Preoperative Dexamethasone Enhances Quality of Recovery after Laparoscopic Cholecystectomy

Effect on In-hospital and Postdischarge Recovery Outcomes

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ABSTRACT

Background: The effect of dexamethasone on quality of recovery after discharge from the hospital after laparoscopic surgery has not been examined rigorously in previous investigations. We hypothesized that preoperative dexamethasone would enhance patient-perceived quality of recovery on postoperative day 1 in subjects undergoing laparoscopic cholecystectomy.

Methods: One hundred twenty patients undergoing outpatient laparoscopic cholecystectomy were randomized to receive either dexamethasone (8 mg) or placebo-saline. A 40-item quality-of-recovery scoring system (QoR-40) was administered preoperatively and on postoperative day 1 to all subjects. Nausea, vomiting, fatigue, and pain scores were recorded at the time of discharge from the postanesthesia care unit and ambulatory surgical unit. Hospital length of stay was also assessed.

Results: Global QoR-40 scores on postoperative day 1 were higher in the dexamethasone group (median [range], 178 [130–195]) compared with the control group (161 [113–194]) (median difference [99% CI], −18 [−26 to −8]; $P < 0.0001$). Postoperative QoR-40 scores in the dimensions of emotional state, physical comfort, and pain were all improved in the dexamethasone group compared with the control group ($P < 0.001$). Nausea, fatigue, and pain scores were all reduced in the dexamethasone group during the hospitalization, as were postoperative analgesic requirements ($P < 0.05$). Total hospital length of stay was also reduced in subjects administered steroids ($P = 0.003$).

Conclusions: Among patients undergoing outpatient laparoscopic cholecystectomy surgery, the use of preoperative dexamethasone enhanced postdischarge quality of recovery and reduced nausea, pain, and fatigue in the early postoperative period.

What We Already Know about This Topic

- Perioperative steroids may reduce pain and nausea after ambulatory surgery, but whether this influences patient-centered outcomes for recovery on the following day is unknown

What This Article Tells Us That Is New

- In 120 patients undergoing outpatient laparoscopic cholecystectomy, 8 mg dexamethasone improved emotional state, physical state, and pain dimensions on the day following surgery of a validated quality of recovery scale

LAPAROSCOPIC cholecystectomy (LC) is one of the most common elective surgical procedures performed in the Western world.[1] Due to advances in anesthetic and surgical management, up to 84% of elective LC patients can be discharged on the day of surgery.[2] However, a variety of metabolic, hormonal, inflammatory, and immune responses are still activated during minimally invasive procedures, which may impair clinical recovery. Methods to attenuate these adverse physiologic responses to surgery may improve outcomes and reduce postanesthesia care unit (PACU) and ambulatory surgical unit (ASU-Phase II) recovery as well as hospital length of stay.

Dexamethasone is among the most potent corticosteroids available, with a biologic half-life of 36–72 h.[3] Dexamethasone is effective, alone or in combination with other antiemetic agents, in reducing nausea and vomiting after laparoscopic procedures.[4] Furthermore, small doses of steroids have been demonstrated to attenuate postoperative pain, improve mood, decrease fatigue, and increase appetite in a va-

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riety of medical and surgical patients.[5–9] The administration of a long-acting steroid like dexamethasone to LC patients may therefore reduce complications and improve the quality of recovery during the first 24 h after surgery.[5,10,11]

The use of patient-based outcome measures has become increasingly important in medical research. Recent advances in anesthetic management and minimally invasive surgical procedures have resulted in reductions in morbidity, enhanced recovery, and an earlier resumption of daily activities.[1] Therefore, the application of instruments that evaluate quality of recovery outcome measures are of importance in assessing the effect of anesthetic interventions in the ambulatory setting. We hypothesized that small-dose dexamethasone (8 mg) treatment would beneficially affect patient-perceived quality of recovery on postoperative day (POD) 1. This primary endpoint was assessed using a 40-item quality-of-recovery scoring system (QoR-40). In addition, the effect of dexamethasone on several early clinical recovery variables during hospitalization (*e.g.*, nausea, vomiting, pain, fatigue) was determined.

