

## Continuous Epidural Analgesia for Colonic Surgery—But What About the Future?

Franco Carli, M.D., M.Phil., and Henrik Kehlet, M.D., Ph.D.

Over the past 3 decades, several studies have explored the effectiveness and efficacy of regional block for abdominal surgery, and it is presently used with satisfactory outcome.<sup>1</sup> Postoperative analgesia for colon surgery can be achieved with either systemic opioids or epidural mixture of local anesthetics and opioids, although evidence suggests superiority of the latter technique.<sup>1</sup> Beside provision of optimal analgesia, thoracic epidural local anesthetics have been shown to attenuate postoperative ileus and, thereby, allow earlier oral nutrition, which by itself improves outcome,<sup>1,2</sup> and to protect the gut from decreased microvascular perfusion caused by hemorrhage and maintain colonic blood flow.<sup>3</sup> Also, ample evidence indicates that the classic catabolic response to abdominal surgery, a key pathogenic factor in postoperative morbidity, can be attenuated, although not completely abolished, by thoracic epidural local anesthetics.<sup>1,2</sup> In contrast to the modulation of endocrine and metabolic responses, inflammatory responses are not modified by epidural block.<sup>2</sup> Thoracic epidural analgesia has also been shown to decrease the incidence of pulmonary morbidity<sup>1,4</sup> and to improve the balance of oxygen supply and demand in the ischemic myocardium in favor of the former.<sup>5</sup>

Although the beneficial physiological effects of continuous epidural analgesia have been recognized, the outcome trials conducted during the past decade have not been able to demonstrate a significant reduction in morbidity, mortality, and hospital stay with this anesthetic and analgesic technique.<sup>6</sup> The explanation hereto is most probably

that these effects have not been utilized in a multimodal postoperative rehabilitation program.<sup>6,7</sup> The realization that the potential advantages of unimodal strategies might be obscured by other perioperative interventions prompted a revisit of the pathogenic factors responsible for postoperative morbidity and delayed convalescence and the necessity to develop multimodal interventions facilitating the acceleration of postoperative recovery programs.<sup>7</sup>

The process of postoperative recovery can be delayed by a series of factors, which are implicated in the pathogenesis of the surgical stress response.<sup>7</sup> The most important available perioperative strategies, besides epidural block, can be mentioned as follows: preoperative optimization of medical fitness, minimally invasive surgery, intraoperative normothermia, perioperative beta blockers, thromboembolic prophylaxis, nausea and vomiting prophylaxis, early enteral nutrition, peripheral opioid antagonists, oxygen therapy, revision of traditional care programs with standardized clinical pathways, and multimodal analgesia obtained with Cox-2 inhibitors, paracetamol, ketamine,  $\alpha_2$ -agonists, gabapentin, glucocorticoids, and intravenous infusion of lidocaine. In addition, avoidance of perioperative fluid excess is essential to reduce ileus and cardiopulmonary morbidity.<sup>8,9</sup> Growing evidence indicates that, within the context of fast-track surgery, the multimodal approach would reduce stress-induced organ dysfunction and morbidity leading to accelerated recovery and improved functional capacity and quality of life after colonic resection.<sup>7,10-12</sup>

For the future, however, the question remains as to whether the application of several therapeutic modalities would provide the same perioperative benefits achieved with epidural block. Can a pharmacological cocktail that could provide similar benefits replace epidural anesthesia and analgesia for colonic resection? In the design of studies to answer this question, several factors must be considered. Obviously, an intensified preoperative education of patients is essential.<sup>7</sup> The role of a preoperative glucose load needs to be explored because several

From the Department of Anesthesia, McGill University, Montreal, Quebec, Canada (F.C.); and Section for Surgical Pathology, Rigshospitalet, Blegdamsvej, Copenhagen, Denmark (H.K.).

Accepted for publication November 17, 2004.

