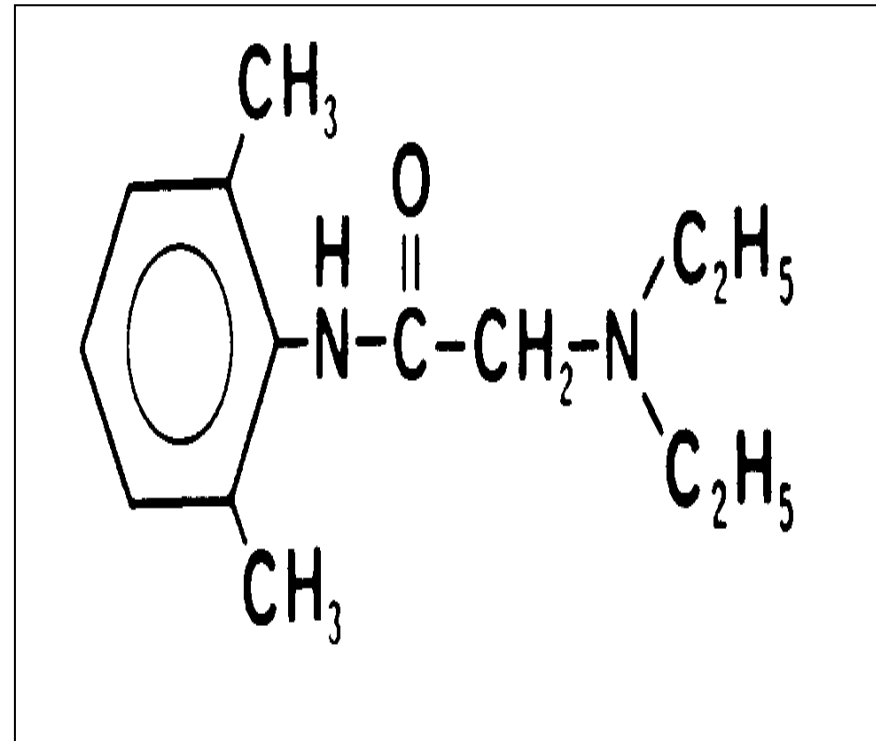

Effect of Low Dose Lidocaine Infusions on Postoperative Analgesic Requirements

J.E. Pellegrini, PhD, CRNA, DNP

Lidocaine

- **Amide Agent**
- *Used as a local anesthetic & antiarrhythmic drug*
 - Epidural
 - Subarachnoid
 - Percutaneous
 - Intravenous



Lidocaine

- Can be used as a primary anesthetic agent
 - Neuraxial administration
 - Central or peripheral nerve blockade
 - Epidural
 - Spinal
 - Bier Block technique etc.
 - Often used as an adjunct or “*bridging agent*” when given in conjunction with general anesthesia
 - Mollify effects of propofol administration
 - 0.5-2 mg/kg to offset pain
 - Rarely given as an integral part of anesthetic plan
-

Lidocaine

- Often viewed as temporizing agent
 - Treatment of acute pain or stimulation
 - Has been shown to possess potent preemptive analgesic properties
 - Traditionally preemptive properties associated with opioids or NSAIDs
 - Can result in significant side effects when used
 - Alterations in hemodynamics
 - Sedation
 - PONV
 - Altered Bowel and Bladder Functioning
 - Coagulation abnormalities (*bleeding dyscrasias*)
-

Lidocaine

■ NSAIDs

- ❑ Often given to offset the side effects produced by opioids
 - ❑ NSAIDs have a positive effect on bowel and bladder function
 - ❑ Not as effective in treating pain from major muscle trauma
 - ❑ Side effects
 - Renal damage
 - Bleeding disorders
 - Allergic responses
-

Lidocaine

- Lidocaine can be used as an agent for multimodal analgesic therapy
 - Lidocaine
 - Peripheral and Central Mode of action
 - Peripherally
 - Localized anti-inflammatory response
 - Centrally
 - Selectively decrease C-fiber activity
-

Lidocaine

- Intravenous lidocaine administration preoperatively & throughout procedure linked to decreasing incidence of hyperalgesia
 - Anti-hyperalgesia- inhibits mechanoreceptors (*prevents cascade of mechanoreceptor stimulation*)
 - Preemptive & Periop admin of IV lidocaine exhibits effects for 36 hrs after surgery
 - Most effective if given preemptively/ postemptively
 - May block postoperative ileus by blocking sympathetic innervation – allowing dominance of parasympathetic innervation in gut
 - May also work by decreasing postoperative inflammatory response (*prostaglandin & other mediators*) in gut
-