Materials and Methods

Study Population

This randomized, double-blind, placebo-controlled investigation was approved by the NorthShore University HealthSystem Institutional Review Board (Evanston, IL), and written informed consent was obtained from all subjects. One hundred twenty patients undergoing elective LC surgery from February 2007 to April 2009 with an anticipated same-day discharge were enrolled. Exclusion criteria included: use of steroids or antiemetic agents within 1 month of surgery, chronic pain requiring opioid treatment, history of allergy to any study medications, severe renal (*i.e.*, serum creatinine more than 1.6 mg/dl) or liver (*i.e.*, liver enzymes more than two times normal values) disease, pregnancy, poor English comprehension, or psychiatric/central nervous system disturbance that would preclude completion of the QoR-40 questionnaire. Patients were excluded after enrollment if the surgical procedure was changed from a laparoscopic to an open approach. Patients were randomized to receive either dexamethasone (dexamethasone group) or placebo-saline (control group) using a computer-generated randomization code. The randomization code for the 120 subjects was provided to the operating room pharmacy before the start of the study; all care providers, researchers, and patients were blinded to group assignments. Study medications were prepared by the operating room pharmacy in 3-ml syringes labeled with the patient's name. Either dexamethasone (8 mg to 2 ml total volume) or saline (2 ml total volume) was drawn into each syringe. Approximately 60 min before the anticipated time of surgical incision, dexamethasone or placebo was administered in 60–90 s to avoid unpleasant symptoms that may occur following rapid dexamethasone injection.

Anesthetic and Surgical Management

All patients received 2 mg of midazolam before transport to the operating room. On arrival to the operating room, standard monitors were applied. Anesthesia was induced with 2.0–2.5 mg/kg propofol, 0.6 mg/kg rocuronium (or 1.0–1.5 mg/kg succinylcholine, if rapid sequence induction was required), and 100 μg fentanyl. Maintenance of anesthesia consisted of 1.5–2.5% sevoflurane, which was titrated to a bispectral index (BIS® system;, Aspect Medical Systems, Newton, MA) of 40–60 and a mean arterial blood pressure value within 20% of baseline measures. Additional fentanyl ($1\ \mu g \cdot kg^{-1} \cdot h^{-1}$) was administered intraoperatively. Ventilation was controlled mechanically to maintain an end-tidal carbon dioxide concentration of 30–34 mmHg using a 50% oxygen-air gas mixture. After tracheal intubation, an orogastric tube was placed to promote emptying the stomach of gastric contents (and removed immediately before tracheal extubation). Additional rocuronium, 5–10 mg, was administered, if needed, to maintain a train-of-four count of 2–3 intraoperatively. Lactated Ringer's solution was used for fluid replacement therapy at a rate of approximately $10\ ml \cdot kg^{-1} \cdot h^{-1}$. Forced-air warming devices (Bair Hugger®; Augustine Medical, Minneapolis, MN) were used to maintain core temperatures above 36.0°C. Neuromuscular blockade was reversed with 50 μg/kg neostigmine and glycopyrrolate before tracheal extubation. All patients received 4 mg ondansetron 30 min before the end of the procedure.

Patients were positioned in the reverse Trendelenburg position. The trocar incision sites were infiltrated with 10 ml of 0.25% bupivacaine. The abdomen was insufflated with carbon dioxide to maintain intraabdominal pressures of approximately 15 mmHg and carefully evacuated at the end of surgery. Laparoscopic cholecystectomy was achieved using four punctures of the abdomen. All surgical procedures were performed by one of three general surgeons experienced (more than 200 procedures) in laparoscopic surgery (equally distributed between the two study groups).

Data Collection

The baseline QoR-40 questionnaire was provided to subjects after informed consent was obtained in the preoperative ASU holding area. Five general quality-of-life dimensions are measured within the QoR-40: physical comfort (12 items), emotional state (9 items), physical independence (5 items), psychologic support (7 items), and pain (7 items). Each item is graded on a five-point Likert scale, and global scores range from 40 (extremely poor quality of recovery) to 200 (excellent quality of recovery). The QoR-40 has been used and validated for patients undergoing general and ambulatory surgical procedures.[12] The QoR-40 scoring system was explained in detail to all subjects, completed in the presence of a research assistant, and reviewed to ensure accurate comprehension of all questions. Study participants were informed that they would be provided with another QoR-40 form to be completed after discharge from the hospital and in-

structed to answer the questionnaire 24 h after leaving the ASU. For patients admitted to the hospital after surgery, the QoR-40 survey was to be completed 28 h after discharge from the PACU (4 h were added to the completion time to account for an average ASU admission after LC). Another brief survey form was to be completed at the same time to determine the presence or absence of adverse symptoms potentially related to steroid administration (*e.g.*, sleeplessness, headache, stomach pain, extremity swelling, intravenous site irritation, increased appetite, blurry vision, or negative mood changes). At the time of discharge from the ASU, ambulatory patients were provided with a QoR-40 questionnaire, the steroid-related symptom form, and a self-addressed, stamped envelope. On the morning of POD1, all subjects were contacted by telephone and reminded to complete the surveys and return all forms to the investigators. Patients admitted to the hospital from the PACU were provided with the surveys directly by a member of the research team on POD1. Forms were to be completed at home if these patients were discharged in the morning.

