



Review

Clinical pharmacist perspectives for optimizing pharmacotherapy within Enhanced Recovery After Surgery (ERAS[®]) programs^{☆, ☆ ☆}



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A B S T R A C T

One of the most durable approaches to perioperative enhanced recovery programming has culminated in the formation of perioperative organizations devoted to improvements in the quality of the surgical patient experience, such as the Enhanced Recovery After Surgery (ERAS[®]) Society. Members of the American College of Clinical Pharmacy (ACCP) Perioperative Care Practice and Research Network (PRN) and officials from the ERAS[®] Society present an opinion that: (1) identifies therapeutic options within each pharmacotherapy-intensive area of ERAS[®]; (2) generates applied research questions that would allow for comparative analyses of pharmacotherapy options within ERAS[®] programs; (3) proposes collaborative practice opportunities between key stakeholders in the surgical journey and clinical pharmacists to manage drug therapy problems and research questions; and (4) highlights examples of pharmacist-led cost savings attributed to ERAS[®] implementation. Clinical pharmacists, working in this manner with the perioperative team across the care continuum, have optimized pharmacotherapy towards measurable outcomes improvements, and stand ready to partner with inter-professional stakeholders and organizations to advance the care of our mutual patients.

1. Introduction

Perioperative enhanced recovery programs have been at the forefront of a major paradigm shift within surgical practice over the last 20 years. One of the most durable approaches has culminated in the formation of perioperative organizations devoted to improvements in the quality of the surgical patient experience, such as the Enhanced Recovery After Surgery (ERAS[®]) Society [1]. The ERAS[®] Society created a unique audit and feedback system that supports perioperative care teams in sustaining high clinical quality and consistency through implementation of over 20 evidence-based strategies, many of which employ pharmacologic therapies. For example, of the 22 components contained within the ERAS[®] Society protocol for elective colorectal surgery, nine areas entail the use of pharmacotherapy to achieve measurable outcome improvements, such as reducing postoperative

complications and hospital length of stay (LOS) [2,3]. With a focus on the identification, prevention, and resolution of drug therapy problems, the clinical pharmacist brings a unique perspective to perioperative teams and collaborative enhanced recovery efforts to optimize patient outcomes. A key role of the clinical pharmacist is to help with evidence based implementation to assure that logistical barriers related to clinical policies, formulary listing, or computer orders, among others, are identified and do not hinder a safe and effective enhanced recovery program.

Clinical pharmacists can add value to enhanced recovery programs through multiple mechanisms. Firstly, dedicated expertise in the areas of pharmacology, pharmacotherapy, medication use, and associated technologies yield an invaluable resource in implementing and optimizing medication-related protocols and processes. The clinical pharmacist is also uniquely positioned as a common bridge for care

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coordination and communication, frequently interfacing with providers across disciplines and throughout the continuum of perioperative care. This often includes having established relationships or frequent modes of contact with all providers involved in surgical care, including surgeon, anesthesiologist, medical consulting prescribers, nursing, and administration. Clinical pharmacists often have training in medication safety, participate in root cause analysis and project management at their institutions, and are part of the ever-growing need for public demonstration of excellence in operational efficiency and action roles in implementation science. Moreover, pharmacists have long advocated for applying a systematic process of care (i.e., obtaining, organizing, and interpreting patient data), system design and thinking, and error prevention/risk management strategies, as evidenced by extensive leadership in organizations like the Institute for Safe Medication Practices (ISMP). Through extensive training and frequent use of medication utilization data in electronic medical records for quality improvement, clinical pharmacists are also adeptly positioned to assist with data collection and analysis of medication-related ERAS[®] elements, such as the use of medications for post-operative nausea and vomiting (PONV), pain management assessments, and adverse drug reactions.

As active partners in advancing the practice and research of enhanced recovery, the representing members of the American College of Clinical Pharmacy (ACCP) Perioperative Care Practice and Research Network (PRN) and officials in the ERAS[®] Society offer the purposes of this opinion paper as follows: (1) to identify therapeutic options within each pharmacotherapy-intensive area of ERAS[®]; (2) to generate applied research questions that would allow for comparative analyses of pharmacotherapy options within ERAS[®] programs; (3) to propose collaborative practice opportunities between key stakeholders in the surgical journey and clinical pharmacists to manage drug therapy problems and research questions; and (4) to highlight examples of pharmacist-led cost savings attributed to ERAS implementation.

