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Dose ranging study on the effect of preoperative dexamethasone on postoperative quality of recovery and opioid consumption after ambulatory gynaecological surgery

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Editor's key points

- Steroids have beneficial effects on some aspects of postoperative recovery.
- There is limited evidence as to the optimal dose of steroid.
- This study demonstrates a dose–response effect of dexamethasone on the quality of recovery after laparoscopic gynaecological surgery.
- Dexmethasone (0.1 mg kg^{-1}) had a positive effect on airway morbidity (such as sore throat) that was not seen with dexamethasone (0.05 mg kg-1), a reduction in opioid consumption, and improvement in all assessed dimensions of quality of recovery.
- The study was not powered to examine adverse effects such as hyperglycaemia or infection.

Background. Glucocorticoids are commonly administered before ambulatory surgery, although their effects on quality of recovery are not well characterized. The purpose of this study was to evaluate the dose-dependent effects of dexamethasone on patient recovery using the Quality of Recovery 40 questionnaire (QoR-40) after ambulatory surgery.

Methods. This prospective, double-blind trial studied 106 female subjects undergoing outpatient gynaecological laparoscopy. Subjects were randomized to receive saline, dexamethasone 0.05 mg kg^{-1} or dexamethasone 0.1 mg kg^{-1} before induction. The primary outcome was global QoR-40 at 24 h. Postoperative pain, analgesic consumption, side-effects, and discharge time were also evaluated.

Results. Global median (IQR) QoR-40 after dexamethasone 0.1 mg kg^{-1} 193 (192–195) was greater than dexamethasone 0.05 mg kg^{-1} 179 (175–185) (P=0.004) or saline, 171 (160–182) (P<0.005). Median (IQR) morphine equivalents administered before discharge were 2.7 (0–6.3) mg after dexamethasone 0.1 mg kg^{-1} compared with 5.3 (2.4–8.8) mg and 5.3 (2.7–7.8) mg after dexamethasone 0.05 mg kg^{-1} and saline (P=0.02). Time to meet discharge criteria was 30 min shorter after dexamethasone 0.1 mg kg^{-1} compared with saline (P=0.005). At 24 h, subjects receiving dexamethasone 0.1 mg kg^{-1} had consumed less opioid analgesics, reported less sore throat, muscle pain, confusion, difficulty in falling asleep, and nausea compared with dexamethasone 0.05 mg kg^{-1} and saline.

Conclusions. Dexamethasone demonstrated dose-dependent effects on quality of recovery. Dexamethasone 0.1 mg kg^{-1} reduced opioid consumption compared with dexamethasone 0.05 mg kg^{-1}, which may be beneficial for improving recovery after ambulatory gynaecological surgery.

Keywords: anaesthesia; general, gynaecological, recovery; recovery, postoperative, pain, postoperative, dexamethasone, postoperative nausea and vomiting

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Single dose glucocorticoids such as dexamethasone are commonly administered perioperatively to ambulatory surgery patients. Preoperative dexamethasone has an established role in nausea and vomiting prophylaxis.[1] The effect of steroids in reducing postoperative pain and opioid consumption have been demonstrated after ambulatory surgery;[2 3] although these effects have primarily been demonstrated at high doses of steroids that are not routinely used in clinical practice.[4] High doses of steroids are also associated with side-effects such as hyperglycaemia and immune suppression which may delay discharge or result in a hospital admission.[5]

Corticosteroids may have other beneficial or detrimental effects on patient recovery. They can generate a subjective sense of well-being, independently of their disease status, which can lead to a faster discharge from the hospital.[6] In addition, the anti-inflammatory effects of dexamethasone may decrease the incidence and severity of airway morbidity which may lead to patient dissatisfaction after anaesthesia and surgery.[7 8] Conversely, corticosteroids can produce symptoms of insomnia and depression that may delay the return to daily activities, a primary goal in outpatient surgery.[6] The dose dependency of these effects has not been well characterized after ambulatory surgery.

The Quality of Recovery 40 questionnaire (QoR-40) is a multidimensional instrument that was specifically developed and validated to evaluate the health status of patients after anaesthesia and surgery.[9] It can be particularly useful when an intervention affects various aspects of patient recovery, as is the case for corticosteroids such as dexamethasone. The purpose of this study was to evaluate the dose-dependent effects of dexamethasone on the quality of recovery, postoperative airway morbidity, and opioid analgesic use after ambulatory gynaecological surgery.

Methods

This study was a prospective, randomized, double-blind placebo controlled trial. Clinical trial registration for this study can be found at www.clinicaltrials.gov; registration identified: NCT01052038. Study approval was obtained from the Northwestern University Institutional Review Board, and written informed consent was obtained from all the study participants. Eligible subjects were ASA physical status I and II females undergoing outpatient gynaecological laparoscopy. Patients with a history of recent respiratory tract infection (<1 month), current use of an opioid analgesic or corticosteroid, pregnancy, or anticipated difficult airway were not enrolled. Reasons for exclusion from the study after study drug administration included: difficult airway defined by more than two laryngoscopic attempts by the attending anaesthesiologist and conversion from a laparoscopic to an open laparotomy. A bedside airway examination was performed and the Mallampati classification was recorded. Subjects were randomized using a computer-generated table into three groups: saline, dexamethasone 0.05 mg kg^{-1}, and dexamethasone 0.1 mg kg^{-1}. Group assignments were sealed in sequentially numbered opaque envelopes that were opened by a research nurse not involved with the subjects' care. The study drug was administered in 100 ml of normal saline as an infusion over 10 min, when the patient was in the preoperative holding area. The anaesthesia care team was blinded to group allocation.

