±58.6 L/min on initiation of the intravenous infusion, 143.0±72.7 L/min at 30 minutes, and 143.3±70.5 L/min at 45 minutes in the placebo group. The difference in peak expiratory flow from initiation of the infusion to 30 and 45 minutes later (calculated as means of the 30- and 45-minute values) was significantly different for the two groups (25.1±35.7 L/min vs 7.4±33.3 L/min; P=.03); the difference was also significant when expressed as percentage increase (22.4%±28.5% vs 6.1%±24.4%; P=.01). There was a statistically nonsignificant trend toward a reduced need for hospitalization in the magnesium sulfate group as compared with the placebo group (28.1% vs 41.9%; P=.25). There were no significant changes in the other parameters with either treatment.
Conclusions: Magnesium sulfate, 1.2 g over 20 minutes after β-agonist administration, is safe and modestly efficacious in the treatment of acute exacerbations of chronic obstructive pulmonary disease, and its bronchodilator effect is greater than that of a β-agonist given alone and lasts beyond the period of magnesium sulfate administration.

(1995;155:496-500) Morton S. Skorodin, MD, et al, 11A VAMC, Honor Heights Drive, Muskogee, OK 74401.

Treatment of Deep Venous Thrombosis With Low-Molecular-Weight Heparins: A Meta-analysis

Background: An intravenous course of unfractionated heparin adjusted on the basis of the activated partial thromboplastin time is the initial treatment of choice for most patients with venous thromboembolism. Recently introduced low-molecular-weight heparin preparations can be administered subcutaneously, once or twice daily, without laboratory monitoring. We quantitatively assessed the relative efficacy and safety of low-molecular-weight heparin vs standard heparin for the initial treatment of deep venous thrombosis.
Methods: English-language reports of randomized trials were identified through a MEDLINE search (1984 through 1994) and a complementary extensive manual search. Reasons for exclusion from the analysis were no heparin dosage adjustments, the lack of use of objective tests for deep venous thrombosis, duplicate reports, preliminary reports of data later presented in full, dose-ranging studies that used higher doses of low-molecular-weight heparin than are currently in use, and the failure to provide blind end-point assessment. We assessed the incidence of symptomatic recurrent venous thromboembolic disease, the incidence of clinically important bleeding, and mortality.
Results: Ten of the 19 identified trials satisfied the predetermined criteria. The relative risk reductions for symptomatic thromboembolic complications (53% [95% confidence interval, 18% to 73%]), clinically important bleeding (68% [95% confidence interval, 31% to 85%]), and mortality (47% [95% confidence interval, 10% to 69%]) were all statistically significantly in favor of low-molecular-weight heparin.
Conclusions: Low-molecular-weight heparins administered subcutaneously in fixed doses adjusted for body weight and without laboratory monitoring are more effective and safer than adjusted-dose standard heparin. Since low-molecular-weight heparins may not be interchangeable and the conclusions of our meta-analysis are based mainly on the findings of three trials that used two different low-molecular-weight heparins, definitive randomized controlled trials for the other low-molecular-weight heparins are required.

(1995;155:601-607) Anthonie W. A. Lensing, MD, PhD, et al, Academic Medical Center H-2, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands.

Effects of Acute Psychological Stress on Serum Lipid Levels, Hemoconcentration, and Blood Viscosity

Background: While there is substantial evidence that psychological stress enhances risk for coronary artery disease, the mechanisms underlying such an influence remain unclear. We examined the effects of short-term psychological stress on serum lipid levels, hemoconcentration, fibrinogen level, and plasma viscosity.
Methods: Forty-four healthy young adults were randomly assigned to perform a distinctly frustrating cognitive task for 20 minutes (stress condition) or to rest quietly for the same period (control condition).
Results: Relative to controls, stressed subjects showed significant increases in blood pressure and heart rate; total, low-density, and high-density lipoprotein cholesterol levels; hematocrit; hemoglobin level; and total protein concentration. Stressed subjects also showed significant reductions in plasma volume and increased plasma viscosity and estimated whole-blood viscosity compared with controls. A similar trend in fibrinogen level was not statistically significant. Individual differences in blood pressure and heart rate response to stress correlated highly with changes in total cholesterol levels and hematocrit.
Conclusions: Our investigation provides further evidence that exposure to short-term mental stress elicits hemoconcentration with associated increases in serum lipid concentration, hemostatic factors, and blood viscosity.

(1995;155:615-620) Matthew F. Muldoon, MD, et al, Old Engineering Hall, Room 506, University of Pittsburgh, Pittsburgh, PA 15260.