Lidocaine

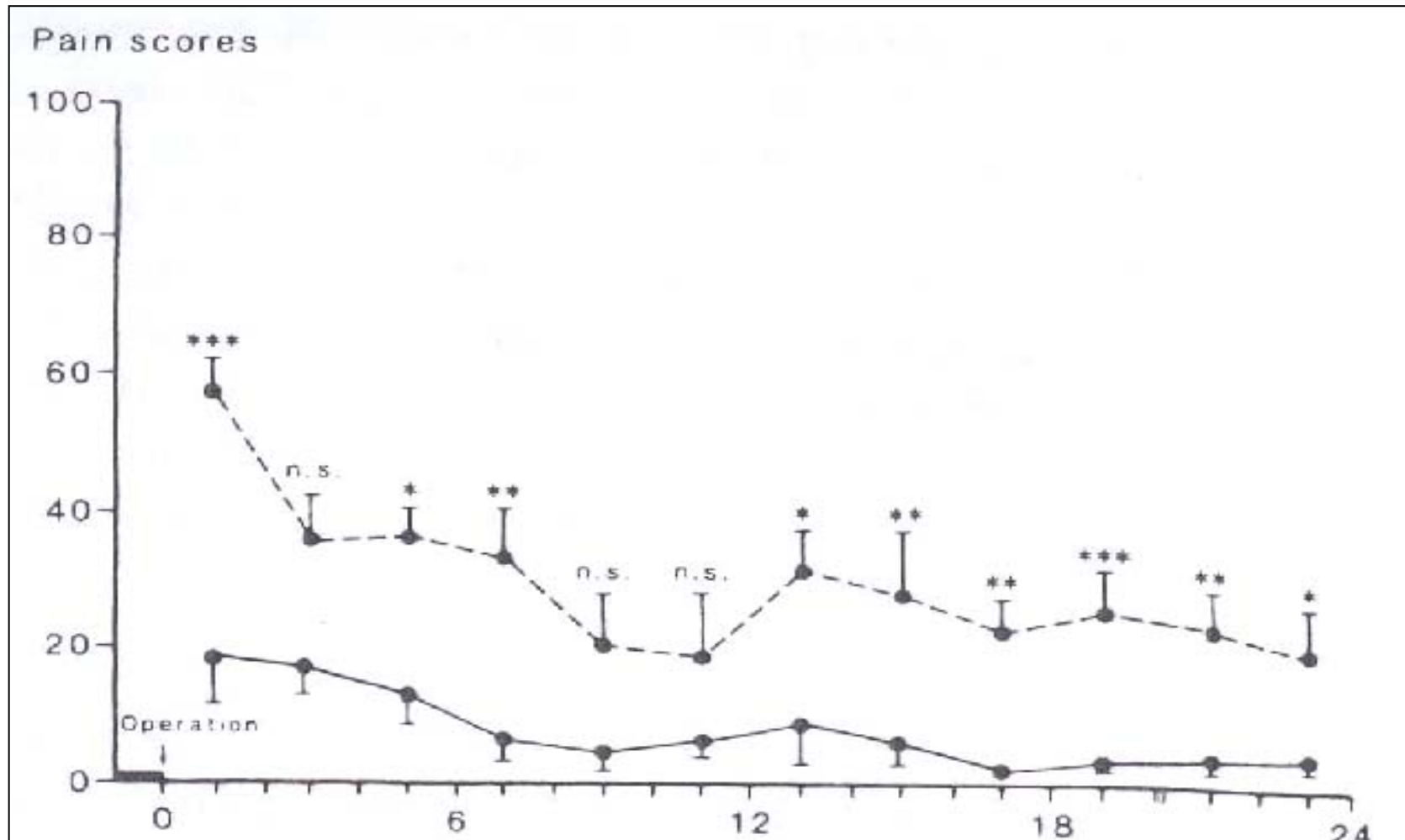
- Act in similar fashion to NSAIDs in relation to maintenance of abdominal reflexes
 - Decrease in postoperative ileus
 - Best if administered preemptively and continued throughout the course of surgical intervention
 - Will continue to provide effect for several hours after discontinuation
 - Routinely given in bolus of 1-2 mg/kg and maintenance infusion of 0.5-2 mg/kg/hr
-

Lidocaine

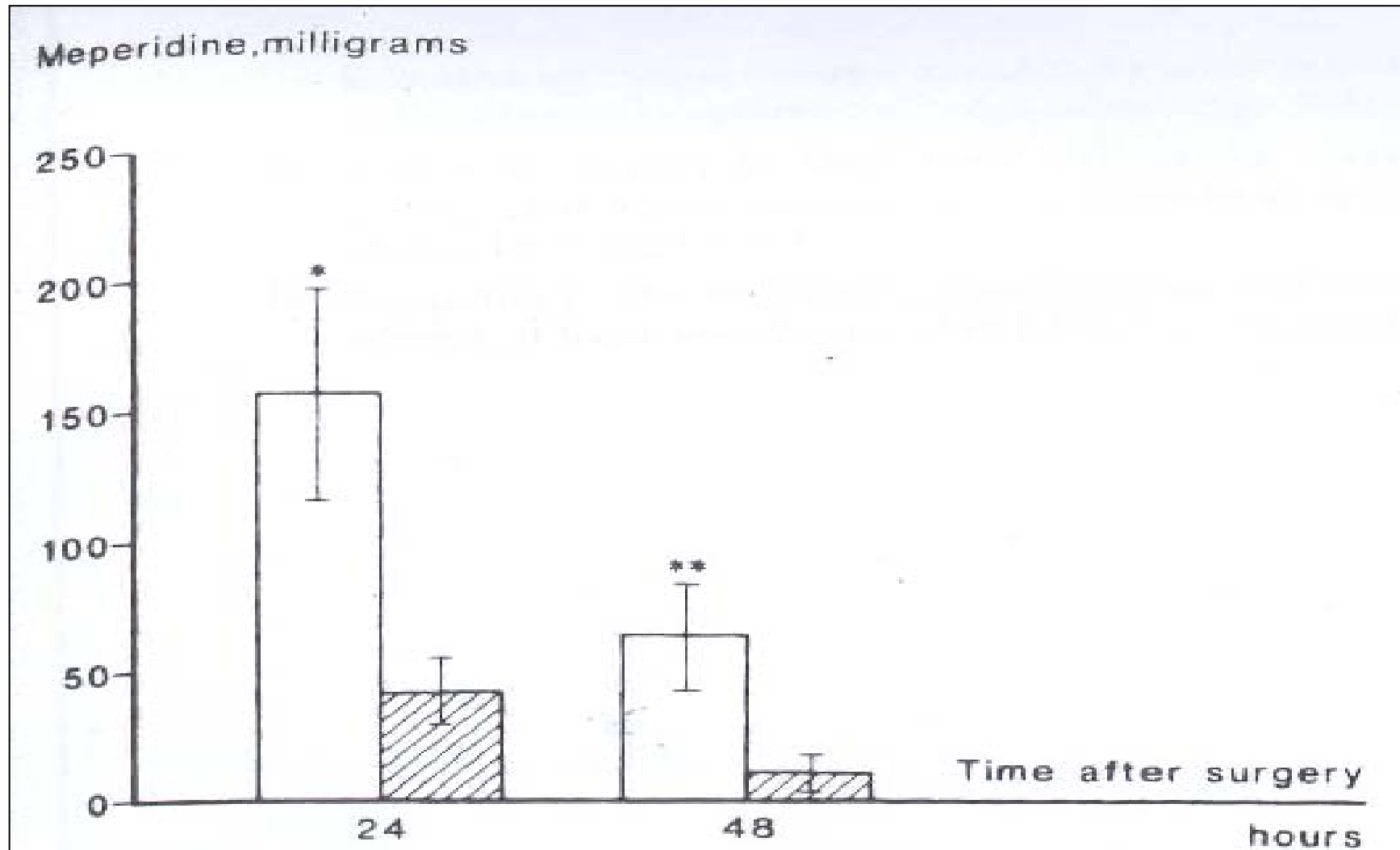
- Useful adjunct in abdominal surgeries
 - Hysterectomy patients
 - Retro pubic prostatectomy patient
 - Open Cholecystectomy
 - Laparoscopic Cholecystectomy
 - Found not to be useful when used in same admixture as morphine PCA
 - Cassuto et al. (open cholecystectomy)
-