In the preoperative ASU holding area, the presence or absence of nausea or vomiting within the previous 12 h was determined. The level of fatigue in the preoperative holding area was measured using a 4-point ordinal scale (0 = none, 1 = mild fatigue, 2 = moderate fatigue, 3 = severe fatigue). Pain intensity was measured (at rest and with movement, supine to sitting) using a 100-mm visual analog scale (VAS). At the time of discharge from the PACU, subjects were again questioned by a blinded research assistant about the presence or absence of nausea and vomiting during the admission. These findings were confirmed with the PACU nursing staff (*i.e.*, episodes of nausea and vomiting were recorded on a postoperative data collection form). Pain and fatigue scores were also quantified at this time as previously noted. Nausea, vomiting, pain, and fatigue evaluations were again performed by the research assistant at the time of discharge from the postoperative ASU. These VAS pain assessments (preoperatively, at discharge from the PACU, at discharge from the postoperative ASU) were used for data analysis.

After PACU admission, patients were assessed for the presence of nausea or vomiting every 15 min by PACU nurses. The need for rescue antiemetics (4 mg ondansetron) was determined. On arrival to the PACU, patients were asked to quantify pain on an 11-point verbal rating scale (VRS, 0 = no pain, 10 = worst pain imaginable) by PACU nurses to determine the need for analgesic agents. Hydromorphone (0.25 mg, mild pain; 0.5 mg, moderate to severe pain) was used for postoperative analgesia and titrated to achieve pain scores of lower than 2 on the 11-point VRS. Total doses of hydromorphone required to provide acceptable analgesia during the admission were noted. PACU nurses also evaluated patients every 15 min using an Aldrete scoring system; the times required to meet discharge criteria (score $\geq$ 8 of 10 points) and to achieve actual discharge were recorded.

During ASU admission, episodes of nausea and vomiting and the need for rescue antiemetics were recorded. ASU nurses evaluated subjects for pain using the 11-point VRS every 30 min. Patients with a VRS score of 4 or greater were treated with one or two oral pain medication tablets (5 mg hydrocodone, 500 mg acetaminophen). The times from ASU admission until first oral intake and first unassisted ambulation were determined. Fitness for discharge from the ASU to home (*i.e.*, awake and alert, minimal nausea and pain, stable vital signs with standing, ambulate without assistance, tolerate oral intake) was measured every 30 min. The times required to meet discharge criteria and to achieve actual discharge were noted. Pain scores, as assessed *via* VRS by PACU and ASU nurses, were used to guide analgesic administration; this information was not part of data analysis. Patient management in the PACU in ASU reflected standard clinical practices.

Statistical Analysis

The primary endpoint of the study was the QoR-40 score on POD1. Mean QoR-40 scores of 167 ± 23 out of 200 possible points were reported in a previous investigation of general surgical patients on POD1.[12] Two groups with sample sizes of 30 subjects each achieve 80% power to detect a difference of 17 between the null hypothesis that both group means are 167 and the alternative hypothesis that the mean of group 2 is 184 with known group standard deviations of 23 and with a significance level (α) of 0.05 using a two-sided two-sample *t* test. Low return rates may occur with questionnaires to be completed after hospital discharge; therefore, a total of 120 patients were enrolled in the present investigation to ensure an acceptable survey response rate .

Categorical data were compared using Fisher exact test (NCSS, Kaysville, UT). The 95% CIs for the differences in percentages were calculated using the Farrington and Manning score. Ordinal data and continuous data that were not normally distributed are presented as median and range. These data were compared between groups using the Wilcoxon rank sum test and within groups using the Wilcoxon signed rank test (StatsDirect, Cheshire, United Kingdom). The median differences and their 99% CIs were calculated for the comparisons involving the primary outcome variables while the 95% CIs of all other median differences were calculated. Normally distributed continuous data are presented as mean ± SD. These data were compared using the unpaired *t* test (NCSS). Mean differences and their 95% CIs were calculated.

To help minimize the chance of a type I error, the criterion for rejection of the null hypothesis was a two-tailed $P < 0.01$ for comparisons involving the primary outcome variable. A value of $P < 0.05$ was used for all other comparisons.

Results

A total of 120 patients were enrolled in this clinical trial. The laparoscopic procedure was converted to an open procedure

Table 1. Patient Characteristics (n = 120)

	Control Group	Dexamethasone Group	Difference (95% CI)	*P* Value
Number	59	56		
Sex, men:women	20 (33.9%):39 (66.1%)	19 (33.9%):37 (66.1%)	0% (−17.2% to 17.1%)	1.000
Age, yr	49.2 ± 16.5	−51.4 ± 15.7	−2.2 (−8.2 to 3.7)	0.464
Weight, kg	82.5 ± 23.9	79.0 ± 17.5	3.5 (−4.3 to 11.2)	0.379
Height, cm	167.4 ± 9.0	166.2 ± 10.4	1.2 (−2.4 to 4.8)	0.501
ASA physical status	2 (1–3)	2 (1–3)	0 (0 to 0)	0.331
Smoking history	9 (15.3%)	10 (17.9%)	−2.6% (−16.7% to 11.3%)	0.804
Drinking history	1 (1.7%)	5 (8.9%)	−7.2% (−17.8% to 1.2%)	0.108
Hypertension	14 (23.7%)	24 (42.9%)	−19.1% (−35.5% to −1.9%)	0.047
Asthma	2 (3.4%)	5 (8.9%)	−5.5% (−16.4% to 3.9%)	0.264
Sleep apnea	8 (13.6%)	4 (7.1%)	6.4% (−5.3% to 18.5%)	0.363
Thyroid disease	6 (10.2%)	6 (10.7%)	−0.5% (−12.8% to 11.4%)	1.000