All subjects were premedicated with 0.04 mg kg^{-1} intravenous (i.v.) midazolam. Propofol 1–2 mg kg^{-1} was administered for anaesthesia induction, a remifentanil infusion (0.1 mcg kg^{-1} min^{-1}) was begun, and rocuronium 0.6 mg kg^{-1} i.v. was administered to induce muscle paralysis. Subjects were ventilated via a face mask until disappearance of all twitches on the train-of-four (TOF) monitor (EZ Stim II, Life Tech, Stafford, TX, USA). Tracheal intubation was initially attempted by an anaesthesia resident physician or a certified registered nurse anaesthetist under supervision of an attending anaesthesiologist. The number of intubation attempts, total time to intubation, and the need for cricoid pressure to improve laryngoscopy grade were recorded. Anaesthesia maintenance was achieved using remifentanil, titrated to keep the mean arterial pressure within 20% of baseline, and sevoflurane titrated to bispectral index (Aspect Medical System Inc., Norwood, MA, USA) between 40 and 60. Additional doses of rocuronium were administered to maintain the TOF between 1 and 3 twitches. During maintenance, patients received a mixture of air and oxygen to keep $F_{I_{O_2}}$ between 0.4 and 0.6. All gases were delivered though a humidified circuit. All patients had an orogastric tube placed.

At the end of the procedure, at removal of the laparoscopic instruments, the remifentanil infusion was stopped and the patient received hydromorphone 10 μg kg^{-1} i.v. Neuromuscular blockade was antagonized using neostigmine 0.05 mg kg^{-1} and glycopyrrolate 0.01 mg kg^{-1}. Patients also received ketorolac 30 mg i.v., ondansetron 4 mg, and metoclopramide 10 mg before the end of the procedure. Before extubation, the subject's mouth was suctioned with a 14 French soft suction catheter and the presence of blood in the aspirate was noted. Subjects were extubated when they were able to perform a 5-s head lift and follow verbal commands.

In the post-anaesthesia recovery room, subjects were asked to rate their pain upon arrival and at regular intervals on a 0–10 numeric rating scale (NRS) for pain, where 0 means no pain and 10 is the worst pain imaginable. Nausea and vomiting were also assessed at the same intervals and recorded as present or absent. Hydromorphone 0.2 mg i.v. was administered every 5 min to maintain an NRS pain score <4 of 10. The time to first hydromorphone administration was recorded. Discharge readiness was assessed by using the Post Anesthesia Discharge Scoring System (PADSS),[10] scored every 15 min until patients met discharge criteria. At discharge, subjects were instructed to take ibuprofen 400 mg orally for mild pain (<4 of 10) or hydrocodone 10 mg plus paracetamol 325 mg for pain > 4 of 10 every 4 h as needed.

Subjects were assessed at 1, 3, and 24 h after the procedure and were asked about the presence or absence of a sore throat and to rate pain related to the sore throat at rest and with swallowing using an NRS for pain (where 0 is no pain and 100 is the worst sore throat pain ever experienced by the patient). At 3 h after the surgery, they were also questioned regarding the presence of cough using a previously described[11] grading scale where 0=no cough or scratchy throat, 1=minimal scratchy throat or cough, 2=moderate cough similar to a cold, or 3=severe cough, greater than a cold. The presence and severity of hoarseness was also evaluated as 0=no evidence of hoarseness occurring any time since your operation, 1=no evidence of hoarseness at the time of interview, but hoarseness was present previously, 2=hoarseness at the time of interview, that was noted only by the patient, or 3=hoarseness that was easily noted at the time of interview.[11]

Subjects were contacted 24 h after the procedure by an investigator unaware of group allocation and were asked about analgesic consumption and the QoR-40 questionnaire was administered (Table 1). Perioperative data collected included subject's age, height, weight, American Society of Anaesthesiologist physical class, surgical duration, intraoperative remifentanil use, total i.v. fluids, and total amount of hydromorphone in PACU.

The primary outcome measure was the global QoR-40 aggregate score. Global QoR-40 scores range from 40 to 200 for representing very poor to outstanding quality of recovery. The mean QoR-40 in female patients after anaesthesia and surgery has been reported to be 162, and the sample was estimated to detect a difference of 10 points in the quality of recovery among the dexamethasone and placebo groups.[9] A sample size of 34 per group was estimated for the three study groups to be compared. The total sample of 102 subjects achieves 81% power to detect differences among the means using an *F*-test and a one-way analysis of variance at a 0.05 significance level. The common standard deviation within a group was assumed to be 26.[9] To account for drop-outs, 120 subjects were randomized. The sample size calculation was made using PASS version 8.0.13 release date 14 January 2010 (NCSS, LLC, Kaysville, UT, USA).