Lidocaine

- Cassuto et al.
 - Open cholecystectomy patient trial
 - Small study (20 patients)
 - Bolus dose 100 mg followed by continuous infusion of 2 mg/kg/hr for next 24 hours
 - Decreased Pain Scores Postoperatively
 - Significant decrease in postoperative analgesic requirements (*24 hour totals – MSO₄ Equiv*)
 - 9.4 ± 2 mg (*Lidocaine group*)
 - 29.4 ± 2.5 mg (*Control group*)
-



From: Cassuto J et al. Inhibition of postoperative pain by continuous low-dose intravenous infusion of lidocaine. Anes Analg 1985; 64: 971-4.



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Lidocaine

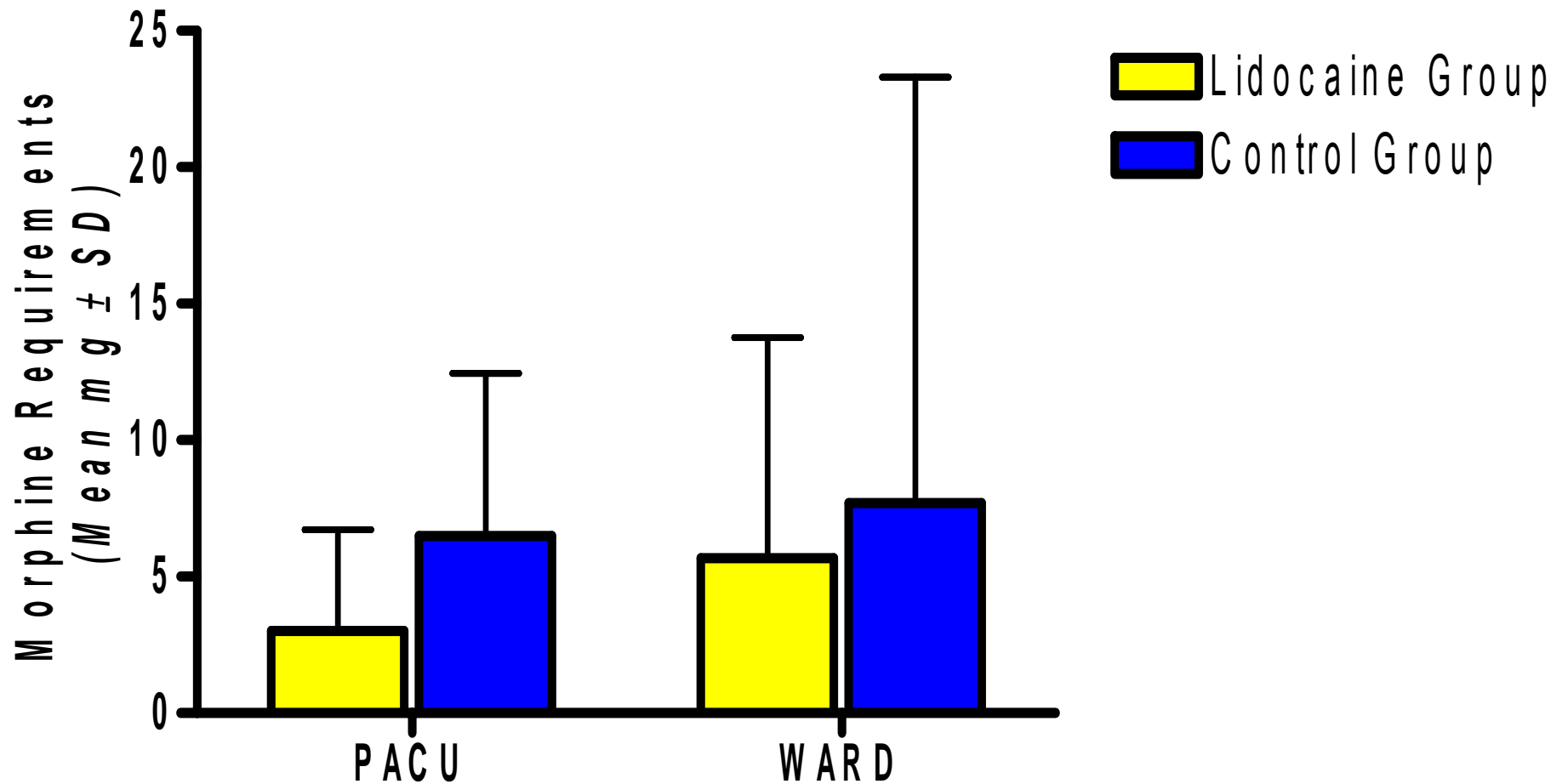
- Cassuto Trial

- Serum levels obtained and no toxicity noted
 - No systemic toxic effects observed
 - Greater analgesia afforded beyond 24 hour infusion time period
 - Problems
 - 24 hour infusion requiring PACU stay
 - Small number of patients
 - Only done on healthy open cholecystectomy patients
-

