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Should clopidogrel be discontinued before laparoscopic cholecystectomy?

Katherine Anderson, M.D., Daniel C. Jupiter, Ph.D., Stephen W. Abernathy, M.D., Richard C. Frazee, M.D.*

Baylor Scott & White Health, 2401 South 31st Street, Temple, TX 76508, USA

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Abstract

BACKGROUND: The perioperative management of clopidogrel remains an area of controversy.

METHODS: An institutional review board-approved retrospective review of patients undergoing a laparoscopic cholecystectomy while on clopidogrel from 2008 to 2012 was performed. These patients were then matched with a nonclopidogrel cohort based on American Society of Anesthesiologists score and emergent or elective surgery. Intraoperative estimated blood loss, operative time, length of stay, and 30-day morbidity were compared.

RESULTS: Thirty-six clopidogrel and 36 control patient records were analyzed. There were no significant differences in age, body mass index, sex, or incidence of coronary artery disease, diabetes, hyperlipidemia, and congestive heart failure. Estimated blood loss averaged 50 mL in the clopidogrel group and 47 mL in the control group (P = nonsignificant). There were no significant differences in operative time, 30-day morbidity, or length of stay between the 2 groups.

CONCLUSIONS: Laparoscopic cholecystectomy performed on patients maintained on clopidogrel during the perioperative period did not produce an increase in blood loss, operative time, 30-day morbidity, or length of stay.

As the mean age of the general population has risen, the number of patients treated with preventative anticoagulation has significantly increased. Clopidogrel is a common antiplatelet drug utilized for cardiovascular, peripheral vascular, and cerebrovascular event prevention. It belongs to a class of thienopyridines that inhibit adenosine diphosphate-induced platelet aggregation by blocking the platelet receptor.[1] The effect on platelet function cannot be medically reversed, and 5 to 7 days of cessation are needed for platelet function to normalize.[2] Clopidogrel cessation, however, is associated with an increased risk of cardiovascular thrombotic events.[3–5] Premature discontinuation of antiplatelet therapy is a strong predictor of stent thrombosis after a percutaneous coronary intervention.[6] Furthermore, even in patients without stents, cessation of clopidogrel is associated with adverse thrombotic events.[7]

Surgeons face a dilemma when patients on anticoagulation medications need an invasive procedure. The risk of a thromboembolic event if an antiplatelet medication is discontinued must be weighed against the risk of bleeding if the drug is continued perioperatively. Although several studies have analyzed this issue in cardiac surgery,[8–13] little has been published regarding perioperative clopidogrel for abdominal surgery. There is a lack of evidence comparing the clinical risks and benefits of temporary interruption of antiplatelet therapy. Current recommendations for general

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* Corresponding author. Tel.: +1-254-724-2593; fax: +1-254-724-8587.
E-mail address: RFRAZEE@sw.org

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surgeons include performing a risk assessment for patients on antiplatelet drugs needing a noncardiac procedure. For patients who are not at high risk for cardiac events, current guidelines recommend cessation of clopidogrel 7 days before the operation.[14] Other studies recommend deferring surgery until clopidogrel is no longer mandatory.[15] Our study examines the question of continued perioperative use of clopidogrel specific to laparoscopic cholecystectomy, and whether this common abdominal operation can be performed safely without clopidogrel cessation.

Methods

An institutional review board-approved retrospective chart review of adult patients at our institution who underwent a laparoscopic cholecystectomy while on clopidogrel from 2008 to 2012 was performed. The medical record numbers for all patients who underwent a laparoscopic cholecystectomy from 2008 to 2012 were obtained. A total of 36 patients who underwent laparoscopic cholecystectomy while on clopidogrel were analyzed. These patients were matched with a separate cohort (control group) based on the American Society of Anesthesiologists (ASA) score and indication for surgery. Specifically, the 36 clopidogrel patients were cross-tabulated by emergent or elective surgery and ASA 2, 3, or 4. For each stratum of this table, the same number of patients who had cholecystectomy without clopidogrel were randomly selected and included for analysis.