The Shapiro–Wilks, Anderson–Darling and Kolmogorov–Smirnov tests were used to test the hypothesis of normal distribution. Normally distributed interval data are reported as mean [standard deviation (SD)] and were evaluated with one-way ANOVA. Non-normally distributed interval data and ordinal data are reported as median [interquartile range (IQR) or median absolute deviation (MAD)] and were analysed using the Kruskal–Wallis *H* test. *Post hoc* comparisons were made using the Tukey–Kramer or Dunn's test with Bonnferoni correction for multiple comparisons. Categorical variable were evaluated using a χ^2 statistic. Estimates of exact *P*-values were determined for the χ^2 and the Mann–Whitney test using a Monte Carlo method with 10 000 samples and confidence limits of 99%. All reported *P*-values are two-tailed. Statistical analysis was performed using NCSS 2007 7.1.20, release date 19 February 2010 (NCSS, LLC, Kaysville, UT, USA) and IBM® SPSS® Statistics 19 (Version 19.0.0, IBM Corporation, Somers NY).

Table 1 Quality of recovery questionnaire 40 (QoR-40). All items scored on a five-point (1–5) Likert scale. Positive characteristics scored 1=none of the time to 5=all of the time. Negative characteristics scored 5=none of the time to 1=all of the time

Sphere of recovery	Positive items	Negative items
Physical comfort	Able to breathe easily	Nausea
	Have had a good sleep	Vomiting
	Been able to enjoy food	Retching
	Feel rested	Feeling restless
		Shaking/twitching
		Shivering
		Feeling cold
		Feeling dizzy
Emotional state	Have a feeling of general well-being	Had bad dreams
	Feeling in control	Feeling anxious
	Feeling comfortable	Feeling angry
		Feeling depressed
		Feeling alone
		Had difficulty falling asleep
Physical independence	Have normal speech	
	Able to wash, brush teeth, shave	
	Able to look after your own appearance	
	Able to write	
	Able to return to work/usual home activities	
Psychological support	Been able to communicate with MD	Feeling confused
	Able to communicate with family/friends	
	Able to communicate with visiting healthcare worker	
	Having support from family/friends	
	Getting support from visiting healthcare worker	
	Able to understand instructions and advice	
Pain		Moderate pain
		Severe pain
		Headache
		Muscle pains
		Backache
		Sore throat
		Sore mouth

