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High-dose perioperative corticosteroids in steroid-treated patients undergoing major colorectal surgery: necessary or overkill?

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Abstract

BACKGROUND: Steroid-treated patients undergoing major colorectal surgery are routinely treated with high-dose steroids (HDS) to prevent perioperative adrenal insufficiency and cardiovascular collapse. However, there is no evidence to support this practice.

METHODS: A retrospective analysis of 97 consecutive steroid-treated patients with inflammatory bowel disease who underwent major colorectal surgery was performed. The incidence of hemodynamic instability and surgical outcomes were compared in patients treated with perioperative low-dose steroids (LDS) versus HDS.

RESULTS: Forty-three patients were treated with HDS, and 54 patients received LDS. There was no significant difference in hemodynamic instability between HDS-treated (74%) and LDS-treated (78%) patients. No patients required rescue HDS for adrenal insufficiency.

CONCLUSIONS: Steroid-treated patients with inflammatory bowel disease undergoing major colorectal surgery appear to have no clinically significant hemodynamic instability when managed with LDS versus HDS. A prospective study assessing perioperative steroid dosing in patients with inflammatory bowel disease is in progress.

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Perioperative high-dose steroids (HDS) are considered the standard of care for corticosteroid-treated patients undergoing major colorectal surgery. This practice is based largely on case reports from the 1950s of postoperative cardiovascular collapse and death in 2 patients whose preoperative steroids were abruptly discontinued before surgery.[1,2] Since that time, it has become standard practice to administer perioperative high-dose intravenous (IV) steroids to all steroid-treated patients undergoing surgery to prevent perioperative adrenal insufficiency and hemodynamic collapse.[3,4] Because steroid-treated patients may have continued adrenal insufficiency for up to 1 year after stopping steroid therapy, this practice is also recommended for patients off steroids at the time of surgery who have previously been treated with steroids <12 months before surgery.[5] However, there is no biochemical or clinical evidence to support this practice.

Accordingly, we retrospectively compared the effect of perioperative low-dose steroids (LDS) or HDS on perioperative hemodynamic and surgical outcomes in steroid-treated patients with inflammatory bowel disease (IBD) undergoing major colorectal surgery at our institution. We hypothesized that steroid-treated patients undergoing major

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colorectal surgery may be managed safely with LDS instead of HDS in the perioperative period.

Methods

Study population

A chart review was performed on consecutive steroid-treated patients with IBD undergoing major colorectal surgery at our institution by 2 colorectal surgeons between January 2009 and September 2010. Patients were included if they were (1) on steroids at the time of surgery or (2) off steroids but had previously been treated with steroids <1 year before surgery. Patients were excluded if their steroid doses were <5 mg oral prednisone or if the duration of steroid therapy was <1 week, because these patients are thought not to develop significant suppression of their hypothalamic-pituitary-adrenal axis.[5] This study was approved by the Cedars-Sinai Medical Center institutional review board (IRB #23006).

Steroid dosing

Patients received 1 of 2 perioperative steroid dosing regimens, HDS or LDS. HDS-treated patients received IV hydrocortisone 100 mg at the time of surgical incision and 100 mg intravenously every 8 hours for another 24 hours and were then tapered to oral prednisone over the next 3 days. On hospital discharge, prednisone was either discontinued or tapered. LDS-treated patients were administered one third of the IV hydrocortisone equivalent of the daily preoperative steroid dose (IVED) at the time of surgical incision, then one third IVED every 8 hours for the first 24 hours after surgery. Patients subsequently were treated with one quarter IVED every 8 hours starting on postoperative day (POD) 1, followed by one sixth IVED every 8 hours on POD 2 and every 12 hours starting on POD 3. On POD 4 or when the patient was tolerating a regular diet, oral prednisone equal to the most recent IV hydrocortisone dose was resumed. At the time of discharge, prednisone was tapered in most patients. Patients off steroids at the time of surgery but previously treated with steroids <1 year before surgery, who were assigned to the LDS treatment group, received no perioperative steroids.