Data are No. (%) of patients, mean ± SD, or median (range) unless otherwise indicated. Patient characteristics with an incidence of > 8% are described. There were no differences in the incidence of myocardial infarction, congestive heart failure, atrial fibrillation, chronic obstructive pulmonary disease, liver disease, noninsulin-dependent diabetes, cerebral vascular disease, or peripheral vascular disease between groups.

ASA = American Society of Anesthesiologists; CI = confidence interval; Drinking history = more than three alcoholic beverages per day.

in 5 patients; these subjects (3, dexamethasone; 2, control) were excluded from further analysis. Preoperative characteristics, intraoperative parameters, and recovery variables during the hospitalization were collected for 56 patients in the dexamethasone group and 59 patients in the control group. There were no significant differences between groups in age, weight, height, sex, preexisting medical conditions (with the exception of a higher incidence of hypertension in the dexamethasone group), or American Society of Anesthesiologists physical status (table 1). The presence or absence of symptoms of nausea, vomiting, fatigue, or pain in the immediate preoperative period did not differ between groups (table 2). Intraoperative management data are presented in table 3. There were no differences between groups in any intraoperative variables.

Global and dimensional QoR-40 scores are presented in table 4. Surveys were completed on POD1 by 91 of the 115 study subjects (79.1%), with no significant differences in completion rates between the dexamethasone and control groups. Baseline preoperative global and dimensional (emotional state, physical comfort, psychologic support, physical independence, and pain) QoR-40 scores did not differ between the study groups. However, on POD1, global QoR-40 scores were significantly lower (*i.e.*, poorer quality of recovery) in the control group (global QoR-40 score, 161) than the dexamethasone group (178, $P < 0.0001$). QoR-40 scores in the dimensions of emotional state (35 *vs.* 41, $P < 0.0001$), physical comfort (45 *vs.* 51, $P < 0.001$), and pain (26 *vs.* 31, $P < 0.0001$) were all significantly lower in the control group compared with the dexamethasone group on POD1. No differences in scores were noted between the two groups in the dimensions of psychologic support and physical independence.

Recovery parameters in the PACU are described in table 5. The incidence of nausea was reduced in the dexamethasone group (12.5% *vs.* 37.3% control group, $P = 0.003$). The frequency of vomiting events was low in both groups and not significantly different. Fewer patients in the dexamethasone group required treatment for nausea or vomiting. Severity of postoperative pain at rest and with movement was reduced in the dexamethasone group at the time of discharge from the PACU; median VAS pain scores were lower in the dexamethasone group at this time (median difference between groups 10 mm, $P < 0.05$). In addition, the percentage of patients requiring treatment for pain was lower in the dexamethasone group (71.4% *vs.* 96.6% control group, $P < 0.001$) as was the median total dose of hydromorphone needed to achieve acceptable postoperative analgesia ($P < 0.001$). There were no differences between groups in the amount of time required to meet and achieve PACU discharge criteria.

Recovery characteristics in the ASU are presented in table 6. There were no significant differences between the dexa-

Table 2. Preoperative Parameters (n = 120)

	Control Group	Dexamethasone Group	Difference (95% CI)	*P* Value
Nausea, Y:N	10 (17.0%):49 (83.0%)	10 (17.9%):46 (82.1%)	−0.9% (−15.3% to 13.2%)	1.000
Vomiting, Y:N	2 (3.4%):57 (96.6%)	1 (1.8%):55 (98.2%)	1.6% (−6.4% to 10.0%)	1.000
Level of fatigue	1 (0–3)	0.5 (0–3)	0 (0 to 0)	0.650
VAS Pain				
At rest	0 (0–50)	0 (0–80)	0 (0 to 0)	0.425
With movement	0 (0–55)	0 (0–80)	0 (0 to 0)	0.635

Data are No. (%) of patients or median (range) unless otherwise indicated.

CI = confidence interval; VAS = visual analog scale (100-mm scale).