1.1. Therapeutic options within each pharmacotherapy-intensive area of ERAS[®]

Because one of the missions of the ERAS[®] Society is to produce guidelines for an international audience, guidance for pharmacotherapy selections within each sub-specialty area and for individual patients is not prescriptive, since each country has a different array and availability of pharmaceuticals and dosage forms approved for use. This is a huge opportunity to partner with the clinical pharmacist as part of the implementation team to assure evidence based medicine and local safety, effectiveness, feasibility and value is aligned. Areas in which pharmacotherapy is referenced directly in ERAS[®] protocols include: (1) pre-anesthetic medication; (2) prophylaxis against venous thromboembolism (VTE); (3) antimicrobial prophylaxis and skin preparation; (4) standard anesthetic protocol; (5) PONV prophylaxis; (6) perioperative fluid management; (7) prevention of postoperative ileus; (8) pre-, intra-, and post-operative analgesia; and (9) postoperative control of glucose. Moreover, considerations for pre-, intra-, and post-operative clinical functions and activities, such as patient education, medication reconciliation, and risk assessment address pharmacotherapy-related decisions within each phase of preparation and recovery.

While the degree of compliance with ERAS[®] elements is known to be predictive of a better surgical outcome [4], many unanswered pharmacotherapeutic questions remain. The significance of each ERAS[®] element, as well as the clinical contribution of optimal pharmacotherapy in terms of the relative importance of each element to reductions in post-surgical complications and LOS, is unknown. Table 1 summarizes the pharmacotherapy options available for the identified ERAS[®] protocol sections, with highlighted areas proposed for initial pharmacotherapy data collection. In all identified areas, for example, there are no comparative analyses that document the drugs of first choice for colonic procedures (e.g. low molecular weight heparin verses heparin for VTE prophylaxis, metronidazole with cefazolin or with

ceftriaxone for surgical antimicrobial prophylaxis, etc.), and pertinent patient-specific risk stratification has largely yet to be explored. Key elements of compliance do matter to overall outcomes and adherence to as many clinically appropriate elements as possible leads to best outcomes [5,6]. Pharmacists have been key team members in this best practice optimization at hospitals and health systems across North America. These activities include preemptive educational sessions for all involved providers, at the patient level for order review and verification, for each patient with clinical monitoring, daily multi-disciplinary rounds, and both short- and long-term educational programs for staff and patient counselling. Moreover, medication reconciliation at discharge and follow up Medication Therapy Management (MTM) have been incorporated into the practices of many clinical pharmacists to facilitate the patient's ability to adhere to appropriate medication use between transitions of care.

1.2. Comparative research for pharmacotherapy options within ERAS[®] programs

It is likely that variance exists within and among ERAS[®] programs regarding drugs of first choice for each ERAS[®] pharmacotherapy element. Clinical pharmacists are also well positioned to lead prospective, randomized controlled trials to robustly assess comparative efficacy and costs of care related to peri-operative medication strategies and associated patient outcomes, as has been done with one peri-articular injection comparison in total knee replacement surgery [7]. To establish a “proof of concept” for the introduction of comparative pharmacotherapy analysis into ERAS[®], it would be important to identify and prioritize correlations between the severity of postoperative complications and pharmacotherapy that exist in the literature. In addition, because ERAS[®] is an established program with a standardized data set, collection process, and audit system (ERAS[®] Interactive Audit System, EIAS), the selection of the first therapeutic areas to collect pharmacotherapy utilization may be a natural extension of the standard collection process. Additionally, to avoid potential confounders in a pilot study's research design, the therapeutic areas selected need to be independent of the program's bowel-related functional changes.

With these factors in mind, enhanced recovery programs could consider two initial elements for further data collection regarding medication use in surgical patients, focusing on elements associated with the most frequent and severe post-operative complications: (1) antimicrobial prophylaxis; and (2) venous thromboembolism prophylaxis. Additional data regarding agent selection and dosing regimens can be collected in a pilot study of surgery patients selected at random from one or more sites. This comparison would provide additional guidance for optimizing pharmacotherapy choices in relation to reduced postoperative complication severity and could serve as the basis for further in-depth data collection for other ERAS[®]-related pharmacotherapy options. While data collection began with colorectal surgery, many specialty areas, such as pancreatic/liver surgery, bariatrics, urologic surgery, and gynecologic oncology have benefitted from a similar framework with modifications for the specific patient population.