Lidocaine

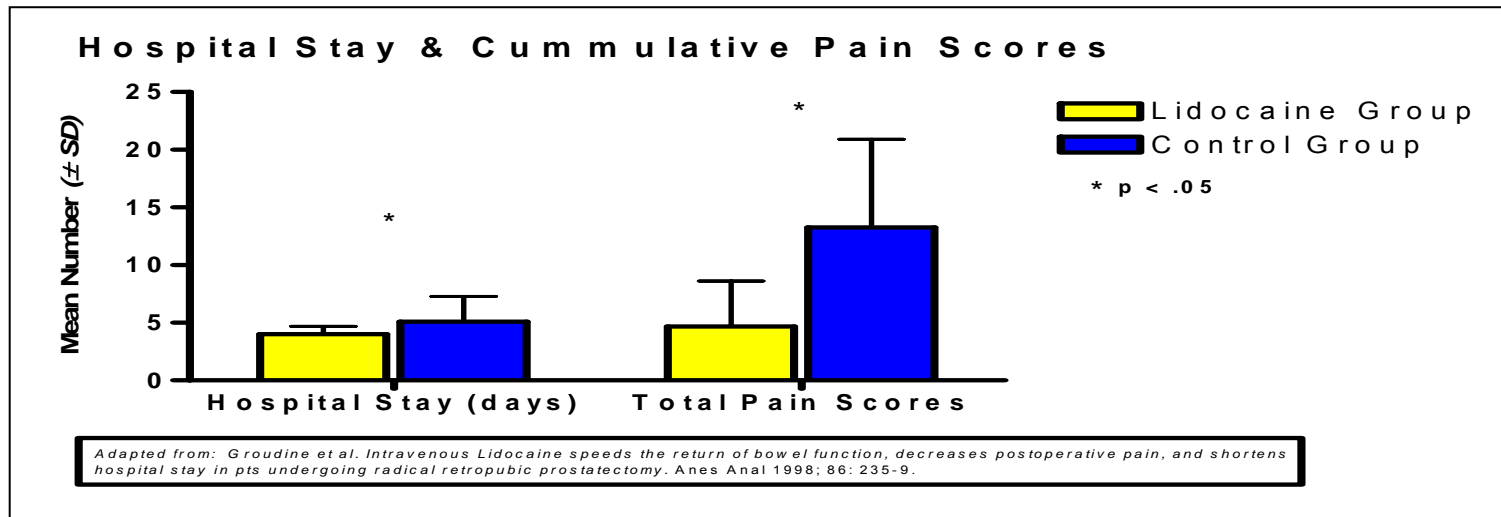
- Groudine et al Trial
 - ❑ Enrolled Patients undergoing Retro pubic radical prostatectomy
 - ❑ Bolus dose of 1.5 mg/kg
 - ❑ Infusion started (2-3 mg/kg/hr) immediately after induction and continued throughout surgery
 - ❑ Infusion DC'd 60 minutes following skin closure
 - ❑ Noted significant decreases in pain scores and analgesic requirements postoperatively
-

Postoperative Analgesic Requirements



Adapted from: Groudine et al. Intravenous Lidocaine speeds the return of bowel function, decreases postoperative pain, and shortens hospital stay in pts undergoing radical retropubic prostatectomy. Anes Anal 1998; 86: 235-9.

Groudine et al Study



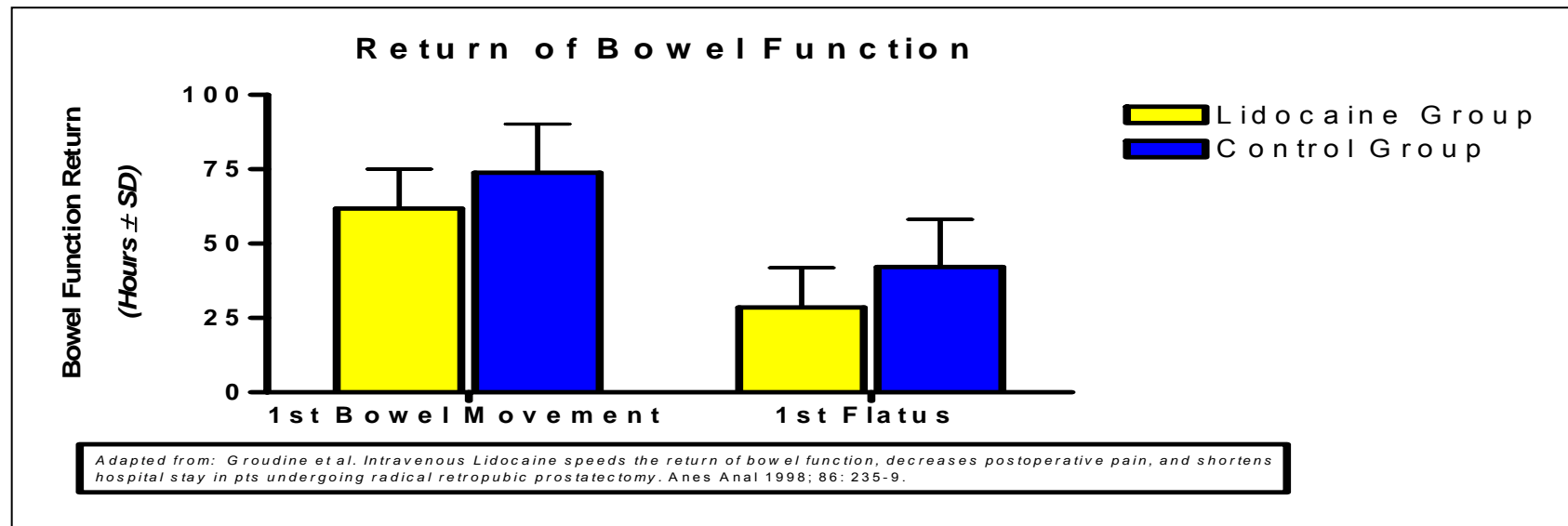
■ Discharge to Home

- 4 ± 0.69 days (*Lidocaine Group*)
- 5.1 ± 2.18 days (*Control Group*)