The choice of the perioperative steroid dosing regimen was solely at the discretion of the attending surgeon. The LDS algorithm was slowly implemented over time. At the beginning of the study period, LDS were administered to low-risk patients (ie, patients off steroids at the time of surgery or those patients on lower dose steroids preoperatively), at the attending surgeon's discretion. With more experience, the LDS algorithm was implemented for patients on higher dose steroids. Toward the end of the study period, all patients undergoing surgery by either surgeon were assigned to LDS.

Clinical characteristics and surgical outcomes

Detailed clinical profiles were retrospectively generated using chart review. Demographic information, preoperative characteristics, and perioperative outcomes were recorded. Preoperative, intraoperative, and postoperative vital signs were assessed. Maximum and minimum values for heart rate (HR), systolic blood pressure (SBP), and body temperature in the operating room, postoperative care unit, and each POD 0 to 7 were recorded. Hemodynamic instability was defined as HR > 100 beats/min, HR < 60 beats/min, or SBP < 90 mm Hg. Fever was defined as temperature ≥ 38°C and hypothermia as temperature < 35°C.

Postoperative complications occurring during the 30-day period beginning from the time of surgery were recorded. These complications were classified as either medical or surgical and were further characterized as being either major or minor in nature on the basis of definitions established in a prior study.[6] If a patient had >1 complication, the most severe complication or the complication that was the most likely the source for the others was included.

Statistical analysis

All data were entered into a standardized database computer program (Excel; Microsoft Corporation, Redmond, WA). Online statistical analysis software was used for all data analysis. Categorical variables were compared using Fisher's exact test (GraphPad Software, San Diego, CA). Numerical variables not normally distributed were compared using Mann-Whitney nonparametric tests (http://www.statpages.org). All hypothesis testing was 2 sided, with P values < .05 considered statistically significant.

Results

The study cohort consisted of 97 operations performed in 74 patients with IBD. Operations performed are shown in Table 1. Forty-eight patients (49%) were on steroids at the time of surgery, including 32 patients treated with HDS and 16 patients treated with LDS. Forty-nine patients (51%) were off steroids but had been previously treated with steroids <1 year before surgery. This patient subgroup included 11 patients treated with HDS and 38 patients treated with LDS. Overall, there were 43 patients (44%) in the HDS group and 54 patients (56%) in the LDS group. Except for lower median preoperative hemoglobin in the HDS group compared with the LDS group, there were no significant differences in demographic variables and clinical characteristics between the HDS and LDS patient groups (Table 2). For patients on steroids at the time of surgery, the median steroid dose at the time of operation in prednisone equivalents was 20 mg/d (range, 5–60 mg/d) for the HDS group and 38 mg/d (range, 5–70 mg/d) for the LDS group. For patients off steroids, the maximum steroid dose in the past

Table 1 Surgical procedures performed

Operation performed	Study Cohort (n = 97)	HDS (n = 43)	LDS (n = 54)
Ileal pouch-anal anastomosis	28	12	16
Ileocolic resection	24	14	10
Subtotal colectomy	19	11	8
Ileostomy closure	18	3	15
Proctocolectomy	5	2	3
Ileostomy creation	1	1	0
Ileostomy revision/ takedown Enterocutaneous fistula	1	0	1
Small bowel resection/ strictureplasty	1	0	1

year in prednisone equivalents was 25 mg/d (range, 15–60 mg/d) for the HDS group and 40 mg/d (range, 5–60 mg/d) for the LDS group. For patients off steroids at the time of surgery, the median time from last steroid dose to surgery was 3 months (range, .1–11 months) for the HDS group and 5.5 months (range, .5–12 months) for the LDS group. Two patients (5%) in the HDS group and 4 patients (7%) in the LDS group had been off steroids for ≤1 month at the time of surgery. These differences in steroid dosing between the 2 patient groups were not statistically significant.