Decisions About Life-Sustaining Treatment: Impact of Physicians' Behaviors on the Family

Background: Despite the growing availability of advance directives, most patients in the intensive care unit lack written directives, and, therefore, consultation with families about treatment decisions remains the rule. In the context of decision making about withdrawing life-sustaining treatments, we investigated which physician and nurse behaviors families find supportive and which behaviors increase the family's burden.
Methods: We conducted intensive 1- to 2-hour-long individual interviews using a semistructured interview protocol with 32 family members of patients without advance directives whose deaths followed a stay in the intensive care unit and withdrawal of treatment. We analyzed more than 700 pages of verbatim interview data using content analysis techniques and achieved more than 90% interrater agreement on data codes.
Results: Themes emerged as families identified selected physician and nursing behaviors as helpful: encouraging advanced planning, timely communication, clarification of families' roles, facilitating family consensus, and accommodating family's grief. Behaviors that made families feel excluded or increased their burden included postponing discussions about treatment withdrawal, delaying withdrawal once scheduled, placing the full burden of decision making on one person, withdrawing from the family, and defining death as a failure.
Conclusions: Study findings provide an increased understanding of the unmet needs of families and serve to guide physicians and nurses in reducing actions that increase families' burdens as they participate in treatment withdrawal decisions.

(1995;155:633-638) Virginia P. Tilden, RN, DNSc, FAAN, et al. Correspondence to Susan W. Tolle, MD, School of Medicine, L101, Oregon Health Sciences University, 3181 SW Sam Jackson Park Rd, Portland, OR 97201-3098.

ARCHIVES OF NEUROLOGY

The Risk of Stroke in Patients With First-Ever Retinal vs Hemispheric Transient Ischemic Attacks and High-grade Carotid Stenosis

Background: The prognosis of amaurosis fugax has been considered to be favorable compared with that of hemispheric transient ischemic attacks. However, this has remained uncertain for patients with significant carotid stenosis as the assessment of progression of the disease has been confounded when patients undergo carotid endarterectomy. In the North American Symptomatic Carotid Endarterectomy Trial, patients with high-grade (70% to 99%) carotid stenosis were randomized to receive either medical or surgical treatment, thus making an unconfounded analysis possible.
Method: We identified 129 medically treated patients with high-grade carotid stenosis who had their first-ever transient ischemic attack as the entry event into the trial. Fifty-nine patients with retinal transient ischemic attacks (RTIAs) were compared with 70 patients with hemispheric transient ischemic attacks (HTIAs).
Results: Patients with HTIAs were older, with a higher prevalence of most risk factors for stroke. Average time of delay from the onset of transient ischemic attacks to medical treatment was longer for patients with RTIAs than for patients with HTIAs (48.5 vs 15.2 days). Kaplan-Meier estimates of the risk of ipsilateral stroke at 2 years were 16.6%±5.6% for patients with RTIAs and 43.5%±6.7% for patients with HTIAs (P=.002 for the difference in risk between RTIAs and HTIAs). From corresponding Cox's proportional hazards regression analyses, the risk of ipsilateral stroke ranged from 11.2% to 28.9% for patients with RTIAs and from 37.4% to 96.3% for patients with HTIAs across stenoses, spanning 75% to 95%. Overall, the relative risk of ipsilateral stroke (HTIAs compared with RTIAs) was 3.23 (95% confi-

dence interval, 1.47 to 7.12), regardless of the degree of high-grade stenosis.
Conclusion: To our knowledge, this study is the first report on the expected outcome for medically treated patients with high-grade (70% to 99%) carotid stenosis in whom the first-ever event was either an RTIA or HTIA. The presence of RTIAs carries a considerable risk of ipsilateral strokes, particularly at higher degrees of stenosis. However, in comparison with HTIAs, patients with RTIAs still have a better prognosis.

(1995;52:246-249) Jonathan Y. Streifler, MD, et al. Reprint requests to Henry J. M. Barnett, MD, The John P. Robarts Research Institute, 100 Perth Dr, PO Box 5015, London, Ontario, Canada N6A 5K8.