Reprint requests: Franco Carli, M.D., Montreal General Hospital, 1650 Cedar Avenue, Montreal, Quebec, H3G 1A4 Canada. E-mail: Franco.carli@mcgill.ca

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1098-7339/05/3002-0005\$30.00/0

doi:10.1016/j.rapm.2004.11.003

studies that included abdominal procedures have shown such an intervention leads to a decreased endocrine metabolic response, including less postoperative insulin resistance.<sup>13</sup> The role of minimally invasive (laparoscopic) colonic resection needs to be further explored, as past systematic reviews have shown less pain and hospital stay compared with open surgery and traditional care.<sup>14</sup> These beneficial effects taken into consideration may, therefore, question whether epidural analgesia is necessary with laparoscopic colonic resection. Thus, 2 randomized studies may suggest that the reduced physiological disturbances and pain with laparoscopic surgery may not require an additional continuous epidural analgesia and its physiological effects to improve outcome.<sup>15,16</sup>

However, the design in previous randomized studies has not been optimal regarding the composition and duration of epidural analgesia. Furthermore, a double-blind randomized study that compared laparoscopic versus open colonic resection combined with epidural analgesia and multimodal rehabilitation could not demonstrate any differences in early postoperative recovery, including pain and ileus.<sup>17</sup> The question, therefore, remains to be answered as to whether the same effect is obtained by laparoscopic surgery and epidural analgesia on pain and ileus.

Postoperative ileus is one of the limiting factors for early recovery after colonic surgery; however, recent developments of a peripherally acting  $\mu$  opioid antagonist may have important implications because the selective peripheral gut effect counteracts the inhibitory effect of systemic opioid on gastrointestinal motility, thereby reducing ileus, but with preserved analgesia.<sup>18</sup> In the future, such pharmacological treatment of ileus may alleviate the need for epidural analgesia within a multimodal rehabilitation context.

Because sufficient dynamic pain relief is a prerequisite for early recovery and because continuous epidural analgesia is the hitherto most effective postoperative pain treatment after colonic surgery, future trials with multimodal analgesia should be instituted to investigate whether such techniques may replace epidural analgesia. Such pain regimens may not be far in the future, because several agents such as NSAIDs or Cox-2 inhibitors combined with paracetamol may improve analgesia,<sup>19</sup> but until now these agents have not been explored in combination with other analgesics such as ketamine,<sup>20</sup> gabapentin,<sup>21</sup> and  $\alpha_2$ -agonist, all of which by themselves have some analgesic effects. Such a multimodal analgesic "soup" may, in the future, alleviate the need for epidural analgesia.

Finally, other pharmacological modifiers of the

surgical stress response such as glucocorticoids,<sup>22</sup> insulin, with its demonstrated antiinflammatory effects,<sup>23</sup> and beta-blockers and anabolic agents,<sup>24</sup> separately or in combination, may provide beneficial physiological effects like those obtained by epidural analgesia.

Assessment of the quality of recovery provided by such multimodal interventions must be relevant to the patient, in the sense that it should capture outcome measures that are valid and meaningful to the recovery process, such as quality of functional pain relief, time-based ambulation, vitality, general health perception, mental and physical function, and functional exercise capacity. Additionally, detailed assessment of the quality of postoperative recovery during and after the immediate perioperative period would be needed to assess costs of care, use of hospital resources, and anesthesia and surgical outcomes (postoperative nausea and vomiting, readmission, ileus, and infections).<sup>7,25</sup>

In summary, enough evidence exists to currently recommend continuous epidural analgesia with a combination of local anesthetic and opioid to enhance recovery after colonic surgery, provided that the beneficial physiological effects of epidural analgesia are utilized in a multimodal rehabilitation program. However, recent developments of pharmacological modification of surgical stress responses, multicomination analgesia therapy, availability of peripheral opioid antagonists, and minimally invasive surgery may call for future randomized clinical trials to reassess the need for epidural analgesia in colonic (and other abdominal) surgery.

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