A comparison of postoperative outcomes and surgical morbidity between the HDS and LDS patient groups is shown in Table 3. Although there was significantly higher intraoperative blood loss in the HDS group compared with the LDS group, the number of patients needing blood transfusions was not significantly different between the patient groups. There was no significant difference in the total volume of IV fluids administered or the volume of IV fluids per kilogram body weight for the HDS and LDS patient groups. However, there was a statistically insignificant trend for more IV fluid boluses in the LDS group (28%) compared with the HDS group (12%). Postoperative complications in HDS group occurred in 10 patients (23%) and included peristomal or anterior abdominal wall abscess requiring incision and drainage (n = 2); wound infection, opened and packed (n = 2); malignant hyperthermia in a patient requiring vasopressors and intensive care unit (ICU) admission (n = 1); enterocutaneous fistula managed conservatively (n = 1); intra-abdominal abscess treated with computed tomography–guided drainage (n = 1); dehydration secondary to high ileostomy output requiring readmission and conservative management (n = 1); urinary retention requiring reinsertion of indwelling catheter (n = 1); and pulmonary embolism managed with systemic anticoagulation (n = 1). In the LDS group, 12 patients (22%) developed complications, including small bowel obstruction or ileus requiring readmission, managed conservatively (n = 2); high ileostomy output and dehydration requiring readmission and conservative management (n = 2); postoperative bleeding responsive to blood transfusion (n = 2); urinary retention requiring reinsertion of indwelling catheter (n = 2); wound dehiscence requiring reoperation (n = 1); parastomal hernia requiring reoperation (n = 1); anaphylaxis to postoperative antiemetic requiring vasopressors and ICU admission (n = 1); and portal vein thrombosis managed with systemic anticoagulation (n = 1). There was no mortality in the entire study cohort within the 30-day postoperative period. In

Table 2 Demographic and clinical characteristics

Variable	Study Cohort (n = 97)	HDS (n = 43)	LDS (n = 54)	*P*
Age (y)	39 (15–76)	38 (18–66)	40 (15–76)	.47
Men/women	47/50	20/23	27/27	1.00
BMI (kg/m^2)	22.2 (14–40)	22.4 (17–37)	22.1 (14–40)	.57
Medical comorbidities	32 (33%)	16 (37%)	16 (30%)	.52
Prior abdominal surgery	56 (58%)	23 (53%)	33 (61%)	.54
ASA score	2 (1–4)	2 (2–4)	2 (1–3)	.88
Preoperative anti-HTN/β-blocker medications	7 (7%)	3 (7%)	4 (7%)	1.00
Indication for surgery				.38
Ulcerative colitis	64 (66%)	26 (61%)	38 (70%)	
Crohn's disease	31 (32%)	16 (37%)	15 (28%)	
Indeterminate colitis	2 (2%)	1 (2%)	1 (2%)	
Preoperative hemoglobin (g/dL)	12.5 (8–18)	11.9 (8–17)	13 (9–18)	.03
Steroid dose at time of surgery*	30 (5–70)	20 (5–60)	38 (5–70)	.83
Preoperative maximum steroid dose*	25 (5–60)	25 (15–60)	40 (5–60)	.94
Time from last steroid to surgery (mo)	4 (.1–12)	3 (.1–11)	5.5 (.5–12)	.12
Off steroids ≤1 mo	6 (12%)	2 (5%)	4 (7%)	.69

Data are expressed as median (range) or as number (percentage).
ASA = American Society of Anesthesiologists; BMI = body mass index; HTN = hypertensive.
*Expressed as prednisone equivalents.

Table 3 Surgical outcomes

Outcome	Study Cohort (n = 97)	HDS (n = 43)	LDS (n = 54)	*P*
Operating room time (min)	205 (67–424)	205 (67–370)	201 (69–424)	.23
Intraoperative blood loss (cm^3)	100 (5–2000)	150 (5–2000)	100 (5–800)	.02
Total IV fluid (cm^3)	9,617 (4,210–34,904)	9,295 (4,650–34,904)	10,117 (4,210–32,201)	.45
Total IV fluid (cm^3/kg)	149 (54–531)	149 (57–453)	150 (54–531)	.51
IV fluid bolus required	20 (21%)	5 (12%)	15 (28%)	.08
Blood transfusion	9 (9%)	5 (12%)	4 (8%)	.50
Postoperative complications	22 (23%)	10 (23%)	12 (22%)	1.00
Major surgical	13	7	6	
Minor surgical	6	2	4	
Major medical	3	1	2	
Minor medical	0	0	0	
Length of hospital stay (d)	5 (3–13)	5 (3–13)	5 (3–9)	.96