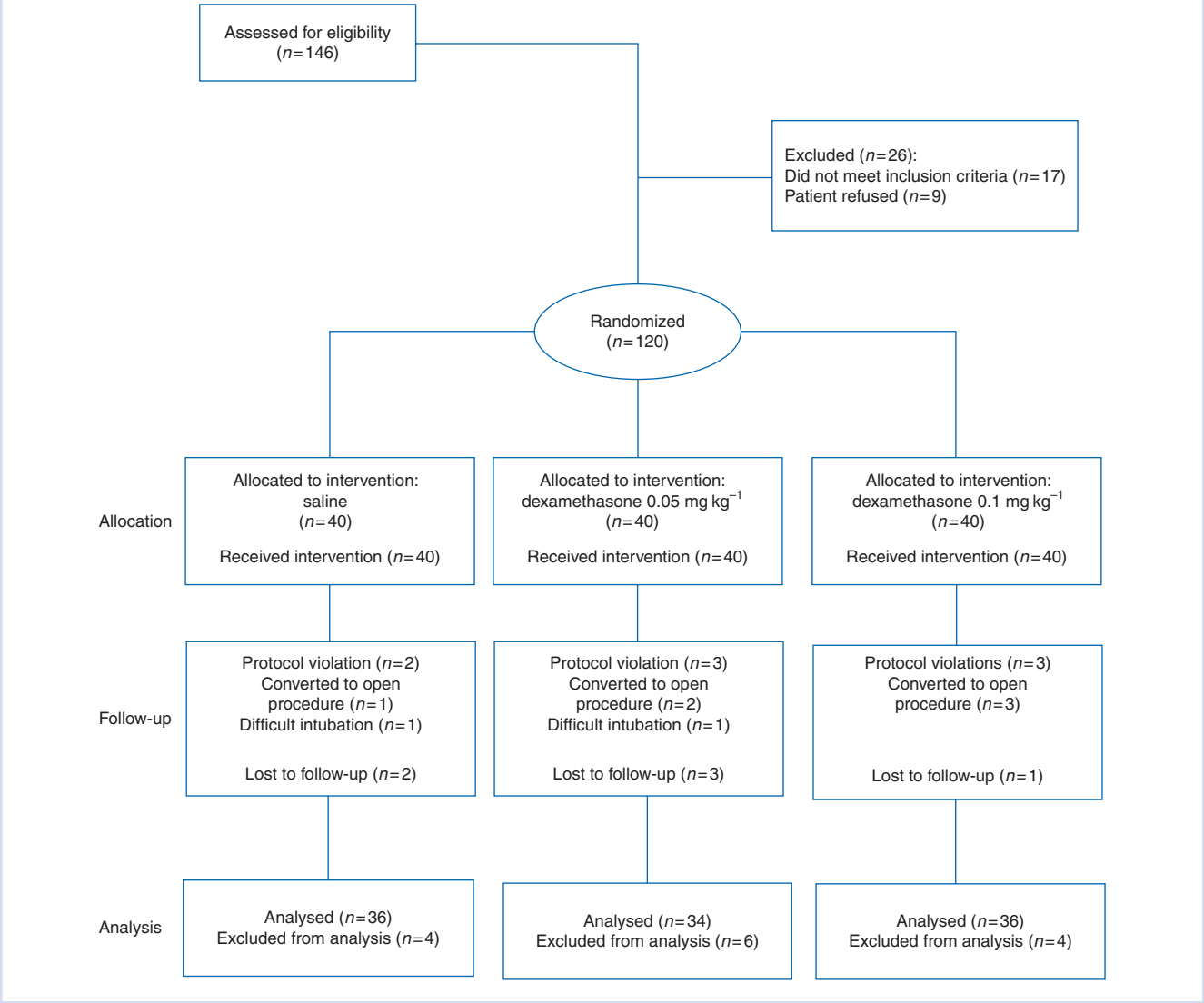

Fig 1 Consort flow study diagram.

Results

The details of the conduct of the study are shown in Figure 1. One hundred and twenty subjects were randomized and 106 completed the study. Patients were enrolled consecutively from January 2010 through September 2010. Patient's baseline characteristics and surgical factors were not different among groups (Table 2).

The median (IQR) global recovery score (QoR-40) 24 h after discharge in the dexamethasone 0.1 mg kg^{-1} group was 193 (192–195) which was greater than the score for the dexamethasone 0.05 mg kg^{-1}, 179 (175–185) ($P=0.004$) or saline, 171 (160–182) groups ($P<0.005$). The dimensions of the QoR-40 questionnaire are shown in Figure 2. The dexamethasone 0.01 mg kg^{-1} group reported higher median scores in every dimension of the QoR-40 compared with saline and in the physical independence and pain dimensions compared with dexamethasone 0.05 mg kg^{-1}.

Responses to individual items of the QoR-40 in the physical comfort, emotional state, psychological support, and pain dimension that demonstrated differences among groups are shown in Table 3. The effect of dexamethasone 0.05 mg kg^{-1} on recovery scores are most apparent in physical comfort dimension in restfulness and reduced retching compared with saline. In the other QoR-40 dimensions, anxiousness, bad dreams, and moderate pain were reduced compared with saline. The effects of dexamethasone 0.1 mg kg^{-1} compared with saline were seen in all dimensions of the QoR-40 questionnaire. In addition, dexamethasone 0.1 mg kg^{-1} demonstrated a greater effect on sore throat and muscle pain, reduced confusion, difficulty in falling asleep and a reduced median nausea score compared with dexamethasone 0.05 mg kg^{-1}.

NRS pain scores and opioid consumption in the first hour in the recovery room did not differ among groups (Table 4). Cumulative opioid consumption by discharge was lower in

Table 2 Subject characteristics preoperative and operative data. Data presented as mean(SD), median (IQR), or *n*(%)

	Saline ($n=36$)	Dexamethasone 0.05 mg kg^{-1} ($n=34$)	Dexamethasone 0.1 mg kg^{-1} ($n=36$)	*P*-value
Age	36 (11)	36 (7)	39 (11)	0.23
Body mass index (kg m^{-2})	25.3 (6.3)	24.9 (6.3)	25.3 (4.4)	0.75
ASA physical status (*n*)				
I	22	17	18	0.57
II	14	17	18	
Mallampati class (*n*)				
I	22	18	16	0.38
II	14	16	20	
Intubation attempts (*n*)				
One	31	32	30	0.42
Two	5	2	6	
Cricoid pressure applied (*n*)				
Yes	12	11	13	0.96
No	24	23	23	
Time to perform intubation (s)	12 (10–16)	12 (11–17)	14 (9–20)	0.71
Blood with suction at end of case (*n*)	4	5	9	0.31
IV fluids	1373 (472)	1350 (428)	1410 (675)	0.95
Total remifentanil dose (μg)	500 (350–750)	618 (407–927)	575 (400–750)	0.66
Surgical duration (min)	81 (60–115)	90 (72–126)	78 (60–112)	0.16

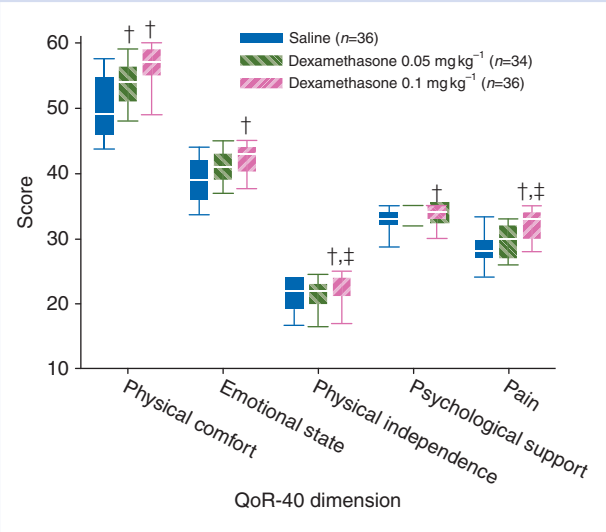

Fig 2 Box plot of dimensions of QoR-40 questionnaires completed 24 h after outpatient gynecological laparoscopic surgery. Median values shown as solid line within box of 25 and 75th percentile values. Whiskers represent 5th and 95th percentile values. Single daggers mean different from saline, $P=0.05$. Double daggers mean different from dexamethasone 0.05 mg kg^{-1}, $P=0.05$. Data were compared using the Kruskal–Wallis and the multiple comparison *Z*-value test (Dunn's test) with Bonferroni correction.