Migraine Prophylaxis With Divalproex

Objective: To compare the effectiveness and safety of divalproex sodium (Depakote) and placebo in the prophylaxis of migraine headache.
Design: Multicenter, double-blind, randomized, placebo-controlled investigation, having a 4-week, single-blind placebo baseline phase and a 12-week treatment phase (4-week dose adjustment, 8-week maintenance).
Setting: Eight headache/neurology clinics throughout the United States.
Patients: One hundred seven patients randomized to divalproex or placebo (2:1 ratio): 70 receiving divalproex and 37 receiving placebo.
Intervention: Divalproex and placebo dosages titrated in blinded fashion during dose adjustment period to achieve actual/sham trough valproate sodium concentrations of approximately 70 to 120 mg/L.
Measurements and Main Results: During the treatment phase, the mean migraine headache frequency per 4 weeks was 3.5 in the divalproex group and 5.7 in the placebo group ($P \leq .001$), compared with 6.0 and 6.4, respectively, during the baseline phase. Forty-eight percent of divalproex-treated patients and 14% of placebo-treated patients showed a 50% or greater reduction in migraine headache frequency from the baseline phase ($P < .001$). Among those with migraine headaches, divalproex-treated patients reported significantly less functional restriction than placebo-treated patients and used significantly less symptomatic medication per episode. No significant treatment group differences were observed in average peak severity or duration of individual migraine headaches. Treatment was stopped in 13% of divalproex-treated patients and 5% of placebo-treated patients because of intolerance (P, not significant).
Conclusions: Divalproex is an effective prophylactic drug for patients with migraine headaches and is generally well tolerated.

(1995;52:281-286) Ninan T. Mathew, MD, et al, Houston Headache Clinic, 1213 Hermann Dr, Suite 350, Houston, TX 77004.

ARCHIVES OF PEDIATRICS & ADOLESCENT MEDICINE

Gravid Students: Characteristics of Nongravid Classmates Who React With Positive and Negative Feelings About Conception

Objective: To determine whether gravid classmates affect nongravid students' feelings about conception.
Method: Cross-sectional survey of a school-based clinic population. We asked 130 nulliparous high school students who were seeking routine health care at an urban school-based clinic to complete an anonymous questionnaire concerning risk factors for and attitudes about teen pregnancy.
Results: The respondents were grouped according to the effect that contact with gravid classmates had on their desire for conception: increased desire (n=13), no change in desire (n=59), and decreased desire (n=49). The analysis disclosed no significant group differences for age (mean±SD, 16.3±1.2 years), sex (65% female), welfare use (20%), or living situation (85% lived with a parent). The increased-desire group had significantly more sociodemographic risk factors for teen pregnancy than did the groups with no change and decreased desire. The group with increased desire was significantly more likely than the other two groups to be failing in school (54% vs 44% and 12.2%; $P < .001$), to have low education goals (15.4% vs 3.4% and 0%; $P = .02$), to be unhappy with their family support (69.2% vs 27.1% and 29.8%; $P = .01$), to be concerned about sterility (30.8% vs 8.6% and 6.1%; $P = .03$), not to be using contraceptives (77% vs 35.6% and 30.6%; $P < .01$), to want a pregnancy within 2 years (61.5% vs 25.4% and 12.2%; $P < .001$), and to have a sexual partner who wanted a pregnancy within 2 years (61.5% vs 13.6% and 8.2%; $P < .0001$).
Conclusions: Our findings support the study hypothesis that never-pregnant students in the increased-desire group had more sociodemographic risk factors for teen pregnancy than did students in the groups with no change or decreased desire. The results of this study may help to ally concerns about the adverse effect that the increased prevalence of gravid students in American schools might have on the childbearing attitudes of never-pregnant students.

(1995;149:272-275) Catherine Stevens-Simon, MD, and Constance Boyle, CHA. Reprints not available.

Establishing Clinically Relevant Standards for Tachypnea in Febrile Children Younger Than 2 Years

Objective: To determine values for defining tachypnea in febrile children younger than 2 years that best identify those at risk for pneumonia.
Design: Prospective case series.
Study Patients: Children younger than 2 years pre-

senting to the emergency department of a children's hospital with a temperature of 38°C or higher.
Interventions: Using a standardized method, respiratory rates were obtained on eligible children for 1 year. Study patients were classified as having pneumonia or no pneumonia based on clinical evaluation and chest radiograph findings. Receiver operating characteristic curves were constructed to select the values for respiratory rate that maximized sensitivity and specificity of tachypnea as a sign of pneumonia.
Results: Data were analyzed for 572 children; pneumonia was present in 42 (7%). The diagnostic utility of tachypnea was maximal when cutoff values for respiratory rates of 59/min in infants younger than 6 months, 52/min in those aged 6 through 11 months, and 42/min in those aged 1 to 2 years were selected. Based on these definitions, tachypnea as a sign of pneumonia had a sensitivity of 73.8%, specificity of 76.8%, positive predictive value of 20.1%, and negative predictive value of 97.4%.
Conclusions: Tachypnea, as defined in this study, is an important predictive sign of pneumonia in febrile children younger than 2 years. Conversely, the absence of tachypnea obviates the need for chest radiography in most settings.