1.3. Collaborative practice opportunities between key stakeholders in the surgical journey

Beyond addressing medication comparative efficacy research questions, we propose greater collaborative efforts between clinical pharmacists and the perioperative care team at all levels to advance ERAS[®]-related practice and research. The ACCP has long advocated that pharmacists work in a collaborative manner with physicians and other healthcare providers to achieve the best possible patient outcomes [8,9]. Clinical pharmacists have directly facilitated or led the development of ERAS[®] protocols and care sets/pathways to optimize best practice evidence for use of medications. Evolving literature exists documenting the impact of clinical pharmacist collaborative practice

Table 1
Pharmacotherapeutic options within each ERAS[®] element for elective colorectal surgery.³

ERAS element	Pharmacotherapeutic option
Preanesthetic medication	<ul style="list-style-type: none"> • No anxiolytics, or • fentanyl with midazolam; • fentanyl with propofol; • remifentanyl with midazolam; or • remifentanyl with propofol
Prophylaxis against venous thromboembolism	<ul style="list-style-type: none"> • No opioid, or risk-stratified opioid use • With/without APAP, Gabapentinoids, anti-inflammatories with proactive criteria to modify for patient comorbidities • Weight-adjusted or not, and • Enoxaparin; • Tinzaparin; • Dalteparin; or • Unfractionated heparin • Direct oral anticoagulants • Duration of therapy, hospital only or extended prophylaxis at home, patient stratification
Antimicrobial prophylaxis and skin preparation	<ul style="list-style-type: none"> • Cefazolin/metronidazole; weight-adjusted or not; or. • Ceftriaxoneone/metronidazole; or • Other antibiotic agents or combinations (2nd generation cephalosporins, quinolones, carbapenems) • Duration – pre-op only vs. 24 hr post op, intra-op re-dosing strategy • Povidone-iodine or chlorhexidine topical antiseptics • Role of pre-operative screenings and decolonization strategies
Standard anesthetic protocol	<ul style="list-style-type: none"> • Fentanyl, sufentanil or remifentanyl • Sevoflurane or desflurane or isoflurane • Roles/indications for TIVA (total intravenous anesthesia), MAC (monitored anesthesia care) • Depth of sedation, use of paralytics and their reversal, patient stratification
PONV prophylaxis	<ul style="list-style-type: none"> • Ondansetron or granisetron; • with or without dexamethasone; • with or without droperidol or aprepitant or additional agents • Degree of combination therapy patient stratification (high risk v. low risk of PONV)
Perioperative fluid management	<ul style="list-style-type: none"> • Lactated Ringer's solution or 0.9% sodium chloride solution; with/without fluid boluses • Total daily IV fluids goal (i.e. less than 2.5 L) • Optimal monitoring strategies, patient stratification • * Euvolemia is goal
Prevention of postoperative ileus	<ul style="list-style-type: none"> • Neuraxial and regional anesthetic strategies -epidural, intrathecal injections, peripheral blocks • Role and associated dosing strategy of intravenous opioid- patient-controlled analgesia (PCA) vs. intermittent as needed IVP • Optimal ways to maximize multimodal analgesia with proactive criteria to modify for patient comorbidities and reduce opioid consumption across phases of care • Scheduled laxative regimen or as needed/triggered • Choice of bowel regimen mechanism of action, individual medication agents and degree of combination • Alvimopan or none • Role of non-pharmacologic therapies (i.e. pre-operative nutrition and fiber intake, chewing gum, etc.)
Postoperative analgesia	<ul style="list-style-type: none"> • Fluid management with the goal of balancing fluids • Acetaminophen (APAP); route of administration • Mixed COX1/2 or COX2 active anti-inflammatory; route of administration (oral preferred) and dosing strategy with proactive criteria to modify for patient comorbidities • Gabapentinoid or none with proactive criteria to modify for patient comorbidities • Morphine or hydromorphone; parenteral or oral (oral preferred) • Influence of patient comorbidities and optimal risk stratification techniques to minimize adverse events
Postoperative control of glucose	<ul style="list-style-type: none"> • Basal/bolus/correction or sliding scale • Insulin lispro/aspart or regular for bolus • Insulin glargine, insulin detemir or other for basal • Initiation of insulin infusion • Care set/pathway in place for management • Optimal perioperative glucose goals and appropriate monitoring based on degree of patient insulin resistance

within perioperative care and enhanced recovery programs [10–14], including preoperative antimicrobial prophylaxis [15], venous thromboembolism risk assessment and prophylaxis [16], postoperative nausea and vomiting prevention, pain management [17], and glycemic control [18]. The American Society of Health-system Pharmacists has a well-developed, inter-professional, and consensus-driven guidance on surgical prophylaxis that could easily be incorporated into ERAS[®] programs for every specialty and sub-specialty [15].

In addition, several studies have identified clinical pharmacist practices that lead to improved outcomes in perioperative patients. Ramrattan and associates [19] created evidence-based bedside clinical “drug rules” in conjunction with surgeons that served as the basis for increased collaboration. Charpiat and colleagues [20] documented prescription errors that had clinical implications in a 4-year ward study of pharmacist practices, which led to improvements in the quality of recommendations. Neville et al. [21] identified over 1000 interventions within 6 months that resulted in fewer adverse drug events, lower medication costs, and decreased hospital length of stay. Indeed, these and other controlled studies illustrate the value of clinical pharmacists

in perioperative patient care units as well as operating theaters and post-anesthesia care settings.