the 0.1 mg kg^{-1} dexamethasone group compared with the dexamethasone 0.05 mg kg^{-1} group and saline groups. The presence and intensity of sore throat at 1 h was similar among groups but both the incidence and severity of sore throat were less in the dexamethasone groups compared with saline at 3 and 24 h (Table 4). The presence of sore throat was less in the dexamethasone 0.1 mg kg^{-1} group compared with saline at 24 h, but the incidence and severity was not different between dexamethasone groups. The severity of coughing among the groups was similar at 3 h, but less at 24 in the dexamethasone 0.1 mg kg^{-1} group compared with dexamethasone 0.05 mg kg^{-1} or saline. Hoarseness was reduced in patient perceived severity in the dexamethasone 0.1 mg kg^{-1} group compared with dexamethasone 0.05 mg kg^{-1} and saline groups at 3 and 24 h. Time to meet discharge criteria was decreased after dexamethasone 0.1 mg kg^{-1} compared with the saline. Post discharge 24 h opioid/paracetamol consumption was less in the 0.1 mg kg^{-1} dexamethasone group compared with dexamethasone 0.05 mg kg^{-1} and saline. Ibuprofen consumption did not differ among groups in the first 24 h.

Discussion

The important finding of this study was the dose-dependent effect of dexamethasone on quality of recovery after outpatient gynaecological surgery. Dexamethasone 0.1 mg kg^{-1} but not 0.05 mg kg^{-1} reduced nausea and vomiting and opioid consumption in the recovery room, sore throat, coughing, and hoarseness at 3 h post-surgery and reduced time to discharge readiness. The quality of the post-discharge recovery assessed at 24 h was improved with dexamethasone 0.1 mg kg^{-1} compared with both saline and dexamethasone 0.05 mg kg^{-1}. Patients receiving dexamethasone 0.1 mg kg^{-1} reported improvement in physical, emotional, psychological, and pain domains compared with placebo. They also had less severe airway morbidities at 24 h. Most

Table 3 Differences in QoR-40 items among groups. Data presented as median (MAD). †Different from saline. ‡Different from dexamethasone, 0.05 mg kg^{-1}. Data analysed using the Kruskal–Wallis *H* test. *Post hoc* comparisons made using Dunn's test with Bonnferoni correction at a corrected $P=0.05$. *=All items scored on a five-point (1–5) Likert scale. ¶Positive characteristics score range; 1=none of the time to 5=all of the time. §Negative characteristics score range; 1=all of the time to 5=none of the time

Sphere of recovery	Item	Group	Scores median (MAD)	Distribution of responses (%)				
				1	2	3	4	5
Physical comfort	Breathe easily¶	Saline	4 (0)	0	0	11	61	28
		Dexamethasone 0.05 mg kg^{-1}	4 (1)	0	0	6	44	50
		Dexamethasone 0.1 mg kg^{-1}	5 (0)†	0	0	0	24	76
	Good sleep¶	Saline	3 (1)	0	22	31	22	25
		Dexamethasone 0.05 mg kg^{-1}	4 (0.5)	0	6	26	50	18
		Dexamethasone 0.1 mg kg^{-1}	4 (1)†	3	8	13	30	46
	Enjoy food¶	Saline	4 (1)	0	6	31	38	25
		Dexamethasone 0.05 mg kg^{-1}	4 (0)	0	3	12	73	12
		Dexamethasone 0.1 mg kg^{-1}	5 (0)†,‡	2	3	11	27	57
	Feel rested¶	Saline	4 (1)	0	11	28	42	19
		Dexamethasone 0.05 mg kg^{-1}	4 (1)†	0	0	18	41	41
		Dexamethasone 0.1 mg kg^{-1}	5 (0)†	0	0	5	38	57
	Nausea§	Saline	4 (1)	0	14	14	36	36
		Dexamethasone 0.05 mg kg^{-1}	4 (1)	0	0	26	26	47
		Dexamethasone 0.1 mg kg^{-1}	5 (0)†,‡	0	0	3	24	73
	Retching§	Saline	4 (1)	0	3	6	44	47
		Dexamethasone 0.05 mg kg^{-1}	5 (0)†	0	0	0	21	79
		Dexamethasone 0.1 mg kg^{-1}	5 (0)†	0	0	0	11	89
	Vomiting§	Saline	5(0)	0	8	6	28	58
		Dexamethasone 0.05 mg kg^{-1}	5(0)	0	0	0	21	79
		Dexamethasone 0.1 mg kg^{-1}	5(0)†	0	0	0	5	95
	Feeling restless§	Saline	4(1)	0	0	3	47	50
		Dexamethasone 0.05 mg kg^{-1}	5(0)	0	0	0	23	76
		Dexamethasone 0.1 mg kg^{-1}	5(0)†	0	0	0	11	89
	Shivering§	Saline	5(0)	0	0	3	22	75
		Dexamethasone 0.05 mg kg^{-1}	5(0)†	0	0	0	3	97
		Dexamethasone 0.1 mg kg^{-1}	5(0)	0	0	3	5	92
	Feeling cold§	Saline	4(1)	0	0	0	75	25
		Dexamethasone 0.05 mg kg^{-1}	5(0)†	0	0	3	21	76
		Dexamethasone 0.1 mg kg^{-1}	5(0)†	0	0	0	27	73
Emotional state	General well-being§	Saline	4(0.5)	0	8	25	50	17
		Dexamethasone 0.05 mg kg^{-1}	4(0.5)	0	6	9	50	35
		Dexamethasone 0.1 mg kg^{-1}	5(0)†	0	0	16	24	60
	Feel in control¶	Saline	4(1)	0	0	28	47	25
		Dexamethasone 0.05 mg kg^{-1}	4(1)	0	3	18	29	50
		Dexamethasone 0.1 mg kg^{-1}	5(0)†	0	0	5	38	57
	Feeling comfortable¶	Saline	3(1)	0	8	44	28	20
		Dexamethasone 0.05 mg kg^{-1}	4(1)	0	3	15	53	29
		Dexamethasone 0.1 mg kg^{-1}	4(1)†	0	0	16	35	49
	Bad dreams§	Saline	5(0)	0	0	0	36	64
		Dexamethasone 0.05 mg kg^{-1}	5(0)†	0	0	0	6	94
		Dexamethasone 0.1 mg kg^{-1}	5(0)†	0	0	0	13	87
	Feeling anxious§	Saline	5(0)	0	0	3	23	74
		Dexamethasone 0.05 mg kg^{-1}	5(0)†	0	0	0	0	100
		Dexamethasone 0.1 mg kg^{-1}	5(0)	0	0	0	13	87
	Difficulty falling asleep§	Saline	4(1)	0	0	36	31	33
		Dexamethasone 0.05 mg kg^{-1}	4(1)	0	3	32	32	33
		Dexamethasone 0.1 mg kg^{-1}	5(0)†,‡	0	3	13	19	65