Table 3. Perioperative Parameters

	Control Group	Dexamethasone Group	Difference (95% CI)	*P* Value
Anesthesia time, min	96.8 ± 30.3	89.5 ± 25.3	7.2 (−3.1 to 17.6)	0.168
Fentanyl dose, μg	180 ± 64	176 ± 55	4 (−18 to 26)	0.726
Rocuronium dose, mg	47.8 ± 18.1	44.6 ± 11.5	3.2 (−2.4 to 8.9)	0.257
Crystalloid, ml	1,136 ± 404	1,146 ± 388	−11 (−157 to 136)	0.884
Estimated blood loss, ml	25 (10–200)	25 (25–600)	0 (0 to 0)	0.253
Final OR temperature, °C	36.14 ± 0.58	36.16 ± 0.43	−0.03 (−0.22 to 0.16)	0.763

Data are mean ± SD or median (range) unless otherwise indicated.
CI = confidence interval; OR = operating room.

methasone and control groups in the percentage of patients requiring inpatient admission. The incidence (21.7% *vs.* 56.8%) of nausea was less in the dexamethasone group than in the control group, and the need for treatment of nausea/vomiting symptoms was reduced in subjects administered steroids (all $P < 0.005$). As observed in the PACU, the frequency of vomiting episodes did not differ between groups. Degree of fatigue was significantly lower (improved) in the dexamethasone group compared with the control group ($P = 0.005$). Although VAS pain scores and analgesic requirements were lower in the dexamethasone group, these differences were not significantly different in the ASU. Times needed to meet discharge criteria (median difference, 40 min, $P = 0.024$) and achieve actual discharge (median difference, 55 min, $P = 0.009$) were less among patients receiving dexamethasone. Total hospital length of stay was less in the dexamethasone group (median difference, 70 min, $P = 0.003$).

The survey of adverse events potentially attributable to the use of steroids was completed by all patients who returned the QoR-40 forms (table 7). There were no differences between the two groups in the incidence of reported adverse events, with the exception of increased appetite in the dexamethasone group. No patients required readmission for complications related to surgery, such as wound infection.

Discussion

As the safety of anesthesia delivery and surgical techniques has improved, assessment of quality of recovery has become an important primary endpoint in outcomes research. In the present investigation, we observed that the preoperative administration of 8 mg dexamethasone significantly enhanced patient-reported quality of recovery during the first 24 h after discharge from the hospital (or during a similar time period for patients requiring inpatient admission). Furthermore, dexamethasone use reduced the incidence of nausea, fatigue, and pain during the early postoperative period and reduced hospital length of stay after LC surgery.

Table 4. Quality of Recovery (QoR-40) Dimensions and Global Scores

	Control Group	Dexamethasone Group	Saline *vs.* Dexamethasone Median Difference (99% CI)	*P* Value
Number (pre-/postoperative)	59/45	56/46		
QoR-40 dimensions				
Emotional state				
Preoperative	41 (24–45)	41.5 (27–45)	0 (−2 to 2)	0.913
Postoperative day 1	35 (17–45)	41 (25–45)	−5 (−7 to −3)	< 0.0001
Physical comfort				
Preoperative	56 (36–60)	55 (30–60)	1 (−1 to 3)	0.458
Postoperative day 1	45 (30–59)	51 (28–60)	−6 (−9 to −1)	< 0.001
Psychological support				
Preoperative	35 (25–35)	35 (28–35)	0 (0 to 0)	0.839
Postoperative day 1	35 (20–35)	35 (26–35)	0 (0 to 0)	0.799
Physical independence				
Preoperative	25 (20–35)	25 (15–25)	0 (0 to 0)	0.701
Postoperative day 1	21 (6–25)	21 (13–25)	−1 (−3 to 1)	0.155
Pain				
Preoperative	34 (17–35)	34 (19–35)	0 (−1 to 1)	0.854
Postoperative day 1	26 (14–34)	31 (20–35)	−5 (−7 to −3)	< 0.0001
Global QoR-40				
Preoperative	189 (124–200)	190 (150–200)	0 (−4 to 5)	0.856
Postoperative day 1	161 (113–194)	178 (130–195)	−18 (−26 to −8)	< 0.0001

Data are median (range) unless otherwise indicated.
CI = confidence interval.

Table 5. Postanesthesia Care Unit Parameters (n = 120)

	Control Group	Dexamethasone Group	Difference (95% CI)	*P* Value
Nausea, Y:N	22 (37.3%):37 (62.7%)	7 (12.5%):49 (87.5%)	24.8% (9.3–39.5%)	0.003
Vomiting, Y:N	5 (8.5%):54 (91.5%)	0 (0%):56 (100%)	8.5% (1.8–18.4%)	0.058
Treat nausea and vomiting, Y:N	11 (18.6%):48 (81.4%)	3 (5.4%):53 (94.6%)	13.3% (1.5–25.9%)	0.044
Level of fatigue	2 (0–3)	1 (0–3)	0 (0–1)	0.055
VAS pain at rest	40 (7–100)	32.5 (0–75)	10 (0–15)	0.030
VAS pain with movement	50 (7–100)	40 (0–95)	10 (0–15)	0.022
Treat pain, Y:N	57 (96.6%):2 (3.4%)	40 (71.4%):16 (28.6%)	25.2% (13.0–38.6%)	< 0.001
Hydromorphone, mg	1 (0–3.5)	1 (0–3)	0.5 (0–0.75)	< 0.001
Time to criteria for PACU discharge met, min	80 (25–420)	70 (10–201)	9 (−2 to 20)	0.117
Time to PACU discharge, min	100 (55–430)	91 (43–201)	10 (−1 to 24)	0.085

Data are No. (%) of patients or median (range) unless otherwise indicated.
CI = confidence interval; PACU = postanesthesia care unit; VAS = visual analog scale (100-mm scale).

