of pathogens is skin, proper preoperative skin antisepsis is crucial to minimize postoperative infections.

The main objective of this large, prospective randomized trial was to determine whether preoperative skin cleansing with chlorhexidine–alcohol is more protective against infection than treatment with povidone–iodine. All patients received systemic antibiotics preoperatively.

Patients (n = 849) undergoing clean-contaminated surgery in six hospitals were randomized to receive preoperative skin preparation with either chlorhexidine–alcohol scrub or povidone–iodine scrub and paint. The incidence and type of surgical-site infection occurring within 30 days after surgery were recorded. The relative risk of surgical site infection among patients who received chlorhexidine–alcohol scrub versus povidone–iodine was 0.59 (95% CI, 0.41–0.85).

<table>
<thead>
<tr>
<th>Chlorhexidine–Alcohol (n = 409)</th>
<th>Povidone–Iodine (n = 440)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean yr ± SD</td>
<td>53.3 ± 14.6</td>
<td>52.9 ± 14.2</td>
</tr>
<tr>
<td>Abdominal surgery, %</td>
<td>72.6</td>
<td>70.0</td>
</tr>
<tr>
<td>SSI, %</td>
<td>9.5</td>
<td>16.1</td>
</tr>
<tr>
<td>Superficial incision</td>
<td>4.2</td>
<td>8.6</td>
</tr>
<tr>
<td>Deep incision</td>
<td>1.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Sepsis from SSI</td>
<td>2.7</td>
<td>4.3</td>
</tr>
<tr>
<td>Organ space</td>
<td>4.4</td>
<td>4.5</td>
</tr>
<tr>
<td>SSF by surgery type, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal surgery</td>
<td>12.5</td>
<td>20.5</td>
</tr>
<tr>
<td>Nonabdominal surgery</td>
<td>1.8</td>
<td>6.1</td>
</tr>
</tbody>
</table>

SSI = surgical-site infection.

**Interpretation**

For clean-contaminated surgery, surgical-site infection was significantly reduced in patients who received chlorhexidine–alcohol compared with 10% povidone–iodine skin preparation. Improving skin antisepsis can decrease skin and deep surgical-site infections but not organ infections.


Postpartum hemorrhage (PPH) is a major contributor to maternal morbidity and mortality worldwide, and the risk of dying is 100 times higher in developing countries likely because of limited skilled personnel, uterotonic drug access, and other resources. Currently, oxytocin is the accepted standard of treatment for PPH; however, it is difficult to store and administer in resource-poor settings. Another uterotonic agent, misoprostol, is a low-cost and easy-to-use alternative.

These two double-blind, large, randomized, multicenter trials compared the effects of oxytocin and misoprostol in postpartum women who were or were not exposed to oxytocin during labor in Egypt, Turkey, and Vietnam. After diagnosis of PPH and randomization, patients received either 40 IU oxytocin intravenously or 800 µg misoprostol sublingually and placebo for the other treatment (i.e., saline placebo pills or intravenously administered saline). The primary outcomes were the proportion of women who stopped bleeding within 20 min of treatment and those with more than 300 ml blood loss after treatment. Active bleeding was controlled within 20 min in the majority of patients regardless of the treatment group (see table on next page).

**Critical Care Medicine**

Jean Mantz, M.D., Ph.D., Editor

Red blood cell transfusion is associated with infection and extracerebral complications after subarachnoid hemorrhage. *Neurosurgery* 2010; 66:312–8

It is unclear at what degree of anemia, red blood cell transfusion should be recommended for patients in intensive care units. An association between red blood cell transfusion and poor clinical outcome has been demonstrated in multiple clinical trials. This may also affect the outcomes of patients with subarachnoid hemorrhage.

This retrospective analysis from a prospective observational database at a level I trauma center examined the interaction between red blood cell transfusion and medical complications in patients with subarachnoid hemorrhage. Patients with grade I–V subarachnoid hemorrhage, at least one confirmed aneurysm, surgical occlusion of the ruptured aneurysm, and intensive care unit stay for more than 24 h, were included.
Patients who received transfusions were generally older, male, and had worse Hunt and Hess clinical grades at admission compared with patients who did not receive transfusions. The mean daily hemoglobin during the intensive care unit stay was 11.0 g/dl. The majority of patients (n/11005289) experienced a favorable outcome; however, 81 died and 51 patients were severally disabled or vegetative at the 6-month follow-up. Red blood cell transfusion was significantly associated with the development of extracerebral medical complications (46.0% vs. 29.8%; P/110210.001) even after controlling for age, clinical grade, hemoglobin, and symptomatic vasospasm (odds ratio [OR] 1.8). These extracerebral complications included major medical complications (OR 2.1), any infection (OR 2.8), pneumonia (OR 2.6), sepsis (OR 2.9), and the need for mechanical ventilation (OR 2.8).

**Interpretation**

Patients receiving red blood cell transfusions had more complications, including infections, such as pneumonia and sepsis. More work is needed to determine causation and to develop stricter guidelines for transfusion in patients with subarachnoid hemorrhage.