Emerging societal healthcare challenges continue to underscore the need for diverse expertise and skillsets on healthcare teams to solve complex problems impacting patient outcomes. In the setting of opioid therapy and the current epidemic, the clinical pharmacist is a key resource to assist perioperative healthcare team members in utilizing multimodal pain management, making patient-specific assessments and optimizing pain medication regimens. Clinical pharmacists are also well-positioned to provide patient education and counselling to set safe expectations about pain, minimize prolonged opioid exposure, and increase adherence to safe opioid prescribing practices and medication disposal at the completion of therapy. Opioid prescribing at discharge is an area where clinical pharmacists can help educate and guide prescribers to strongly consider the influence of multimodal ERAS[®] analgesia, individual patient pain scores and actual opioid usage rather than providing a protocolized opioid prescription for all patients. Brandal and colleagues [22] found that while an ERAS[®] protocol for colorectal surgery decreased total morphine equivalents used compared

to non-ERAS[®] protocol, prescribers still provided the same number of opioid doses on discharge prescriptions for patients in both groups. Most shockingly, 70% of patients in the ERAS[®] group with a combination of no preoperative opioid use, low postoperative pain scores, and low postoperative morphine equivalent consumption were still discharged with an opioid prescription.

Additionally, detailed descriptions of pharmacotherapy components of surgical quality improvement projects, such as the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP), NSQIP Pediatric, the NSQIP Trauma Quality Improvement Program and the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP), further stress the importance of collaborative bedside patient care practice [23].

1.4. Examples of pharmacist-led cost savings attributed to ERAS[®] implementation

In a recent review article, ERAS[®], as an example of value-based surgery, was estimated to save between €153 and €6537 per colorectal case, and between US \$1035 and \$8726 for non-colorectal case [24]. Ongoing shifts in hospital payment structures also continue to challenge healthcare teams to provide higher quality of care with greater efficiency and at lower costs. Engaging pharmacists at the time of ERAS[®] protocol design can help address drug inventory, budget, and potential therapeutic alternatives. Moreover, a pharmacist's evaluation of drug therapy can minimize overuse of medications, leverage therapeutic formulary options with evidence-based practices, and provide alternatives to developed protocols in the emergent setting of drug shortages or recalls.

Pharmacists' understanding of hospital operations and policies, quality measures and other metrics have facilitated improvements in systematic care provided. For example, Jordan and colleagues demonstrated improved compliance with pre-operative antibiotic quality measure compliance with implementation of an operating room clinical pharmacist service at a large Level 1 trauma and surgery center. The service was also associated with substantial revenue increase through improved medication charge capture related to a collaboratively optimized anesthesia medication distribution and billing process [25]. Significant improvements in post-operative complications and associated cost-savings through pay-for-performance reimbursement programs were realized in a large total joint arthroplasty population with the integration of a comprehensive clinical pharmacy service [26]. Strong inter-professional relationships between perioperative clinical pharmacists and the surgical team have also proven to be vital in successful stewardship efforts of high-risk, high-cost medications employed in perioperative settings [27]. Vincent and colleagues applied intravenous (IV) acetaminophen (APAP) guidelines within ERAS[®] protocol implementation that saved one Massachusetts medical center over US \$400,000, decreased IV utilization by 83%, increased use of ERAS[®] multi-modal oral pain management strategies by 18%, and almost tripled pharmacist documentation of care provided [28].

2. Summary

In summary, there is evolving literature that validates the collaborative contributions of a clinical pharmacist in peri-procedural areas. ERAS[®] programs are effective in reducing the frequency and severity of post-operative complications and in lowering LOS statistics, but further inter-professional research and practice collaboration are needed to continue optimizing patient outcomes, especially considering trends towards increasing patient and payer complexities. The principles of enhanced recovery serve as the backbone for improved safety and effectiveness for the surgical population as well as parameters for patient specific adjustments for the teams. Clinical pharmacists are involved initially in program development, and work on the perioperative care team caring for each surgical patient. Asking and answering applied

research questions related to comparative drug efficacy within each program element provides an opportunity to strengthen the evidence and quality of pharmacotherapy choices within ERAS[®] pathways, as well as that of the ERAS[®] paradigm entirely. This would provide valuable information for hospitals and surgical practices interested in implementing and evaluating enhanced recovery programs and minimizing misuse or overuse of medications, contributing to improved outcomes and decreased costs. Clinical pharmacists, working in this manner with the perioperative team across the care continuum, are able to optimize pharmacotherapy towards measurable outcomes improvements, and stand ready to partner with inter-professional stakeholders and organizations to advance the care of our mutual patients.

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There is no research data included with this review.

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None to declare.

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