A systematic review by Wu *et al.*[13] reported a high incidence of postdischarge symptoms after outpatient surgery (45%, pain; 42%, drowsiness; 21%, fatigue; 18%, dizziness; 17%, nausea and headaches; 8%, vomiting). The QoR-40 is a 40-item scoring system developed to assess these aspects of recovery after general anesthesia and surgery. A recent systematic review assessed seven instruments used to measure the quality of recovery in ambulatory surgical patients using eight criteria: appropriateness, reliability, validity, responsiveness, precision, interpretability, acceptability, and precision.[14] Only one instrument, the QoR-40, fulfilled all eight criteria. The QoR-40 has been validated for patients undergoing neurosurgical, cardiac, gynecologic, orthopedic, general, urologic, and ambulatory surgical procedures.[12,15,16] These data suggest that the QoR-40 is the best instrument for evaluating the complex and multidimensional process of postoperative recovery.

The effect of dexamethasone on patient-perceived quality of recovery has been investigated in only a few studies. Coloma *et al.*[11] randomized 140 patients undergoing LC surgery to receive 4 mg dexamethasone or saline; both groups received dolasetron. A follow-up telephone call 24 h after surgery was used to quantify quality of recovery using a 100-point VRS. Patients in the dexamethasone group reported higher quality of recovery scores compared with the control group (89 *vs.* 76). Among patients undergoing outpatient anorectal surgery, administration of 4 mg dexamethasone did not improve quality of recovery (assessed using a 10-cm VAS system) at the time of discharge.[17] The reliability of single-item global satisfaction ratings (VRS or VAS) is poor and inadequate for the assessment of the complex process of postoperative recovery.[18,19] In the present investigation, the QoR-40 scoring system was used to evaluate quality of recov-

Table 6. Ambulatory Surgery Unit Parameters for Patients Discharged on the Day of Surgery (n = 120)

	Control Group	Dexamethasone Group	Difference (95% CI)	*P* Value
Admitted, Y:N	15 (25.4%):44 (74.6%)	10 (17.9%):46 (82.1%)	7.6% (−7.7% to 22.6%)	0.371
Nausea, Y:N	25 (56.8%):19 (43.2%)	10 (21.7%):36 (78.3%)	35.1% (15.2–52.4%)	0.001
Vomiting, Y:N	9 (20.4%):35 (79.6%)	4 (8.7%):42 (91.3%)	11.8% (−3.0% to 27.2%)	0.140
Treat nausea and vomiting, Y:N	20 (45.5%):24 (54.5%)	7 (15.2%):39 (84.8%)	30.2% (11.6–47.3%)	0.003
Level of fatigue	1.5 (0–3)	1 (0–2)	1 (0 to 1)	0.005
VAS pain at rest	38.3 ± 22.7	31.5 ± 19.1	6.8 (−2.0 to 15.5)	0.129
VAS pain with movement	46.7 ± 22.3	40.7 ± 20.0	6.0 (−2.9 to 14.8)	0.185
Treat pain, Y:N	39 (88.6%):5 (11.4%)	33 (71.4%):13 (28.6%)	16.9% (0.4–33.1%)	0.065
Oral pain medication tablet(s)	1 (0–3)	1 (0–3)	0 (0 to 1)	0.015
Time				
First oral intake, min	20 (0–215)	20 (0–120)	0 (−5 to 10)	0.929
First unassisted ambulation, min	150 (10–465)	100 (5–380)	20 (−18 to 55)	0.286
Met criteria for ASU discharge, min	227.5 (35–720)	190 (65–470)	40 (5–75)	0.024
ASU discharge, min	265.5 (75–720)	217.5 (95–525)	55 (15–95)	0.009
Total hospital LOS, min	381 (180–930)	316 (175–653)	70 (27–111)	0.003

Data are No. (%) of patients, median (range), or mean ± SD, unless otherwise indicated.
ASU = ambulatory surgery unit; CI = confidence interval; LOS = length of stay; Oral pain medication tablets = 5 mg hydrocodone, 500 mg acetaminophen tablet; PACU = postanesthesia care unit; VAS = visual analog scale (100-mm scale).