■ Total Pain Scores

- 4.67 ± 3.94 (*Lidocaine Group*)
- 13.25 ± 7.65 (*Control Group*)

Groudine et al Study



■ Flatus Return

- ❑ 28.5 ± 13.4 hours (*Lidocaine Group*)
- ❑ 42.1 ± 16.0 hours (*Control Group*)

■ Bowel Movement

- ❑ 61.8 ± 13.2 hours (*Lidocaine Group*)
- ❑ 73.9 ± 16.3 hours (*Control Group*)

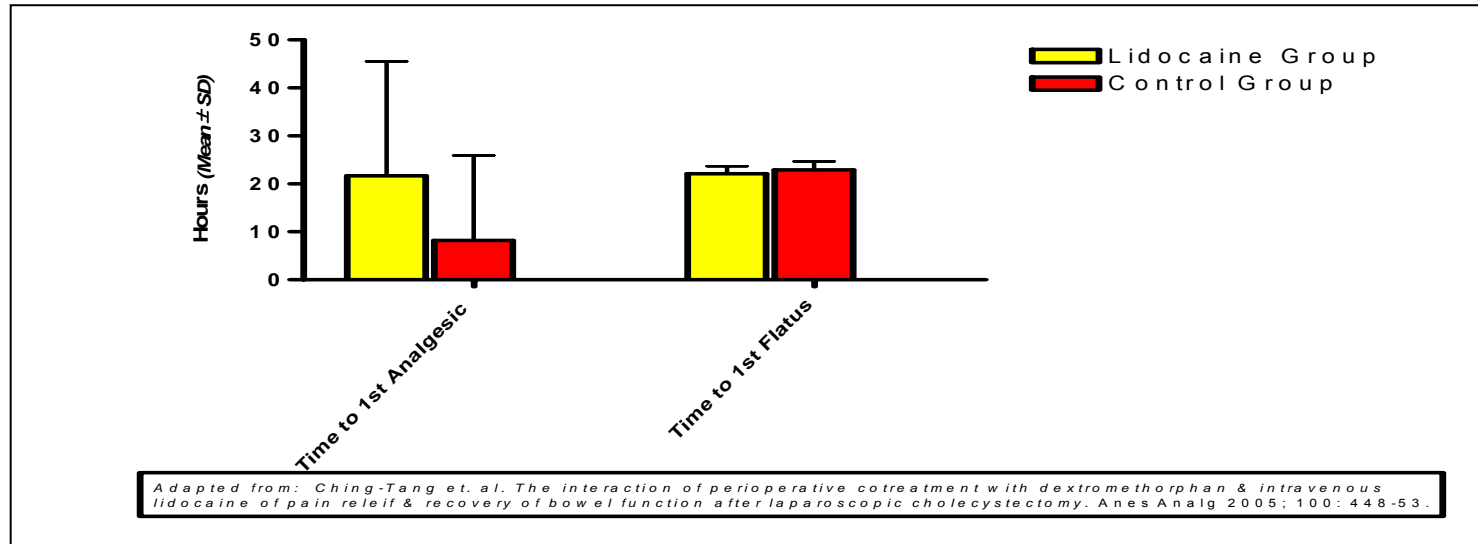
Groudine et al Study

- Differed from Cassuto study in design
 - Bolus
 - Infusion
 - No toxic levels (serological) seen nor systemic toxicity noted in group
 - Did not require extensive monitoring postoperatively
 - Problems
 - Small number (40 subjects total)
 - Less analgesic effects
 - Only enrolled radical prostatectomy patients
-

Lidocaine

- Ching-Tang et al. Study
 - Used a multimodal approach using lidocaine infusion and IM dextromethorphan
 - Laparoscopic cholecystectomy patients
 - 4 group design (Lidocaine infusion, Lido-Dex, Control-Dex, Control only)
 - Lidocaine Group (3 mg/kg lidocaine infusion started 30 minutes before incision & concluded at skin closure)
-

Ching-Tang et al. Study



- **Time to 1st Analgesic**
 - 21.7 ± 23.8 hours (*Lidocaine Group*)
 - 8.2 ± 17.7 hours (*Control Group*)
- **Time to 1st Flatus**
 - 22.1 ± 1.6 hours (*Lidocaine Group*)
 - 22.9 ± 1.8 hours (*Control Group*)

Ching-Tang et al. Study

- Validated analgesic benefit from short term infusion of lidocaine in laparoscopic cholecystectomy patients
 - Inconclusive evidence in relation to return of bowel function
 - Inclusion of Dextromethorphan conflicting variable (study not designed to analyze lidocaine group as independent group –didn't use Solomon design properly)
 - No data reported in relation to time to discharge nor time to first bowel movement
-

Systemic Lidocaine

(Effect on Bowel Function)

- Lidocaine infusions linked to earlier return of bowel function
 - Variable results on postoperative analgesic efficacy
 - Definite advantages in reducing intraoperative analgesic requirements
 - Lidocaine infusions don't appear to slow the time to emergence from GETA
 - Bolus dose 1-1.5 mg/kg on induction
 - Continuous infusion of 2 mg/kg
 - Most trials continue infusions into post-operative period
-

Herroeder S, Pecher s, Schönherr M, Kaulitz G, et al. Systemic lidocaine shortens the length of hospital stay after colorectal surgery: A double-blind, randomized, placebo-controlled trial. *Ann Surg* 2007; 246(2): 192-200.