Continued

Table 3 *Continued*

Sphere of recovery	Item	Group	Scores median (MAD)	Distribution of responses (%)				
				1	2	3	4	5
Psychological support	Feeling confused[§]	Saline	4(0)	0	0	17	69	14
		Dexamethasone 0.05 mg kg^{-1}	4(0)	0	0	15	56	29
		Dexamethasone 0.1 mg kg^{-1}	5(0)[†,‡]	0	0	8	38	54
Pain	Moderate[§]	Saline	3(1)	6	28	39	25	2
		Dexamethasone 0.05 mg kg^{-1}	4(0.5)[†]	0	6	41	50	3
		Dexamethasone 0.1 mg kg^{-1}	4(1)[†]	0	11	19	46	24
	Severe[§]	Saline	4(1)	0	0	8	67	25
		Dexamethasone 0.05 mg kg^{-1}	4(1)	0	0	3	47	50
		Dexamethasone 0.1 mg kg^{-1}	5(0)[†]	0	0	0	30	70
	Headache[§]	Saline	5(0)	0	3	0	42	55
		Dexamethasone 0.05 mg kg^{-1}	5(0)	0	3	0	44	53
		Dexamethasone 0.1 mg kg^{-1}	5(0)[†]	0	0	0	19	81
	Muscle pain[§]	Saline	4(0.5)	0	0	14	50	36
		Dexamethasone 0.05 mg kg^{-1}	4(0)	0	6	18	56	20
		Dexamethasone 0.1 mg kg^{-1}	5(0)[†,‡]	0	3	5	24	68
	Sore throat[§]	Saline	4(1)	0	14	31	39	17
		Dexamethasone 0.05 mg kg^{-1}	4(1)	0	12	23	27	38
		Dexamethasone 0.1 mg kg^{-1}	5(0)[†,‡]	0	0	5	32	63

importantly, opioid consumption in the first 24 h after discharge was reduced with dexamethasone 0.1 mg kg^{-1}.

A major determinant for discharge after ambulatory surgery is the quality of postoperative pain control.[12] In addition to the direct influence of pain on readiness to discharge, side-effects of opioid analgesics such as nausea, vomiting, sedation, and urinary retention can also delay discharge time. The dose-related effects of dexamethasone observed in this study have important clinical implications since practice guidelines for prevention of postoperative nausea and vomiting after ambulatory surgery favour the use of the 0.05 mg kg^{-1} dose.[4] Another factor that may delay discharge and prolong recovery room stay after ambulatory surgery is the presence of a sore throat since pain related to the sore throat could make patients reluctant to go home.[8] Dexamethasone 0.05 and 0.1 mg kg^{-1} reduced sore throat pain compared with saline at 3 h which may have contributed to a faster discharge process. The reduced airway morbidity at 24 h in the dexamethasone 0.1 mg kg^{-1} group compared with both dexamethasone 0.05 mg kg^{-1} and saline represents additional evidence of improved quality of recovery with this dose.

