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# The Use of Exparel in Transversus Abdominus Plane Blocks for Postoperative Pain Control

Kyle Dammann<sup>1</sup>, Amanda Gifford<sup>1</sup>, Rodrique Fontem<sup>1</sup>, and Anna Ng Pellegrino<sup>2\*</sup> <sup>1</sup>Department of Surgery, Saint Luke's University Health Network, Bethlehem, PA, USA <sup>2</sup>Department of Anesthesia, Saint Luke's University Health Network, Bethlehem, PA, USA

## Abstract

**Background:** Overuse of opiates in surgical patients has been associated with dependence and poor patient outcomes. Ultrasound guided transverse abdominal plane (TAP) blocks provide a means for administering nonnarcotic pain control in patients undergoing abdominal surgery. Exparel is a long acting liposomal bupivacaine with a duration up to 72 hours. Here we examined the effect of Exparel TAP blocks on postoperative outcomes in a cohort of surgical patients.

**Methods:** This study was IRB approved. Patients undergoing open abdominal surgery > 18y/o and ASA 1-3 were included, and those with allergies to local anesthesia, advanced liver failure, pregnancy, and dementia were excluded. TAP blocks were performed with ultrasound guidance, and pain scores/outcomes were assessed for five days.

**Results:** Fifty-two patients underwent open abdominal surgery followed by Exparel TAP blocks (n=26) or standard opioid therapy (n=26). Fifty two percent were male, mean age was  $58 \pm 17$  years. Exparel treatment resulted in 50% fewer patients requiring oral morphine equivalents (OME) (61-90) for treatment of severe postoperative pain. Exparel treatment was associated with decreased length of stay  $5\pm 2$  vs  $9\pm 7$  days, reduced incidence of ileus (3% vs 27%), nausea and vomiting (8% vs 42%), readmission (4% vs 12%), and postoperative complications (23% vs 54%). These findings were also associated with a 27% reduction in cost per admission  $\$18,190 \pm\$8700$  with Exparel vs  $\$25010\pm$  \$15423 without Exparel. Exparel reduced the incidence of severe postoperative pain scores by 50% or greater from POD0- 4.

**Conclusion:** Exparel TAP blocks improve postoperative outcomes by reducing OME and acute pain scores associated with reduced length of stay, fewer complications, and average cost per patient. Large randomized multicenter control trials should investigate whether TAP blocks are similarly effective.

**Keywords:** Exparel; Post op pain; Transversus Abdominus; Plane Block; Opioids; Exploratory laparotomy.

### Introduction

Perioperative pain management plays a key role in both patient satisfaction and outcome. Notably, postoperative pain following abdominal surgery is associated with both increased hospital length of stay and readmission [1]. Standard morphine derivatives used for pain control contribute to reduced return of bowel function, nausea, vomiting, urinary retention, and subsequently patient dissatisfaction [2]. This also contributes to an added economic burden on the healthcare system [2]. For years, epidural analgesia has assisted in reduction in narcotic use however still associated with its own risks, notably hypotension and infection. Ultrasound guided transverse abdominus plane (TAP) blocks provide a means for non-narcotic postoperative pain control when epidural is not feasible, or when complicated minimally invasive procedures are converted to open in the operating room. TAP blocks are injected between internal oblique and transversus abdominus fascial plane and with Exparel use (a long acting lipid form of local anesthetic, which is FDA approved), can provide pain relief up to 72 hours [3]. This study's primary goal was to investigate the effect of Exparel TAP blocks on postoperative pain, and opioid requirements following open abdominal surgery. Considering the current opioid epidemic and the negative outcomes associated with narcotics, we also investigated the effect of TAP blocks on post op adverse events.

## Methods

This non-randomized study was IRB approved, IRB# 2016-02. Data was collected from January to September 2019 at Saint Luke's University Health Network in Bethlehem, PA. Patients who underwent open

abdominal surgery > 18y/o and American Society of Anesthesiologists Classification (ASA) 1-3 were included, and those with allergies to local anesthesia, advanced liver failure, pregnancy, and dementia were excluded. Consent was obtained prior to procedure. Exparel was mixed with 0.25% bupivacaine and normal saline. TAP block was performed with ultrasound guidance using a stimuplex needle via hydro dissection technique in the operating room (OR) or post anesthesia care unit (PACU). Pain scores and daily average opioid requirements were collected in PACU and post-operative day(POD) 0-5. We expected to see a30% change in pain scores with a maximum mean of 5/10 points on the pain scale in Exparel group on postop day 0, followed by a maximum of 8/10 on postop days 2-3 and a return to a maximum of 5/10 on postop day 5. In order to detect this range of differences, we required at least 18 patients at alpha = .05 and beta = .80, but we included an additional 10% to account for missing or otherwise unusable data, for a total sample size of 20 Exparel and 20 Non Exparel patients. The electronic medical record (EMR) was reviewed on post-operative day (POD) 0-5 to determine pain scores, and opioid requirements/consumption based on standard OME conversion (Table 1). Standard pain scores from a

\*Corresponding author: Anna Ng Pellegrino MD. Department of Anesthesia, Saint Luke's University Health Network, Email: Anna.NgPellegrino@sluhn.org

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scale from 1-10 were used to document mild (0-3), moderate (4-7), and severe (8-10) pain. Other parameters including adverse events such as postoperative nausea, vomiting, ileus, urinary retention, length of stay, and readmissions were collected from the EMR.