- Enrolled 66 patients undergoing colorectal surgery & randomly assigned to placebo or lidocaine infusion group
 - Bolus dose of 1.5 mg/kg with induction
 - Continuous infusion of 2 mg/kg initiated immediately after induction → 4 hrs postop
 - Measured inflammatory mediators
-

Herroeder S, Pecher s, Schönherr M, Kaulitz G, et al. Systemic lidocaine shortens the length of hospital stay after colorectal surgery: A double-blind, randomized, placebo-controlled trial. *Ann Surg* 2007; 246(2): 192-200.

Medscape®		www.medscape.com	
Variable	Control Group (n = 29)	Lidocaine Group (n = 31)	P/Test
Age (yr)	56.93 ± 12.04	56.13 ± 11.84	0.72/Wilcoxon
Bodyweight (kg)	73.59 ± 13.93	75.88 ± 13.54	0.52/t test
Gender (M/F) (%)	51.7/48.3	61.3/38.7	0.32/Fisher
ASA score (I/II/III) (%)	11.1/77.8/11.1	6.7/66.7/26.7	0.31/Wilcoxon
Nicotine abuse (Y/N) (%)	24.1/75.9	22.6/77.4	0.56/Fisher
Psychoactive drugs intake (Y/N) (%)	3.4/96.6	16.1/83.9	0.11/Fisher
Hypertension (Y/N) (%)	24.1/75.9	48.4/51.6	0.046/Fisher
Ileocecal resection (n)	0	2	
Hemicolectomy (right) (n)	5	5	
Hemicolectomy (left) (n)	4	1	
Subtotal colectomy (n)	1	0	
Proctocolectomy*† (n)	3	1	
Sigmoid resection (n)	8	12	
High anterior rectum resection (n)	3	2	
Low anterior rectum resection† (n)	1	3	
Rectum exstirpation‡ (n)	2	3	
Others†§¶ (n)	2	2	

Data are mean ± SD, unless indicated as (%) or absolute numbers.
 *Ileoanal-pouch.
 †Ileostomy.
 ‡Colostomy.
 §Ileorectal anastomosis (bypass).
 ¶Explorative laparotomy.
 ††Adhesiolysis.
 Y/N indicates yes or no; ASA, American Society of Anesthesiologists.

Source: Ann Surg © 2007 Lippincott Williams & Wilkins

Herroeder S, Pecher s, Schönherr M, Kaulitz G, et al. Systemic lidocaine shortens the length of hospital stay after colorectal surgery: A double-blind, randomized, placebo-controlled trial. *Ann Surg* 2007; 246(2): 192-200.

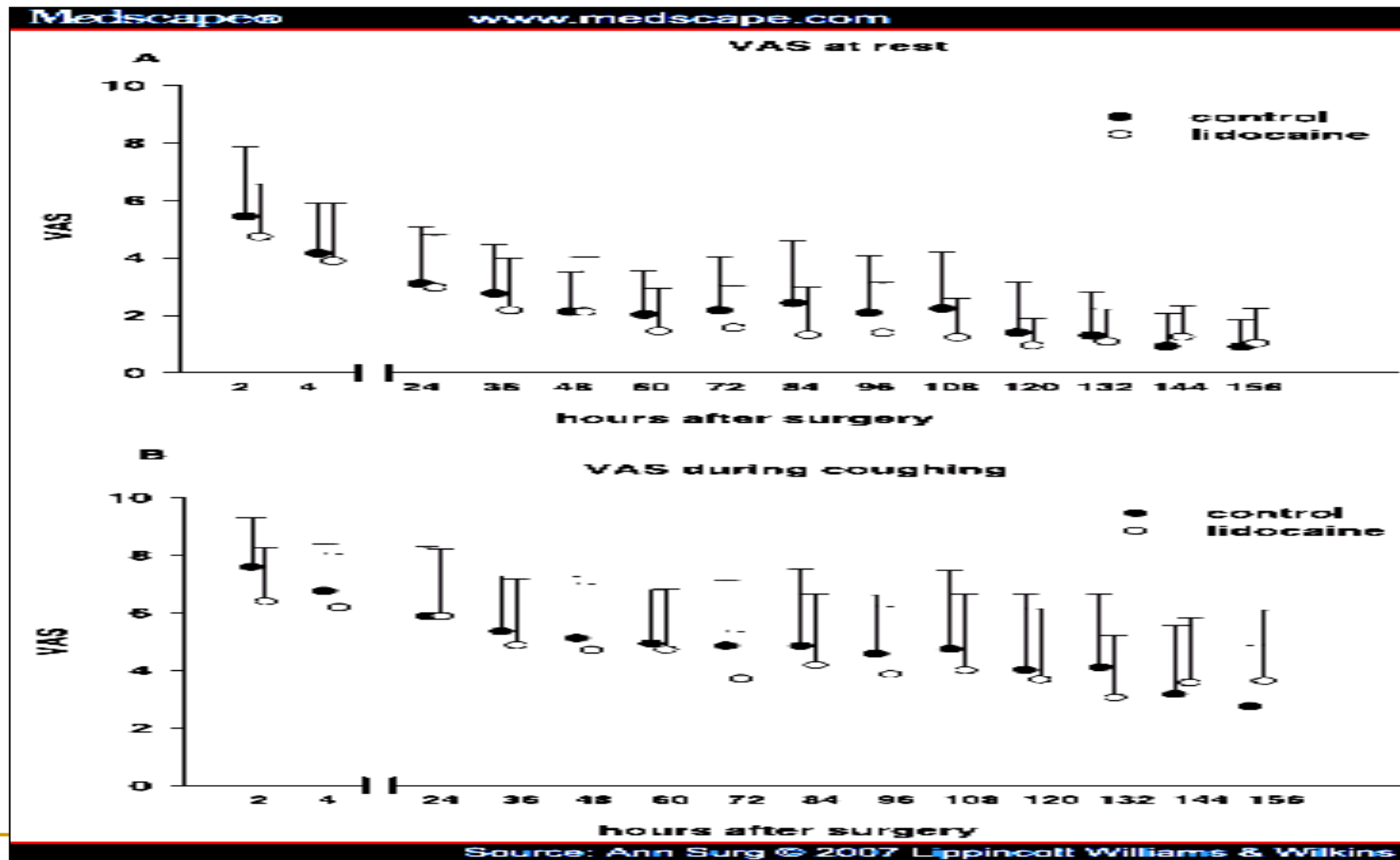
■ Cytokines

- Attenuated levels of IL-6, IL-8, IL-1ra and C3a
 - Differences noted during surgery and following surgery
- Noted that plasma levels of TNF-α and IL-1β did not increase during surgery and IL-10 was unaffected at any time point (*anti-inflammatory cytokine*)
- Cytokines are well known to play role in inflammatory response
 - Inflammation plays key role in promotion of ileus following surgery