Data are expressed as median (range) or as number (percentage).

comparing vital sign profiles between the HDS and LDS patient groups at any time until POD 7, we found no significant difference in overall hemodynamic instability, tachycardia, bradycardia, or hypotension between the 2 patient groups (Table 4). However, on subgroup analysis, patients off steroids at the time of surgery (but previously treated with steroids <1 year before surgery) had a significantly higher incidence of tachycardia when treated with HDS (82%) versus LDS (42%) ($P = .04$). In patients on steroids at the time of surgery, there was a significantly higher incidence of overall hemodynamic instability in the LDS group (100%) compared with the HDS group (72%) ($P = .02$). However, these differences in hemodynamic instability appeared to be clinically insignificant, because in all but 3 patients, hemodynamic instability resolved with no intervention, fluid bolus, or blood transfusion. Two patients in the LDS group were treated with vasopressors. One patient received a single dose of epinephrine and dexamethasone followed by ICU admission for anaphylactic shock immediately after the administration of an antiemetic on POD 4. Another patient was treated with a single dose of intraoperative phenylephrine for intraoperative hypotension after aggressive intraoperative β-blockade. Finally, 1 patient in the HDS group was treated with dantrolene and norepinephrine and admitted to the ICU for malignant hyperthermia. There were no cases of hypotension with SBP falling to <70 mm Hg in the entire study cohort. None of our patients required stress-dose steroids for acute adrenal insufficiency.

Three of 4 patients in the LDS group on preoperative antihypertensive medications or β-blockers developed perioperative hypotension. In 2 of these patients, hypotension was intraoperative and responded simply to IV fluid bolus. One patient whose preoperative antihypertensive medications were continued postoperatively developed transient hypotension on POD 1, which resolved with no intervention. One of 3 patients in the HDS group on preoperative antihypertensive medications or β-blockers developed hypotension in the postoperative care unit, which was corrected easily with IV fluid boluses.

There was an insignificant trend toward a higher incidence of fever in the LDS group (26%) compared with the HDS group (9%). However, all episodes of fever resolved with simple cooling measures or acetaminophen. Although 1 patient in the HDS group developed intraoperative hypothermia of unclear etiology, it was responsive to warming measures.

Table 4 Vital sign profiles of the HDS and LDS patient groups

On Steroids at Time of Surgery?	Perioperative Steroid Dose	Any Hemodynamic Instability	HR (beats/min)			Temperature (°C)	
			>100	<60	SBP < 90 mm Hg	≥38	<35
Yes (n = 48)	HDS (n = 32)	23 (72%)	19 (59%)	12 (38%)	4 (13%)	3 (9%)	1 (3%)
	LDS (n = 16)	16 (100%)*	11 (69%)	4 (25%)	2 (13%)	4 (25%)	0
No (n = 49)	HDS (n = 11)	9 (82%)	9 (82%)†	2 (18%)	2 (18%)	1 (9%)	0
	LDS (n = 38)	26 (68%)	16 42%)	9 (24%)	13 (34%)	10 (26%)	0
Total (n = 97)	HDS (n = 43)	32 (74%)	28 (65%)	14 (33%)	6 (14%)	4 (9%)	1 (2%)
	LDS (n = 54)	42 (78%)	27 (50%)	13 (24%)	15 (28%)	14 (26%)	0

*$P = .02$ versus HDS in patients on steroids at time of surgery.
†$P = .04$ versus LDS in patients off steroids at time of surgery.