Table 7. Postoperative Adverse Effect Potentially Related to Dexamethasone (n = 120)

Adverse Effect, Y:N	Control Group	Dexamethasone Group	Difference (95% CI)	*P* Value
Sleeplessness	19 (42.2%):26 (57.8%)	15 (32.6%):31 (67.4%)	9.6% (−10.2% to 28.8%)	0.391
Headache	17 (37.8%):28 (62.2%)	11 (23.9%):35 (76.1%)	13.9% (−5.1% to 32.1%)	0.178
Stomach pain	26 (57.8%):19 (42.2%)	18 (39.1%):28 (60.9%)	18.7% (−1.9% to 37.7%)	0.095
Extremity swelling	2 (4.4%):43 (95.6%)	0 (0%):46 (100%)	4.4% (−3.4% to 14.8%)	0.242
IV site irritation	6 (13.3%):39 (86.7%)	4 (8.7%):42 (91.3%)	4.6% (−9.0% to 18.8%)	0.522
Increased appetite	0 (0%):45 (100%)	6 (13.0%):40 (87.0%)	−13.0% (−25.7% to −4.7%)	0.026
Blurry vision	1 (2.2%):44 (97.8%)	1 (2.2%):45 (97.8%)	0% (−9.4% to 9.6%)	1.000
Negative mood change	6 (13.3%):39 (86.7%)	6 (13.0%):40 (87.0%)	0.3% (−14.4% to 15.1%)	1.000

Data are No. (%) of patients or median (range) unless otherwise indicated.
CI = confidence interval; IV = intravenous.

ery on POD1. Global QoR-40 scores were significantly higher on POD1 in the dexamethasone group than in the control group. Our findings suggest that overall patient satisfaction with the early recovery process is enhanced when dexamethasone is administered. The most significant differences between the groups were observed in the dimensions of pain, emotional state, and physical comfort.

The effect of dexamethasone on postoperative pain after LC remains controversial. In a randomized investigation by Bisgaard *et al.*,[5] LC patients administered 8 mg dexamethasone 90 min before incision required less postoperative morphine and reported significantly less overall pain compared with control patients. In contrast, other randomized trials reported no reductions in postoperative pain in LC patients receiving 8 mg dexamethasone at induction of anesthesia.[20,21] Timing of steroid administration may be an important factor influencing the intensity of postoperative pain because the biologic onset of action of dexamethasone is 1 to 2 h; dosing of steroids immediately before surgical incision may be less effective in attenuating inflammatory and pain pathways.[5,22] In addition to reducing pain associated with surgical intervention, prophylactic dexamethasone has been reported to reduce the incidence and severity of sore throat following laryngoscopy and tracheal intubation.[23,24] In the present investigation, the administration of dexamethasone 60 min before incision resulted in significant improvements in global symptoms of pain (surgical, muscle, sore throat, and headache) on POD1, as assessed in the QoR-40 pain dimension. Furthermore, reductions in postoperative VAS pain scores and analgesic requirements were observed in this group. Our results provide further evidence for an analgesic effect of dexamethasone extending throughout POD1.

Previous investigators have speculated that the beneficial effect of dexamethasone in facilitating early recovery from surgery is due to a mood-altering effect and ability to produce a general sense of well-being.[11,17] The effect of dexamethasone on postoperative emotions has not been assessed in prior clinical trials. In this investigation, mood/emotional status during the first 24 h after LC surgery was beneficially affected by dexamethasone treatment. QoR-40 scores in the dimension of emotions were significantly improved in subjects randomized to receive preoperative steroids. The improved mood state in the dexamethasone group may have been due to a primary central nervous system effect of steroids.[25] Dexamethasone also attenuates perioperative inflammatory mediator release, which may enhance emotional status indirectly.[26,27] Finally, more effective control of pain among patients receiving dexamethasone may produce beneficial effects on overall emotional status and quality of recovery.[16,28]

The 12 questions in the physical comfort category of the QoR-40 focus primarily on nausea/vomiting and appetite, fatigue and restfulness, feelings of shivering/being cold, and dizziness. We observed that QoR-40 scores in physical comfort category were improved significantly in the dexamethasone group on POD1. These findings are not unexpected. Many clinical trials have demonstrated that dexamethasone is effective in reducing the incidence of postoperative nausea, vomiting, or both.[29] In the present investigation, the incidence of nausea in the PACU and ASU was reduced in subjects randomized to receive dexamethasone. The late antiemetic effects of this steroid likely contributed to improved patient comfort on POD1. Steroids are also effective in stimulating appetite and preventing anorexia,[9] which may enhance convalescence and recovery after surgery. Fatigue is another common postoperative symptom that may negatively affect patient comfort.[5,6] In the present investigation, the intensity of fatigue during hospitalization was reduced in subjects receiving preoperative dexamethasone. The use of a single postinduction dose of dexamethasone has also been reported to decrease the incidence of postoperative shivering and dizziness.[30,31] In summary, we believe that the beneficial effects of dexamethasone on several diverse but interrelated symptoms that determine patient comfort resulted in the overall improved QoR-40 scores observed in this dimension on POD1.