Symptomatic vasospasm is the leading cause of death and permanent disability after subarachnoid hemorrhage. Although the modalities to exclude ruptured aneurysm have been studied extensively, little is known yet about the best management to prevent or to treat vasospasm, which is the leading cause of death and permanent disability after subarachnoid hemorrhage.

This retrospective review assessed 580 patients with subarachnoid hemorrhage, in whom 95 (16%) developed symptomatic vasospasm resulting in a delayed ischemic deficit, and 51 had cerebral infarction. Once diagnosed, patients with symptomatic vasospasm were treated with hypertensive hypervolemic therapy. Clinical improvement was observed in 43% of 89 patients in whom volume expansion was used and 68% of 81 patients in whom pressors were used. Patients with no response to this treatment as clinically assessed 2 h after treatment were more likely to die or to have severe neurologic disability.

**Interpretation**

Although the modalities to treat ruptured aneurysm have been studied extensively, little is known yet about the best management to prevent or to treat vasospasm. Particular attention should be paid to the early detection of asymptomatic vasospasm (present in 30–70% of patients with subarachnoid hemorrhage), for which milrinone has proven efficacy. In addition to hypervolemic hypertensive therapy, the use of repeated neurologic examination, transcranial Doppler, and computed tomography angiography when required should be considered.
Poor sleep quality is associated with late noninvasive ventilation failure in patients with acute hypercapnic respiratory failure. Crit Care Med 2010; 38:477–85

After noninvasive ventilation (NIV) failure, tracheal intubation is required in up to 40% of patients admitted to the intensive care unit (ICU). Approximately 15–25% of patients experience late NIV failure, defined as death, intubation, or maintained NIV for 6 days. There is a need to identify the risk factors associated with late NIV failure to improve outcomes in this poor prognosis patient group.

To determine whether sleep disturbances that occur shortly after initiation of NIV in the ICU are associated with late NIV failure, a prospective study in elderly patients with hypercapnic respiratory failure was conducted. Hypercapnic patients in the ICU (n = 27) who required NIV for more than 48 h were monitored using a 17-h sleep polysomnography for 2 to 4 days after NIV initiation.

Of the 14 patients (52%) with late NIV failure, seven required NIV for 6 days, five died, and two required endotracheal intubation. Abnormal sleep was recorded in seven patients (50%) with late NIV failure compared with one patient (8%) in the NIV success group (P = 0.03). Elderly patients failing NIV had worse sleep quality with greater circadian sleep-cycle disruption and less nocturnal rapid eye movement sleep (6 min [0–12] vs. 26 min [6–49]; P = 0.03) compared with patients successfully treated with NIV. NIV failure was also associated with delirium during the ICU stay (64% vs. 0%).

**Interpretation**

Although recent work suggests that sleep deterioration has the potential to worsen ICU patient outcome, there are little supportive clinical data available. This study is one of the first to provide evidence for an association between sleep deterioration and an increased rate of late NIV failure in elderly, hypercapnic patients. Whether these considerations may be applicable to other specific ICU patient subpopulations remains to be determined.

Corticosteroid treatment and intensive insulin therapy for septic shock in adults: A randomized controlled trial. JAMA 2010; 303:341–8

Progression from infection to septic shock, a major complication of infectious diseases, occurs in part because of disruption of the hypothalamic-pituitary-adrenal axis. Although corticosteroid therapy may offer a survival benefit in these patients, it also induces potentially detrimental hyperglycemia.

This randomized, multicenter study examined blood glucose normalization with intensive versus conventional insulin treatment in patients with septic shock treated with cortico-steroid therapy in the intensive care unit (ICU). Patients with septic shock who presented with multiple organ dysfunction received continuous intravenous insulin infusion (intensive treatment) with hydrocortisone alone (n = 126), continuous intravenous insulin infusion (intensive treatment) with hydrocortisone plus fludrocortisones (n = 129), conventional insulin therapy with hydrocortisone alone (n = 138), or conventional insulin therapy with intravenous hydrocortisone plus fludrocortisones (n = 116).

Blood glucose levels were markedly lower in patients in the intensive insulin therapy group compared with the control group (P < 0.00001). Patients treated with intensive insulin experienced more episodes of severe hypoglycemia (< 40 mg/dl) than those in the conventional treatment group (P = 0.003). In-hospital death (P = 0.50 and P = 0.50) and overall survival (P = 0.78 and P = 0.61) were similar for intensive therapy versus conventional glucose control and hydrocortisone plus fludrocortisones versus hydrocortisone alone groups, respectively. Median length of stay in the ICU was also similar among groups (10 days in the experimental group vs. 9 days in the control group). Significantly, more patients in the fludrocortisone group experienced superinfection compared with the control group (P = 0.02).

**Interpretation**

This robust, multicenter, randomized controlled study confirms and extends previous concerns about intensive insulin therapy in ICU patients. Although the results provided here are negative, it can be accepted that patients with septic shock treated by hydrocortisone benefit neither from intensive insulin therapy nor from addition of fludrocortisone.


Several studies have demonstrated the benefits of daily interruption of sedation including reduced risk of posttraumatic stress disorder, pneumonia, hemorrhage, and other complications. However, continuous sedation remains a standard practice in most hospitals for critically ill patients requiring intubation and mechanical ventilation.