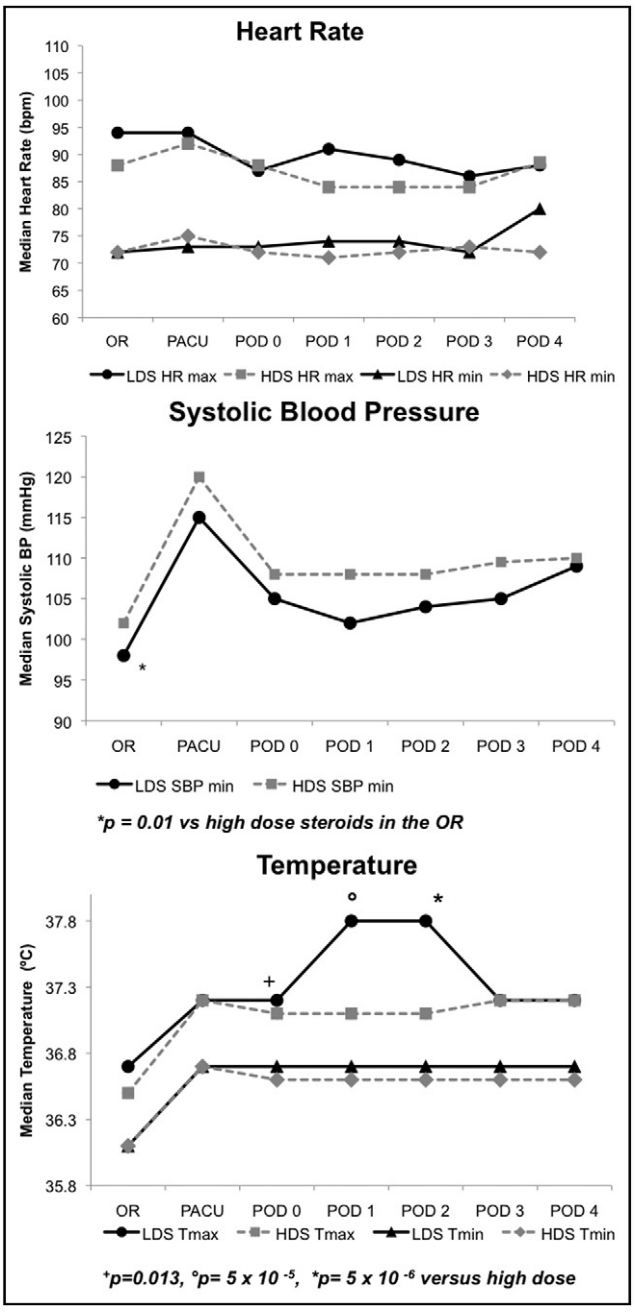

Figure 1 Detailed comparison of hemodynamic characteristics. HR max = maximum HR; HR min = minimum HR; OR = operating room; PACU = postoperative care unit; SBP min = minimum SBP; Tmin = minimum temperature; Tmax = maximum temperature.

For a more thorough comparison of the hemodynamic characteristics between the 2 patient groups, we evaluated maximum and minimum HR, minimum SBP, and maximum and minimum temperatures for the HDS and LDS patient groups in the operating room, postoperative care unit, and PODs 0 through 4 (Fig. 1). The data were analyzed only through POD 4 because the median postoperative hospitalization was 5 days. We found no significant difference in median maximum or minimum HR between the HDS and no steroid patient groups. However, median minimum SBP in the operating room was significantly lower for patients in the LDS group compared with the HDS group ($P = .01$). In addition, median maximum temperature was significantly higher on PODs 0, 1, and 2 for patients in the LDS group compared with the HDS group.