Improvements in early recovery in the dexamethasone group translated into reductions in hospital length of stay. Our findings are in accordance with two previous trials in the ambulatory setting demonstrating that dexamethasone facilitated earlier hospital discharge.[11,17] We observed improvements in several recovery variables during the PACU and ASU admission in the dexamethasone group, which likely resulted in a shorter in-hospital length of stay.

There are several limitations to this investigation. First, the optimal dose of dexamethasone required to enhance postoperative recovery has not been established. A dose of 8

mg was selected for the current investigation based on data that this is the optimal effective dose in the prevention of postoperative nausea or vomiting after LC surgery.[4,21] Future dose-response studies will be required to establish the most appropriate dosing regimen of dexamethasone for optimal postoperative recovery. Second, QoR-40 scores were only collected for 24 h after discharge from the hospital. It is uncertain whether the beneficial effects of dexamethasone persisted beyond POD1. Third, the use of a survey instrument may introduce a response-rate bias; patients with a poorer (or improved) quality of recovery may be less likely to return the QoR-40 questionnaire. However, we observed that response rates did not differ significantly among patients receiving dexamethasone or placebo. Fourth, a multimodal analgesic treatment regimen was not used in our study population. The use of additional postoperative analgesics, such as nonsteroidal antiinflammatory agents, may have affected POD1 QoR-40 scores. Fifth, we observed no complications directly attributable to steroid therapy. However, our study was likely underpowered to detect uncommon adverse clinical outcomes potentially related to steroids (*e.g.*, impaired wound healing, postoperative infection). Finally, although this study was properly powered to detect a difference in the primary outcome, it may not have had sufficient power to detect differences in secondary outcomes, such as the uncommon adverse outcomes mentioned above (*i.e.*, a type II inferential error). In addition, given the large number of comparisons of secondary outcomes made in this study, it is likely that one or two differences in secondary outcomes may have been identified by chance (*i.e.*, a type I inferential error).

In conclusion, our investigation demonstrated that the preoperative administration of a single dose of dexamethasone enhanced recovery after planned outpatient LC surgery. During POD1, patient-perceived quality of recovery was significantly enhanced among patients receiving dexamethasone. Throughout hospitalization, the incidence of nausea was decreased, and fatigue scores were improved in the dexamethasone group. Furthermore, pain scores and requirements for analgesics were reduced after steroid administration. These improvements in recovery translated into reductions in hospital length of stay. Our findings support the belief that small-dose steroid therapy (8 mg dexamethasone) may improve quality of recovery measures after hospital discharge.

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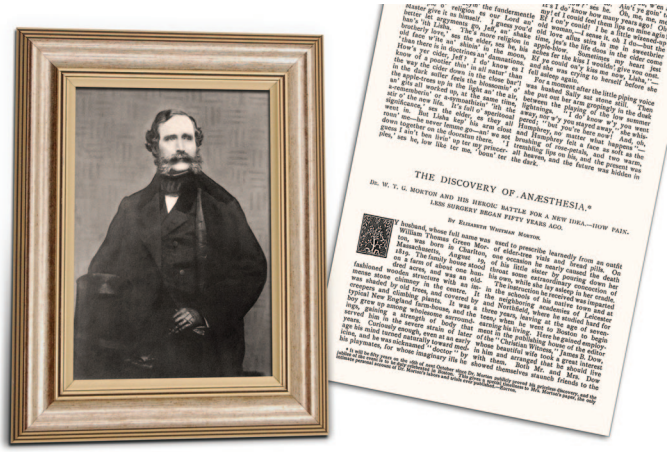
ANESTHESIOLOGY REFLECTIONS

Morton in *McClure's Magazine*


THE DISCOVERY OF ANÆSTHESIA.*

DR. W. T. G. MORTON AND HIS HEROIC BATTLE FOR A NEW IDEA.—HOW PAINLESS SURGERY BEGAN FIFTY YEARS AGO.

By ELIZABETH WHITMAN MORTON.

Eight years after his 1846 public demonstration of surgical anesthesia, a well-dressed William T. G. Morton rested his top hat on one knee as he posed for formal photography by the Boston firm of Silsbee, Case and Company. That image so impressed his daughter Elizabeth Whitman Morton, that she published it in 1896 in her popular *McClure's Magazine* article titled "The Discovery of Anaesthesia. Dr. W. T. G. Morton and His Heroic Battle for a New Idea.—How Painless Surgery Began Fifty Years Ago." Her semicentennial publication honoring her father would eventually be reunited with this large "Silsbee, Case & Co." photoportrait at the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology in Park Ridge, Illinois. (Copyright © the American Society of Anesthesiologists, Inc. This image also appears in the *Anesthesiology Reflections* online collection available at www.anesthesiology.org.)

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