Multimodal analgesic techniques are frequently used to improve postoperative pain management and reduce opioid-related side-effects.[13 14] Several strategies including i.v. local anaesthetics, non-steroidal anti-inflammatory drugs, paracetamol, and *N*-methyl-D-aspartic acid receptor antagonists have been demonstrated to be effective after outpatient surgery.[15] The effect of corticosteroids on postoperative analgesia has not been as consistently demonstrated, and this may represent the wide variation in dexamethasone dosage studied. Wu and colleagues reported lower pain scores in the immediate postoperative period on subjects receiving 5 mg dexamethasone for outpatient anorectal surgery compared with saline;[16] however, in patients undergoing sinus surgery, Al-Qudah and colleagues did not find a difference in postoperative pain scores when comparing 8 mg of dexamethasone with placebo.[17] Jokela and colleagues demonstrated that 10 and 15 mg of dexamethasone had opioid sparing effects after laparoscopic hysterectomy.[18] Likewise, Haval and colleagues demonstrated lower VAS scores at 24 h compared with placebo when 16 mg of dexamethasone was administered to patients undergoing outpatient breast surgery.[19] The results of the aforementioned studies together with the results of the current study suggest that the analgesic and opioid-sparing effect of dexamethasone varies with the dose of dexamethasone administered as well as the type of surgical procedure. We restricted our study to a single type of surgery, outpatient gynaecological laproscopy, and demonstrated that dexamethasone 0.1 mg kg^{-1} provided effective multimodal analgesia; however, we cannot generalize our finding to other surgical procedures.[20]

Several studies in ambulatory patients have evaluated quality of recovery primarily as improvement in postoperative pain, nausea, and vomiting;[21–23] however, this approach has limited significance when not adjusted for patient's level of activity, emotional status, and independence. In the current study, we used the QoR-40 questionnaire,[9] designed to measure patient's health status after surgery and anesthesia.[24–26] In a review of postoperative recovery assessment measures after ambulatory surgery, the QoR-40 was the only test that fulfilled the criteria of: appropriateness, reliability, validity, responsiveness, precision,

Table 4 Postoperative pain management, side-effects, and time to discharge. Data presented as median (IRQ) or *n*(%). †Different from saline. ‡Different from dexamethasone 0.05 mg kg^{-1}. *Post hoc* comparisons made using Dunn's test with Bonnferoni correction to $P=0.05$. §Two subjects in saline group and two subjects in dexamethasone 0.05 mg kg^{-1} group admitted for 23 h observation excluded from analysis

	Saline ($n=36$)	Dexamethasone 0.05 mg kg^{-1} ($n=34$)	Dexamethasone 0.1 mg kg^{-1} ($n=36$)	*P*-value
NRS for pain				
Post anaesthesia care unit admission	4 (0–6)	4 (2–7)	3 (0–6)	0.25
30 min	5 (2–6)	4 (1–6)	3 (0–5)	0.25
60 min	3 (2–4)	2 (0–4)	2 (0–4)	0.32
Required opioid in post anaesthesia recovery room [*n*(%)]	29 (81)	28 (82)	23 (64)	0.13
Time to first opioid administration (min)	15 (10–50)	14 (5–90)	46 (15–75)	0.18
Cumulative opioid consumption (iv morphine equivalents)				
First hour after operation	4.0 (1.4–5.9)	3.3 (1.0–5.5)	2.7 (0–5.3)	0.1
At discharge	5.3 (2.7–7.8)	5.3 (2.4–8.8)	2.7 (0–6.3)†,‡	0.02
Nausea [*n*(%)]	22 (61)	13 (38)	9 (25)†,‡	0.006
Vomiting [*n*(%)]	13 (36)	7 (21)	1 (3)†,‡	0.002
Sore throat present (*n*)				
1 h	25	19	18	0.23
3 h	24	17	10†	0.004
NRS for sore throat pain				
1 h	30 (0–40)	20 (0–30)	10 (0–30)	0.25
3 h				
resting	30 (0 to 40)	2.5 (0–30)†	0 (0–20)†	0.006
swallowing	40 (5–60)	5 (0–40)†	0.5 (0–25)†	0.003
24 h				
Resting	40 (20–47)	20 (0–40)	0 (0–20)†	0.003
Swallowing	50 (30–60)	30 (0–50)	0(0–20)†	0.001
Cough (none/minimal/moderate)				
3 h	4/22/2010	8/18/2008	13/17/6	0.12
24 h	2/18/2016	2/21/2011	14/14/8†,‡	0.001
Hoarseness (none/previous/noted only by patient/easily noticed)				
3 h	2/5/9/20	10/9/12/3	20/6/4/6†	0.0001
24 h	5/10/15/6	11/6/11/6	18/8/6/4†	0.04
Time to meet discharge criteria (min)	120 (105–150)	90 (90–120)	90 (75–112)†,‡	0.005
Discharge time (min)§	270 (224–315)	256 (191–285)	217 (169–287)†,‡	0.05
Pain medication consumption in the first 24 h after discharge				
Ibuprofen (mg)	1600 (800–2000)	1200 (0–2000)	1000 (400–1700)	0.42
Paracetamol (mg)	650 (650–975)	650 (325–1056)	325 (325–650)†	0.03
Opioid (oral morphine equivalents mg)	20 (20–30)	10 (10–32.5)	10 (10–20)†	0.01