Statistics were performed using online calculator and tool found at www.socscistatistics.com.

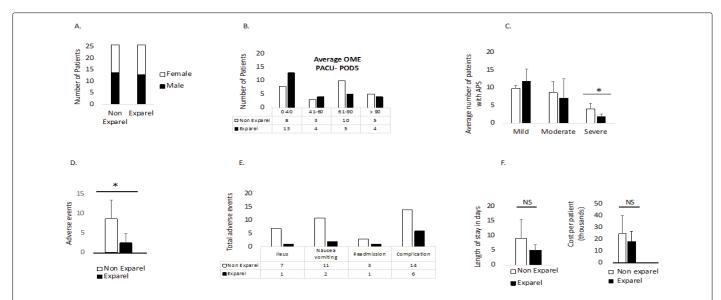
## Results

Fifty-two patients underwent open abdominal surgery followed by Exparel TAP blocks (n=26) or standard therapy (n=26) (Figure 1A). Fifty two percent were male, mean age was  $58 \pm 17$  years. Treatment with ExparelTAP blocks demonstrated a 50% reduction in patients requiring OMEs in the high consumption (61-90) range (Figure 1B). In comparison to standard therapy, the average number of patients with daily OMEs in moderate (41-60) and high (61-90) consumption ranges were also decreased with Exparel treatment (Supplementary Figure 1A). Although not significant, this finding was most apparent from POD2- POD5 ranging from 41-43% decrease in OME on POD2- 3, and 68-73% decrease POD4- 5 (Figure 2A and Supplementary 1B). Exparel TAP blocks were associated with significantly fewer patients reporting severe pain ( $2 \pm 0.7$  vs  $4 \pm 1.6$ ) (p value .004) (Figure 1C). When acute pain scores were stratified, this effect was apparent from POD2-POD4 (Supplementary 1D). ExpareItreatment was also significantly associated with a reduction in non-serious adverse events( $3\pm 2.3 \text{ vs } 9 \pm 4.7$ )(p-value .028) (Figure 1D), demonstrated by reduction in ileus (3% vs 27%), nausea and vomiting (8% vs 42%), readmission (4% vs 12%), and postoperative complications (23% vs 54%) (Figure 1E). Further, ExpareI treatment was associated with decreased length of stay  $5\pm 2$  vs  $9\pm 7$  days, and a 27% reduction in cost per admission \$18,190 ±\$8700 with ExpareI vs \$25010± \$15423 in the standard treatment group (Figure 1F).

In order to further understand the trend in OME reduction from POD2-4 (Figure 2A), and whether there was an association with reduced acute pain scores, we stratified the data by surgical subspecialty. As such, acute care and colorectal surgery patients had reduced OME requirements with Exparel when compared to standard therapy (Figure 2 B-D). This effect was less robust in Surgical oncology, urological, and OBGYN subspecialties (Supplementary Fig 2 A-B). Pain scores were similarly reduced by 75% on POD2 and 50% on POD3- 4 in acute care surgery patients (Figure 3A), and by 40% POD2 in colorectal surgery patients (Figure 3B&C). Such an effect in acute pain scores was less apparent in OBGYN, surgical oncology, and urological surgeries.

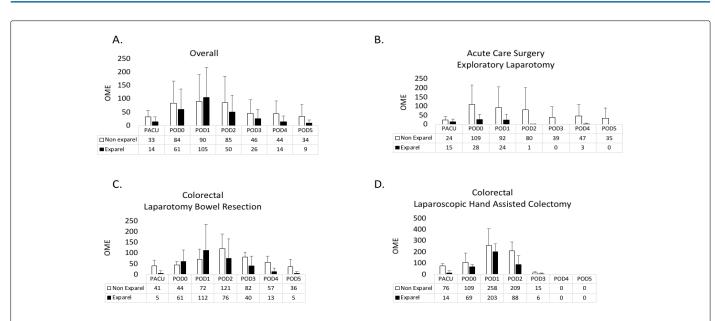
Table 1: Oral morphine equivalent conversion and classification. (Top) Standard conversion of oral and IV opiates converted to oral morphine equivalents. (Bottom) Oral morphine requirements per day classified from low to excessive consumption.