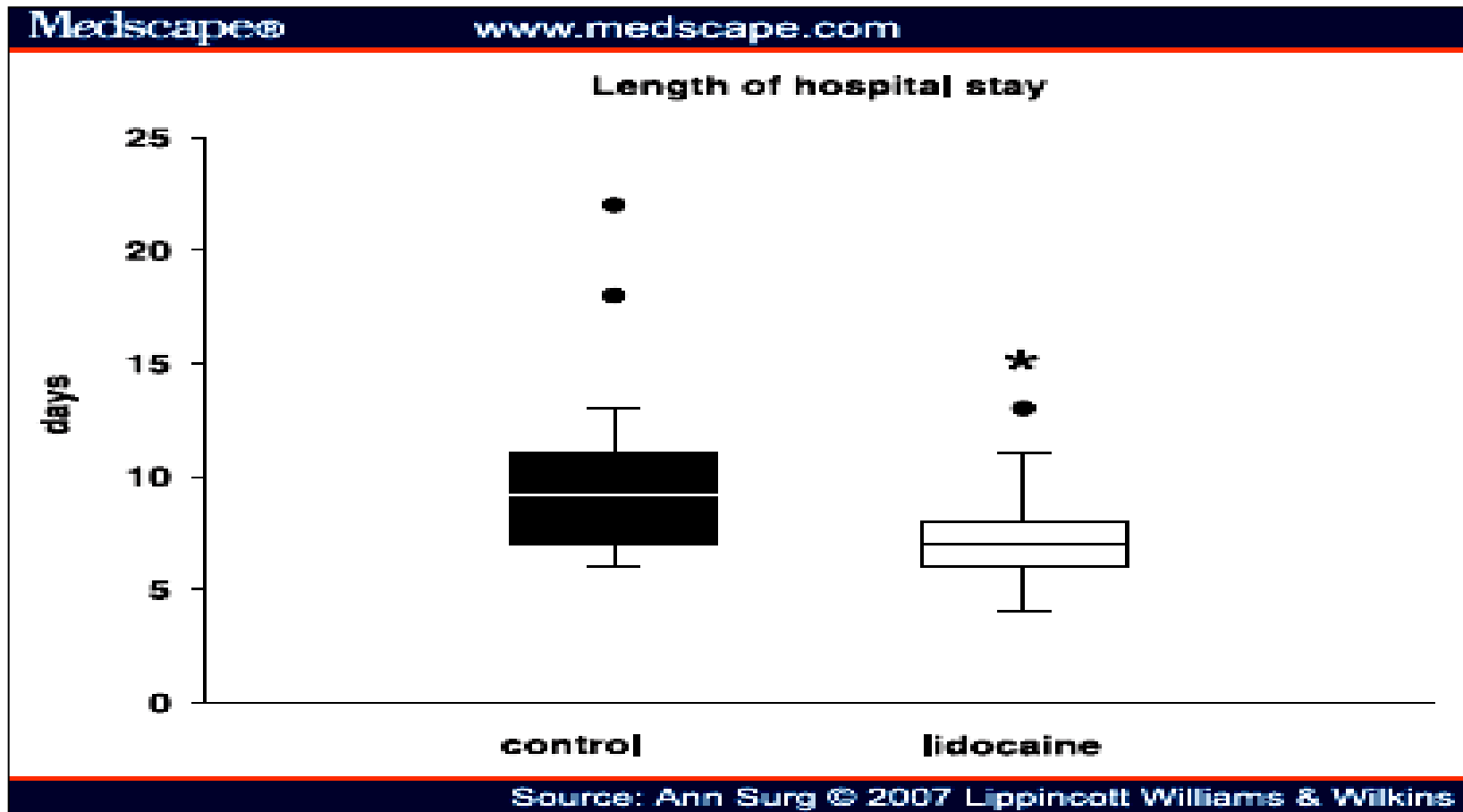
		Medscape® www.medscape.com	
Cytokine	Time	Control Group (n = 29)	Lidocaine Group (n = 31)
IL-6 (pg/mL)	Preop.	10 ± 7	13 ± 7
	End of operation	44 ± 28*	29 ± 17*†
	2-hr Postop.	118 ± 73*	63 ± 50*†
	POD 3	18 ± 11*	11 ± 8†
IL-8 (pg/mL)	Preop.	ND	ND
	End of operation	27 ± 14*	18 ± 12*†
	2-hr Postop.	42 ± 34*	27 ± 19*†
	POD 3	9 ± 7*	6 ± 4*†
IL-1β (pg/mL)	Preop.	3 ± 2	3 ± 2
	End of operation	3 ± 2	3 ± 2
	2-hr Postop.	4 ± 2	3 ± 2†
	POD 3	3 ± 2	3 ± 2
TNF-α (pg/mL)	Preop.	4 ± 3	5 ± 3
	End of operation	5 ± 4	5 ± 3
	2-hr Postop.	5 ± 3	4 ± 3
	POD 3	4 ± 3	5 ± 3
C3a (ng/mL)	Preop.	128 ± 46	138 ± 71
	End of operation	135 ± 56	129 ± 44*†
	2-hr Postop.	287 ± 77*	201 ± 101
	POD 3	187 ± 89*	167 ± 90
IL-1ra (pg/mL)	Preop.	275 ± 163	296 ± 189
	End of operation	1576 ± 934*	987 ± 642*†
	2-hr Postop.	1489 ± 812*	866 ± 537*†
	POD 3	333 ± 196	282 ± 198
IL-10 (pg/mL)	Preop.	ND	ND
	End of operation	32 ± 31*	28 ± 25*
	2-hr Postop.	46 ± 36*	45 ± 31*
	POD 3	ND	ND

Data are mean ± SD.
 *P < 0.05 vs. baseline values.
 †P < 0.05 vs. control patients (RM-ANOVA, corrected with a post hoc Bonferroni test).
 POD indicates postoperative day; ND, nondetectable by the assay used.