interpretability, acceptability, and feasibility.[27] The authors did note that the QoR-40 was not specifically designed for use in ambulatory surgery and therefore the clinical correlate of the change in global QoR-40 values such as those observed in this study are difficult to assess. The responsiveness of this instrument has been assessed in patients evaluated before and after surgery.[9] The calculated standardized response mean of 0.65 was suggested by the authors to represent sensitivity of the instrument to clinically significant changes. In a study of outcomes after cardiac surgery, a poorer quality of life at 3 months was found in subjects that had median QoR-40 global values 10 points less than those with higher QoR-40 values 3 days after cardiac surgery.[28] Days 1 and 3 QoR-40 values were highly correlated. Therefore, we believe that the differences found in QoR-40 in this study represent clinically significant improvement in recovery with dexamethasone compared with saline.

Improved self-reported quality of recovery and reduced emetic symptoms at 24 h after discharge for dexamethasone 4 mg vs control after ambulatory laparoscopic cholecystectomy has previously been reported.[29] The QoR scale used in the aforementioned study was based on a 0–100 self-reported scale and did not evaluate the domains of recovery. We found that dexamethasone 0.05 mg kg^{-1} primarily affected the physical comfort sphere of recovery; whereas dexamethasone 0.1 mg kg^{-1} improved recovery in all domains of the QoR-40. It is likely that at the 0.05 mg kg^{-1}

dose the effects of dexamethasone on the QoR-40 most likely reflect its antiemetic actions, but at 0.1 mg kg^{-1} analgesic and euphoric effects are likely to have contributed to the increase in QoR-40 scores. Patients might have the same level of analgesia assessed by visual analogue scale scores but cannot be compared in terms of quality of recovery if they are unable to resume normal daily activities. In the current study, dexamethasone 0.1 mg kg^{-1} produced better physical comfort score (nausea, vomiting, retching, sleep, ability to eat). They also had greater physical independence scores. The higher dexamethasone group not only had less pain but they were also more active 24 h after surgery. These finding have important economic implication when evaluating costs associated with ambulatory procedures.[30]

The mechanism of the analgesic effect of dexamethasone is multifactorial. It has anti-inflammatory properties by inhibition of phospolipase-A_2, cytokines production, and decreasing polymorphonuclear leucocyte function, suppresses the production of free oxygen radicals and nitric oxide by endothelial cells,[31] and reduces postoperative oedema.[32] We suspect that the anti-inflammatory effects of dexamethasone may be responsible for the reduced clinical symptoms of airway morbidity, since the acute inflammatory reaction produced by the presence of the tracheal tube or direct trauma to the airway mucosa are believed to be mechanisms for the development of postoperative sore throat after procedures requiring tracheal intubation.[33–35]

We administered dexamethasone before the patient was taken to the operating room rather than after induction of anaesthesia which is more commonly done in clinical practice. We did this to optimize the effect of dexamethasone (peak effect 45 min to 1 h) on the stress response during surgical incision and other stress generating portions of surgery especially during the short ambulatory procedures studied. Also, because dexamethasone can produce an excruciating perineal burning in 50–70% of patients, we administered the drug slowly over 10 min diluted in 50 ml of saline.[36 37]

There are limitations to our study. We limited our study to only two doses of dexamethasone and did not evaluate potential side-effects of dexamethasone such as hyperglycaemia, wound healing, and susceptibility to infection. Prior studies have evaluated headache, dizziness, wound infection, and wound healing after dexamethasone use in laproscopic cholecystectomy and a meta-analysis of dexamethasone-related adverse effects did not find an increased risk of these adverse effects at doses of dexamethasone similar to those used in this study.[1] The incidence of wound infection and wound healing problems in clean laparoscopic procedures is extremely low and no antibiotic prophylaxis is given for these procedures. An examination of the charts of the subjects at the follow up visit with the surgeon revealed no reports of problems with wound healing or infection. We limited our study to a single type of surgery with limited amount of a somatic pain component; therefore, our results may not be generalizable to more extensive surgeries. In addition, although the groups were assigned by random allocation and surgical procedure estimates were similar for all cases, the dexamethasone 0.05 mg kg^{-1} group did have more pain ablation procedures, were slightly longer and required more intraoperative remifentanil on examination compared with the saline and dexamethasone 0.1 mg kg^{-1} group, which may have affected the findings of the study. There were, however, no differences in time to meet discharge criteria ($P=0.9$), opioid consumption before discharge ($P=0.3$), or global QoR-40 scores ($P=0.5$) among the surgical procedure groups. The effects of the dexamethasone on quality of recovery observed in this study were in addition to the effects of ketorolac, metaclopramide, and ondansetron which were administered to all patients.

In conclusion, we demonstrated that 0.1 mg kg^{-1} of dexamethasone produced a better quality of recovery with less postoperative pain and better return to normal daily activities after outpatient gynaecological laproscopic surgery when compared with 0.05 mg kg^{-1} of dexamethasone and placebo. The higher dexamethasone dose also produced an opioid-sparing effect, which may be beneficial for improving recovery after ambulatory surgery.

Conflict of interest

None declared.

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