Impact of preoperative anxiolytic on surgical site infection in patients undergoing abdominal hysterectomy

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Background: An increased anxiety may be associated with a higher risk of surgical site infection (SSI), but there is little objective data on the effect of preoperative anxiolytic interventions on SSI. To address this issue, we evaluated the effects of preoperative diazepam on postoperative SSI following abdominal hysterectomy.
Methods: This randomized, double-blinded, placebo-controlled study included 130 patients, American Society of Anesthesiologist physical status 1 or 2. Patients were randomly assigned to receive either oral diazepam 10 mg (n = 65) or placebo (n =65) the night before and 1 hour prior to surgery. The assessment instruments were the Visual Analogue Scale and the State-Trait Anxiety Inventory. SSI was diagnosed according to the criteria of the Centers for Disease Control and Prevention with standard follow-up of 30 days.
Results: The relative risk (RR) was 1.79 (95% confidence interval [CI]: 1.31-2.43), and the number of patients that needed to be treated was 5.2 (95% CI: 2.74-50.76) to prevent 1 additional SSI. The RR for SSI in placebo-treated patients with high postoperative anxiety was 1.65 (95% CI: 1.07-2.56).
Conclusion: Diazepam-treated patients showed lower postoperative anxiety and lower incidence of SSI up to 30 days after surgery compared with placebo in patients undergoing abdominal hysterectomy. (Am J Infect Control 2008;36:718-26.)

Wound infections are among the most common serious complications of anesthesia and surgery.[1] Surgical wound infections can prolong hospitalization[2] and substantially increase the cost of care.[1,3] The first few hours after tissue is contaminated by bacteria constitute a critical period during which wound infection is established,[4] but infections are typically not detected until some days after surgery. The factors that influence the incidence of surgical wound infection include site and complexity of surgery,[3] patient's underlying illness, smoking, obesity,[5,6] blood transfusion, hyperglycemia,[7] presence or absence of hypovolemia,[8] patient's temperature during surgery,[2] use or not of prophylactic antibiotics,[9] and degree to which pain and anxiety are controlled.[10]

Studies published in the health-psychology literature suggest that increased preoperative anxiety is associated with poor postoperative behavioral and clinical recovery.[11,12] Furthermore, numerous reports indicate that preoperative psychologic interventions aimed at reducing preoperative anxiety may also result in improved postoperative behavioral and clinical recovery.[12-14] Additionally, several reports indicate that increased perioperative anxiety and uncontrolled postoperative pain may increase the perioperative neuroendocrine stress response.[14,15] Thus, a possible hypothesis is that factors such as anxiety and pain can stimulate sympathetic vasoconstriction[16,17] and thereby increase the risk of postoperative infection.[18] Accordingly, one can hypothesize that the use of preoperative benzodiazepine can reduce postoperative anxiety and enhance the postoperative clinical recovery process involved in warding off infection. To test this hypothesis, we conducted a randomized, double-blind, placebo-controlled trial to evaluate the effect of preoperative diazepam on the postoperative incidence of surgical site infection (SSI) during the first 30 days following abdominal hysterectomy.

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MATERIALS AND METHODS

Study population

Following ethics committee approval and written informed consent, 130 patients, American Society of Anesthesiologist classification 1 or 2, aged 19 to 60 years,

scheduled to undergo total abdominal hysterectomy, were enrolled in the randomized, double-blind, placebo-controlled study. The patients were undergoing elective abdominal hysterectomy for myomatosis in the Gynecology Service, and all operations were performed by a third-year resident supervised by one of the attending gynecologists. All patients were admitted to the hospital 1 day before surgery, and those patients who did not develop complications were discharged on day 3 postsurgery, on any day of the week. Patients with contraindications to regional anesthesia; mental impairment; chronic pain; or a history of congestive heart failure, valvular heart disease, renal or hepatic disease, psychotropic drug use, and language or communication difficulties were excluded. In addition, patients with a body mass index (BMI) higher than 35 kg/m^2 and those with a history of psychiatric disorder and/or positive screening for minor psychiatric disorders (scores, $\geq$8) on the World Health Organization's (WHO) Self-Reporting Questionnaire (SRQ-20) were excluded.[19] The SRQ-20 measures somatic symptoms, depressive mood, depressive thoughts, and decreased energy.

Randomization and interventions

The treatment allocation method used was advanced simple randomization without blocking or stratification. Before the recruitment phase of the study, 160 envelopes containing all protocol materials were prepared and numbered sequentially. A random number was used to assign each consecutively numbered envelope to receive either 10 mg oral diazepam or placebo the night before (10 PM) and 1 hour prior to surgery, and the envelopes were grouped so that each had an independent 50% probability of being included in either group. A sheet indicating the allocated treatment was then placed in the envelope, and the envelopes were sealed. Throughout the course of the study, the sealed envelopes were removed and opened sequentially by a pharmacy technician, who delivered the tablets of diazepam 10 mg or placebo only after prospective patients had been screened and had consented to participation. No other preoperative medication was given. During the entire protocol time line, blinding and randomization were undertaken by 2 investigators who were not involved in the patient's evaluation. Other individuals involved in the patient's care were unaware of the treatment group to which the patient belonged.

Outcome measures

Our major outcome (SSI) was either of 2 distinct criteria for diagnosis. The first criterion, as in previous studies,[2,20] was that wounds were considered likely to be infected when pus could be expressed from the incision or aspirated from a loculated mass within the wound. The second criterion was based on the Centers for Disease Control and Prevention (CDC)'s National Nosocomial Infections Surveillance (NNIS) system, modified in 1999,[5] in which SSI is classified as being either incisional (superficial or deep) or organ space with a diagnostic period up to 30 days. At all times, the gynecologist examiner was blinded to the aim of the study, preoperative interventions, and all other measures.

Instruments and assessment

The data were collected in the following multiple standardized phases: (1) during the period of preoperative evaluation, a structured questionnaire was used to collect information concerning demographic characteristics, clinical state, and anxiety level; (2) the surgical procedures were assessed using the anesthesiologist's records; (3) during the patients' stay at the hospital, the gynecologists examined the surgical wound daily for the presence of SSI; (4) after discharge, all patients were examined 2 times, at 1 and 4 weeks of follow-up, carried out by a gynecologist in the same hospital, in the outpatient service. Data regarding drug records, medical and diagnostic examinations, reinterventions, other medical procedures, and hospital readmission for treatment of surgical complications were all collected from the patient's records. Two independent, trained data collectors followed a standard method by which they reviewed all clinical and laboratory information available in the hospital. Urinary and respiratory infections were defined by clinical and laboratory criteria. The gynecologist in charge of discharge was blinded to the aim of the study and all other measures. The length of hospital stay was defined as the number of days spent in the hospital.

Assessment of pain and psychologic state

The day prior to surgery, the same anesthesiologist, who provided patients with information on the perioperative course and instructed them regarding the use of the patient-controlled analgesia pump, saw all patients. Moreover, each patient underwent psychologic testing and pain evaluation.

The pain was measured by a 100-mm Visual Analog Scale (VAS), by which scores ranged from no pain (zero) to worst possible pain (100 mm).[21] Incisional pain at rest was defined as the average of pain ratings obtained at 6 and 24 hours following surgery. A 30-mm cut-off point was used to classify the patients into 2 groups: (1) absence of pain or mild pain (scores equal to or less than 30 mm); and (2) moderate, intense, or worst possible pain (scores greater than 30 mm).[21] Incisional pain on coughing, deep breathing, or movement assessed using yes or no type questions and the patient's