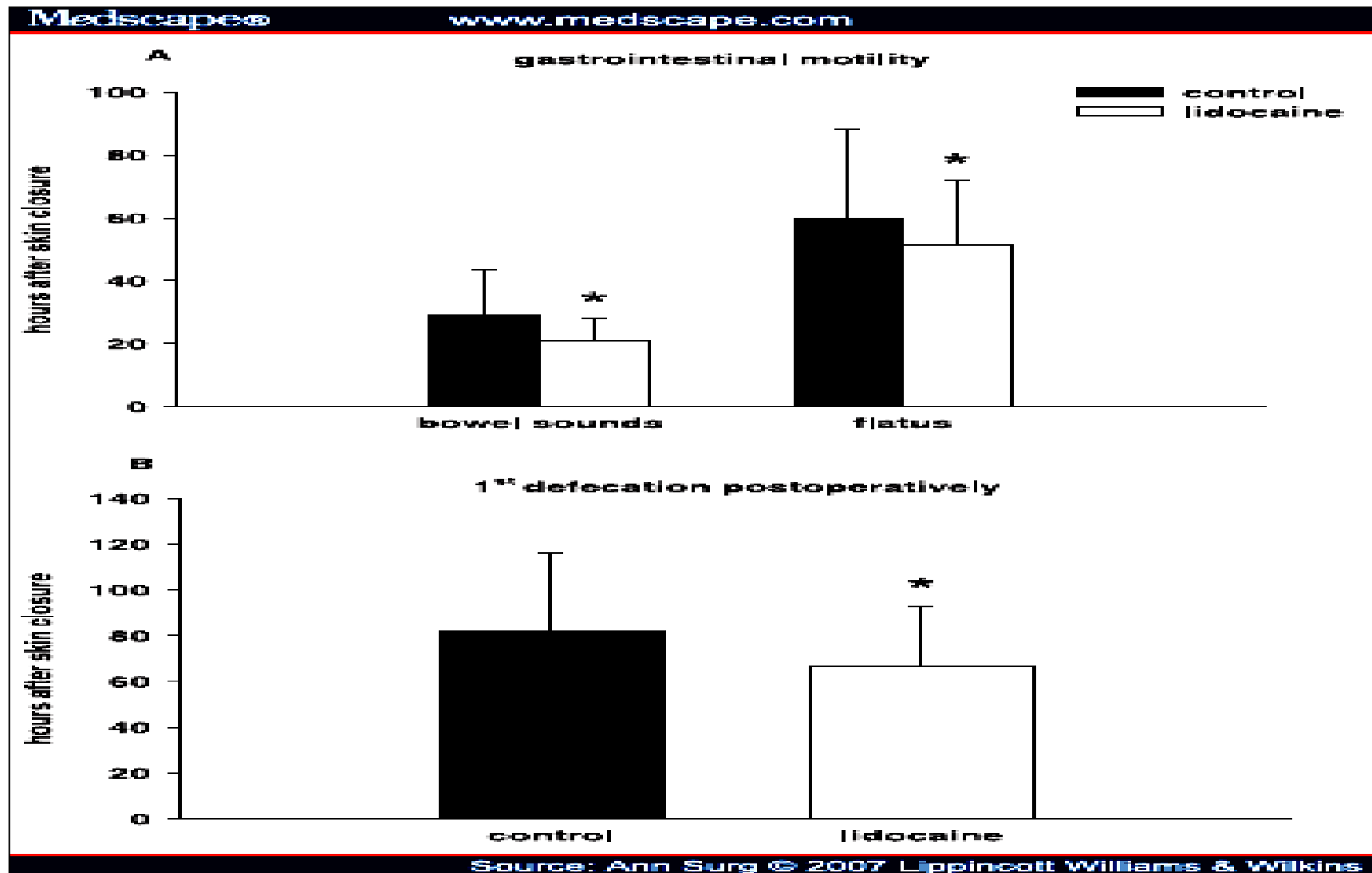
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- Study demonstrated that perioperative systemic lidocaine significantly shortened length of hospital stay by 1 day
 - No differences in length of PACU stay
 - 76 ± 74 versus 84 ± 77 minutes (*control vs lido*)
 - Postoperative ileus estimated to increase the cost of abdominal surgery by 1 billion dollars per year in U.S.
 - Definite advantage in decreasing inflammatory mediators
 - Conflicting results as to how it differs from patients administered thoracic epidural analgesia (*Kuo et al*)
 - Small sample size
 - Weak exclusionary criteria (allowed patients on corticosteroids)
 - Less impact on postoperative analgesia than other studies
 - Did not report overall intraoperative and postoperative analgesic requirements
-

Lidocaine

■ Conclusions

- Lidocaine has been shown to be safe to use
 - Useful in decreasing intraoperative and postoperative analgesic requirements
 - No Toxicity reported in clinical trials when doses of < 3 mg/kg/hr infusions used
 - Definite reduction in postoperative ileus noted in 3 clinical trials
 - Lower total hospital stay requirements when used in major abdominal surgery
 - Lower overall hospital costs
 - Further studies are needed – *current study underway*
-

Lidocaine