This single-center, prospective, randomized trial in Denmark was conducted to assess the interaction of sedation and the duration of mechanical ventilation. Patients received either intravenous analgesics alone or sedation (20 mg/ml propofol for 48 h, 1 mg/ml midazolam thereafter) with daily interruption until awake.

Patients receiving no sedation had significantly more ventilation-free days (n = 55; mean 13.8 days) than those receiving interrupted sedation (n = 58; mean 9.6 days; P = 0.0191). Length of stay was significantly shorter in the no-sedation group in the ICU (13.1 vs. 22.8 days; P = 0.0316) and the hospital (34 vs. 58 days; P = 0.0039) compared with the interrupted-sedation group. No difference was recorded.
in the mortality rates, occurrences of accidental extubations, the need for computed tomography or magnetic resonance imaging brain scans, or ventilator-associated pneumonia. The agitated delirium ($P = 0.0400$) and the use of haloperidol ($P = 0.01$) were more frequent in the no-sedation group.

**Interpretation**

Several studies and randomized trial results have changed clinical practice regarding mechanical ventilation and deep sedation in ICU patients. The current study suggests that no sedation is feasible in mechanically ventilated patients without adverse affects. However, the 1:1 patient:nurse ratio and an additional person to reassure the patient as needed in this study may influence results. Further studies are needed to determine whether these findings could be more broadly applied.

*Suggested by: Bernard de Jonghe, M.D.*

**Pain Medicine**

*Timothy J. Brennan, Ph.D., M.D., Editor*


Because awareness of chronic noncancer pain as an important patient problem is increasing, so is opioid prescribing. This is associated with an increased risk of overdose and opioid overdose fatalities. However, the proportion of risks attributed to patients receiving medically prescribed long-term opioid therapy and the effect of dose are unknown.

The Consortium to Study Opioid Risks and Trends study examined the medical records over an 8-yr period to estimate overall overdose rates among patients receiving long-term opioid therapy for noncancer pain from clinicians and to examine the effect of opioid dose on risk. Data from the Group Health Cooperative in Washington were collected from the records of adult patients who documented the initiation of long-term opioid prescribing for chronic noncancer pain.

The mean age of patients (n = 9,940) was 54 yr, mean follow-up was 42.1 person months, back pain (37.9%) and extremity pain (30.3%) were the most common pain diagnoses, and the mean dose of opioids was 13.3 mg/day of morphine equivalents. The most common opioids prescribed were hydrocodone (46.3%) and oxycodone (24.5%). There were 51 opioid-related overdoses and 6 deaths. Compared with patients receiving 1 to 20 mg/day of morphine equivalent opioids (0.2% annual overdose rate), patients receiving higher opioid doses had a 3.7- and 8.9-fold increase (50–99 mg/day and 100 mg/day or greater, respectively) in overdose risk compared with patients who received low-dose opioids (1–20 mg/day) and a 0.7 and 1.8% annual overdose rate, respectively. Overdose rates were also higher in patients older than 65 years and patients with a history of depression or treatment of substance abuse. An increased overdose risk was also associated with shorter time to filling an original or refill prescription.

**Interpretation**

Although the number of overdoses in this study cohort was small, the study reinforces carefully selecting and closely monitoring patients who are prescribed opioids for chronic noncancer pain. Protocols, such as demonstration of improved quality of life before increasing dose, should be evaluated to attempt to reduce these preventable deaths in patients prescribed high-dose opioids for long-term pain management.


The development and potential application of sensory-selective local anesthetics and long-acting local anesthetics could improve acute pain management and labor analgesia. Chemical permeation enhancers may allow for increased drug flux across cell membranes and hence increase the permeability of sensory selective drugs and the duration of nerve blockade.

This in vivo study tested the effect on thermal nociception of various concentrations of surfactants in combination with quaternary lidocaine derivatives such as QX-314 injected at the sciatic nerve of Sprague-Dawley rats. QX-314 demonstrated concentration-dependent durations of nerve blockade (approximately 1 day at 100 mM), and sensory selective nerve block occurred at some time points. The duration of sensory nerve block from 25 mM QX-314 was prolonged for up to 7 h in combination with a surfactant, 30 mM octyltrimethylammonium bromide (OTAB). Little or no motor block was observed. QX-314 in combination with varying concentrations of another surfactant, sodium octyl sulfate (SOS), produced prolongation of both sensory and motor blockade, but sensory selectivity was observed with 5 mM SOS. Sensory selectivity was imparted to varying degrees by cationic, neutral, and anionic surfactants and also was achieved with another quaternary lidocaine derivative, QX-222.

**Interpretation**

Local anesthetics used for producing prolonged nerve blockade have limitations and side effects including motor blockade. This study, using impermeant sodium channel blockers such as QX-314, suggests that adjuncts to local anesthetic mixtures, such as surfactants, may improve the sensory blockade profile of these drugs and permit better motor function during labor and after surgery.


It is common for seriously injured trauma survivors to experience posttraumatic stress disorder (PTSD). Recent research...