(1995;149:283-287) James A. Taylor, MD, et al, Department of Pediatrics (Mailstop RD-20), University of Washington, 1959 NE Pacific St, Seattle, WA 98195.

Metered-Dose Inhalers With Spacers vs Nebulizers for Pediatric Asthma

Objective: To determine whether the administration of β-agonists by metered-dose inhaler (MDI) with a spacer device is as effective as the administration of β-agonists by nebulizer for the treatment of acute asthma exacerbations in children.
Design: Randomized trial with two arms.
Setting: Urban pediatric emergency department (ED) in Bronx, NY.
Patients: Convenience sample of 152 children 2 years and older with a history of at least two episodes of wheezing presenting to the ED with an acute asthma exacerbation.
Interventions: Patients were randomly assigned to receive standard doses of a β-agonist (albuterol) by an MDI with spacer or by a nebulizer. Dosing intervals and the use of other medications were determined by the treating physician.
Measurements/Main Results: Baseline characteristics and asthma history were recorded. Asthma severity score, peak expiratory flow rate in children 5 years or older, and oxygen saturation were determined at presentation and before admission or discharge. The groups did not differ in age, sex, ethnicity, age of onset of asthma, or asthma severity score at presentation. There were no significant differences between the groups in outcomes, including mean changes in respiratory rate, asthma severity score, and peak expiratory flow rate, oxygen saturation, number of treatments given, administration of steroids in the ED, and admission rate. Patients given MDIs with spacers required shorter treatment times in the ED (66 minutes vs 103 minutes, $P<.001$). Fewer patients in the spacer group had episodes of vomiting in the ED (9% vs 20%, $P<.04$), and patients in the nebulizer group had a significantly greater mean percent increase in heart rate from baseline to final disposition (15% vs 5%, $P<.001$).
Conclusions: These data suggest that MDIs with spacers may be an effective alternative to nebulizers for the treatment of children with acute asthma exacerbations in the ED.

(1995;149:201-205) Katherine J. Chou, MD, et al, 1W20 Jacobi Hospital, Pelham Parkway and Eastchester Road, Bronx, NY 10461.

ARCHIVES OF SURGERY

Long-term Morbidity Following Jejunoileal Bypass: The Continuing Potential Need for Surgical Reversal

Objective: To review the late sequelae of jejunoileal bypass (JIB) and the potential role of late surgical reversal in ameliorating morbidity and mortality following JIB.
Design: Patients who underwent JIB between 1965 and 1977 were contacted and pertinent health-event information was gathered. Early sequelae were defined as disorders occurring within the first 2 years after JIB; late sequelae were those occurring after 2 years. Health events occurring between 0 and 23 years after JIB were documented.
Setting: A private, tertiary referral center.
Patients: Patients underwent JIB for morbid obesity that had failed medical and/or psychiatric interventions.
Main Outcome Measures: Body mass index (BMI) (weight in kilograms divided by the square of the height in meters), diarrhea, electrolyte imbalance, acute and chronic liver disease, renal disease, JIB reversal, reason for JIB reversal, death, and cause of death.
Results: A total of 453 morbidly obese patients underwent JIB. By 2 years following JIB, the mean (±SD) BMI dropped from 49.3±8.1 to 31.1±0.8 and remained as this level until year 15, after which weight gradually increased (BMI, 35.4±3.1). The most severe early complication was acute liver failure, which occurred in 7% of patients and caused seven deaths. At 15 years, the actuarial probability of the most common serious late complications related to JIB were renal disease (37%), with two deaths; diarrhea (29%); and liver disease (10%), with three deaths. One hundred thirty-eight patients (31%) had a bypass reversal. The most common indications for reversal were diarrhea and electrolyte disturbance (29%), renal disease (19%), and liver disease (17%). Fifty-six patients died more than 30 days after JIB; 64% before JIB reversal, 13% at the time of reversal, and 23% subsequently.
Conclusions: Jejunoileal bypass is associated with progressive accrual of serious, sometimes life-threatening complications. Lifelong follow-up for early diagnosis and surgical reversal before life is threatened should reduce the morbidity and mortality associated with this procedure.

(1995;130:318-325) Jay A. Requarth, MD, et al. Reprint requests to Kenneth W. Burchard, MD, Section of General Surgery, Dartmouth-Hitchcock Medical Center, One Medical Center Drive, Lebanon, NH 03756-0001.