Patient demographics, body mass index (BMI), ASA score, preoperative presentation, and preoperative comorbidities were assessed. Patient's preoperative indication for surgery was reviewed and classified as acute cholecystitis, chronic cholecystitis, or gallstone pancreatitis. Comorbidities evaluated included presence of diabetes mellitus, coronary artery disease, obesity, congestive heart failure, chronic obstructive pulmonary disease, and hyperlipidemia. These comorbidities were used to determine if the 2 groups were comparable.

Details from the operation were obtained from the operative report and anesthesia records and included estimated blood loss (EBL) and length of surgery. Charts were reviewed for postoperative morbidities up to 30 days postop. Primary outcomes for comparison were intraoperative EBL and operative time. Secondary outcomes included hospital length of stay and 30-day morbidity.

Demographic factors were compared between the clopidogrel and control groups using *t* test or chi-square/Fisher's exact test for continuous and discrete variables, respectively. Fisher's exact test was used when the number in any cell was less than 5. Similar analyses were carried out for our primary and secondary outcomes.

A secondary analysis was performed on EBL and operative time to test for equivalence. A *t* test determined whether those with clopidogrel were noninferior in terms of EBL and operative time. A difference in 25 mL of blood loss or 30 minutes of operative time was considered a clinically significant difference.

Results

Seventy-two patients (36 clopidogrel group and 36 control group) having laparoscopic cholecystectomy were analyzed (Table 1). The average age was 67.76 years (±12.85, range 33 to 89 years) and 58% (42) of the patients were male. The average BMI was 29.69 (±6.77, range 16 to 48) and 55% (40) of the operations were performed in an acute setting. The indications for surgery were acute cholecystitis in 32 patients (44%), chronic cholecystitis in 32 patients (44%), and gallstone pancreatitis in 8 patients (11%).

There were no significant differences between the 2 groups in terms of age, BMI, sex, or incidence of coronary artery disease, diabetes, hyperlipidemia, and congestive heart failure (Table 1).

EBL was an average of 49.44 mL (range 5 to 300 ml) in the clopidogrel group and 47 mL (range 2 to 300 ml) in the control group ($P = .85$). Operative time was 79.11 versus 63.73 minutes in the clopidogrel and control patients, respectively ($P = .50$). One patient in the clopidogrel group was converted from laparoscopy to open incision and all patients in the control group remained laparoscopic. There were no significant differences in 30-day morbidity (22.22% vs 41.67%, $P = .08$). As shown in Table 2, 8 of the 36 patients receiving clopidogrel had postoperative morbidity. This included acute respiratory failure in 4 patients (50%), infectious related in 3 patients (38%), and exacerbation of heart failure in 1 patient (13%). In the control group, 15 patients had 30-day morbidity. Of these, 6 patients were associated with respiratory failure (40%), 4 (27%) infectious, 4 (27%) related to a cardiac event, and 1 patient (6%) had acute blood loss anemia requiring a transfusion. There was no significant difference in length of stay ($P = .26$). The average stay was 2.86 days in the clopidogrel group (range 0 to 29 days) and 1.75 days (range 0 to 9 days) in the control group.

To further analyze our 2 primary outcomes, EBL and operative time underwent a secondary analysis of equivalence. This showed that the EBL in those with clopidogrel did not exceed 25 mL more than those without clopidogrel ($P = .047$). The operative time of those on clopidogrel did not exceed 30 minutes more than in those without clopidogrel ($P = .005$).

Comments

The incidence of coronary artery disease is estimated to be 50% in Western countries. The rapid increase in obesity has further accelerated the complications of vascular disease.[16] Multiple medical strategies have been developed to address the problem of vascular disease. These include diet modification, cholesterol lowering drugs, and