Oral Morphine Equivalent (OME) Conversion	
5 Oxycodone PO	7.5 OME
1 mg IV morphine	3 OME
1 dilaudid PO	4 OME
50 tramadol PO	5 OME
OME Requirement/day	Consumption
0-40	Low
41-60	Moderate
61-90	High
>90	Excessive

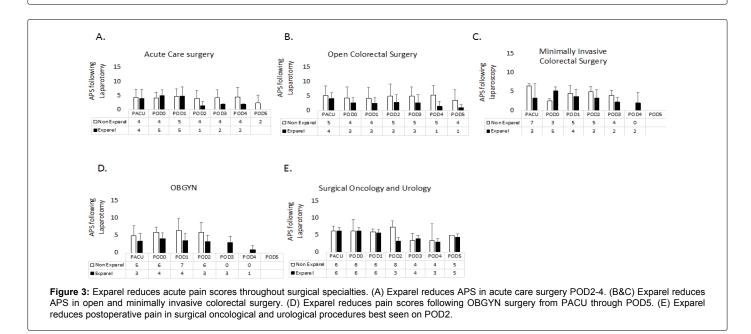


**Figure1:** Exparel improves patient outcomes. (A) Distribution of male and female patients treated with or without Exparel. (B) Oral morphine equivalents required throughout study. X axis indicates morphine equivalents grouped as low (0-40), moderate (41-60), high (61-90), and excessive (>90) consumption. Exparel treated patients required fewer OME (61-90) range. (C) Average number of patients with mild, moderate, and severe pain scores. Exparel treatment resulted in significantly fewer patients with severe pain. (\*<0.05). (D) Exparel significantly reduced non serious adverse events (\*<0.05). (E) Exparel is associated with reduced incidence of non-serious adverse adverse adverse including ileus, postoperative nausea/vomiting, readmission, and postoperative complications. (F) Exparel is associated with reduced length of stay in hospital after abdominal surgery, and associated with decreased average cost per patient, non-significant (NS).

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**Figure 2:** Effect of Exparel in surgical specialties. Oral morphine equivalents (OME) required by patients from PACU through POD5 in Non Exparel (white) (n=26) and Exparel (black) (n=26) treated patients. (A) Daily averages through study overall. Trend in decreased OME from POD2-POD5. (B) Exparel treated acute care surgery patients required fewer OME from PACU through POD5. Data includes exploratory laparotomy procedures including lysis of adhesions, ileostomy creation and take down, gastric ulcer repair, cholecystectomy, and splenectomy in Non Exparel (n=12) and Exparel (n=3) patients. (C) Exparel reduces OME from POD2-POD5 in patients undergoing laparotomy, either small or large bowel resection in Non Exparel (n=5) and Exparel (n=7). (D) Exparel reduces OME requirements from PACU-POD2 in patients undergoing laparoscopic hand assisted colectomy Non Exparel (n=2) and Exparel (n=4).



# Discussion

This study investigated the effect of Exparel TAP blocks on post operative pain and opioid requirements following open abdominal surgery. Here Exparel was associated with reduction in opioid consumption, reduction in severe pain scores, fewer adverse events, decreased hospital cost, and reduced length of stay when compared to standard multimodal therapy.

Baseline data regarding known postoperative pain scores and opioid requirements had not been collected at our institution prior to this study. Similar to our findings, the literature reported reduced narcotic requirements and hospital length of stay, using Exparel TAP blocks after abdominal wall reconstruction [4]. We also showed that Exparel reduced severe acute pain scores, and similar reports have demonstrated Exparel TAP blocks improve pain control following open umbilical hernia repair [5]. Moreover, anorectal Exparel injections significantly reduced cumulative pain scores and opioid requirements following hemorrhoidectomy [6]. Our findings did not support Exparel efficacy in OBGYN cases, however active clinical trials are investigating the effect of TAP blocks in open [7] and laparoscopic gynecological surgery [8], and one recent report demonstrated Exparel blocks reduce IV narcotic requirements after c-section [9]. Nevertheless, our study is the first to investigate the effect of Exparel in open abdominal surgery across multiple surgical specialties. We also observed that Exparel TAP

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blocks were more robust in acute care surgery and colorectal surgery cases in comparison to other specialties.

One of the major limitations of this study is that we lacked the ideal control. Due to the operating room costs, and risk associated with procedure, we chose to compare Exparel TAP blocks to standard therapy rather than performing TAP blocks with Non Exparel controls. Further limitations include the highly subjective nature of pain scores and multiple confounders including patient demographics, and baseline opioid use prior to admission were not taken in to account in our design. Furthermore, chronic pain associated with cancer patients may have dampened the effects of Exparel in the OBGYN and surgical oncology patients in our study.

We were unable to demonstrate that Exparel TAP blocks significantly reduced OME requirements post operatively. There was however as notable trend in OME reduction, especially in the (61-90) range, and a more robust was likely masked due to an under powered study. We did however observe a significant reduction in severe pain scores and non serious adverse events indicating Exparel was effective.

# Conclusion

In conclusion, Exparel TAP blocks improve postoperative outcomes by reducing OME and acute pain scores associated with reduced length of stay, fewer complications, and average cost per patient. Large randomized multicenter control trials should investigate whether TAP blocks are similarly effective.

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