Comments

For >50 years, abdominal surgeons have been administering perioperative HDS to steroid-treated patients undergoing surgery to prevent perioperative adrenal insufficiency and cardiovascular collapse.[3,4] This practice stems largely from case reports from the 1950s of cardiovascular collapse and death in 2 patients whose preoperative steroids were discontinued just before surgery.[1,2] Because steroid-treated patients may have continued adrenal suppression for up to 1 year after stopping steroid therapy, perioperative HDS have also been recommended for patients previously treated with steroids up to 12 months before surgery.[5] However, there is little objective evidence to support this practice. In addition, corticosteroid therapy is not without consequence. Perioperative HDS have been associated with impaired wound healing, immunosuppression, hyperglycemia, hypertension, and deleterious psychological effects.[7]

Various studies have suggested that steroid-treated patients undergoing surgery may be treated with only their baseline corticosteroid doses in the perioperative period.[8–14] However, these studies have focused mostly on organ transplant recipients or included patients on low maintenance doses of corticosteroids undergoing minor or moderate surgical procedures. Patients with IBD represent a unique study cohort because they are frequently on high doses of steroids for a prolonged period, and surgery in these patients often involves major surgical stress. Therefore, it is more than conceivable that data from the organ transplantation literature cannot be reliably applied to steroid-treated patients with IBD undergoing major colorectal surgery.

Data from the present study suggest that in steroid-treated patients with IBD, there is no significant difference in hemodynamic instability when treated with LDS versus HDS. On subgroup analysis of patients on steroids at the time of surgery, there was a significantly higher incidence of hemodynamic instability in the LDS patient group compared with the HDS patient group. However, these episodes of hemodynamic instability were clinically unimportant, because in all but 3 cases, hemodynamic instability resolved with simple measures. In the 3 patients who were treated with vasopressors, hemodynamic instability was clearly due to other medical causes rather than adrenal insufficiency. In addition, no patients required rescue HDS because of adrenal insufficiency.

Tachycardia was the most common factor contributing to hemodynamic instability in the study cohort. In the subgroup of patients off steroids at the time of surgery, tachy-

cardia was significantly more common in the HDS group compared with the LDS group, suggesting that HDS may have a detrimental effect on this subgroup of steroid-treated patients. Surgeons should realize that simply administering HDS to all steroid-exposed patients in the perioperative period may have adverse clinical consequences.

LDS-treated patients had a higher median maximum temperature on PODs 0, 1, and 2 and a trend toward a higher incidence of fever compared with HDS-treated patients. One might argue that this is due to corticosteroid blunting of the natural pyretic response to surgery in HDS-treated patients.[7] By contrast, this may be a sign of adrenal insufficiency, as fever is a common sign of hypoadrenalism.[7] Aside from a higher intraoperative blood loss in the HDS group compared with the LDS group, there was no significant difference in surgical outcomes, complications, or hospital stay between the 2 patient groups, and our results compare well with those of other studies assessing surgical outcome in patients with IBD.[15] Because all cases of hemodynamic instability and fever resolved with simple measures and without serious consequence, it appears that the omission of HDS during and after major colorectal surgery in steroid-treated patients with IBD is feasible and safe.

Some may suggest that our data are not supported by biochemical testing of adrenal insufficiency. Preoperative testing of hypothalamic-pituitary-adrenal axis dysfunction, although readily available, has low specificity for perioperative clinical adrenal insufficiency.[16] Therefore, an abnormal result on preoperative adrenocorticotropic hormone stimulation testing does not accurately predict perioperative hemodynamic instability. Using this test to predict which patients may need perioperative HDS may lead to the overtreatment of patients with biochemical evidence of adrenal insufficiency who may not go on to develop clinical signs or symptoms of perioperative adrenal insufficiency. Selective perioperative biochemical adrenal testing of patients with persistent hemodynamic instability unresponsive to fluid bolus would be a more reasonable method to identify patients with true adrenal insufficiency. However, none of our patients required such testing, because all episodes of hemodynamic instability in our study cohort resolved quickly and with relatively simple measures.

Our study was limited by its retrospective nature and may have been confounded by other factors that may affect hemodynamic instability, such as lower preoperative hemoglobin in the HDS group compared with the LDS group. In addition, because the choice of HDS versus LDS steroid use was dependent solely on surgeon preference, our study may have been affected by selection bias. Despite these limitations, our data suggest that it may be safe to manage patients with IBD undergoing major colorectal with perioperative LDS instead of HDS. A prospective study assessing perioperative steroid dosing in patients with IBD undergoing major colorectal surgery is in progress.

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