Hirosi Kuriyama Award 2007 Memorial Review

Epidural analgesia and gastrointestinal motility after open abdominal surgery—a review

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Abstract

After major abdominal surgery, postoperative ileus is inevitable, and it has always been a challenge for the surgical team to shorten the duration of this period. Based on many clinical and basic reports that affirm the effect on the recovery of gastrointestinal motility, epidural analgesia has been used widely to promote recovery from postoperative ileus. Different techniques have been used to measure gastrointestinal motility in laboratory and clinical investigations. Many of the techniques used in clinical investigations of gastrointestinal motility are controversial because they are subjective. In the laboratory strain gauge force transducer (SGT) can provide objective data on gastrointestinal motility. Nevertheless the significance of SGT in the clinical setting is yet to be confirmed. Therefore in this review we examine both clinical and laboratory outcomes of epidural analgesia on gastrointestinal motility to present the possibility for the development of gastrointestinal motility research with SGTs. We suggest that further investigation using SGTs may lead to the development of objective methods that allow objective assessment of post-surgical gastrointestinal function.

Key words: epidural analgesia, postoperative ileus, animal model, gastrointestinal motility

Introduction

Investigations of the motility of the gastrointestinal tract have been reported since the early 1900s’ (Douglas et al., 1934; Castelton, 1939; Grindlay et al., 1941). With human subjects, intraluminal manometry and gastro-electrograms have been well-established as methods to detect gastrointestinal motility. Nevertheless, these methods require a leading wire to be connected to the external device to receive signals, which limits the availability and duration of recording. This has led to the development of techniques using SGT (Strain Gauge Force Transducers) in...
animal models to investigate basics of gastrointestinal motility (Jacoby \textit{et al.}, 1963; Itoh \textit{et al.}, 1982).

Normal gastrointestinal motility has two different patterns; that in the interdigestive state and that in the digestive state. The interdigestive state is most characteristic, and is often used to investigate abnormality and the recovery of gastrointestinal motility. As a result of severely traumatic conditions such as with major abdominal surgery, the characteristic cyclic pattern of gastrointestinal tract motility disappears. After operation, the interdigestive migrating contractions (IMC) eventually shows recovery (Tsukamoto \textit{et al.}, 1999; Nakayoshi \textit{et al.}, 2007).

Clinically, temporary paralysis of the intestine is inevitable after major abdominal surgery. Prolongation of this state may induce abnormal bacterial growth in the intestine and increase morbidity and mortality (Nieuwenhuijs \textit{et al.}, 1998). Therefore it is a challenge for the surgical team to shorten the duration and intensity of this intestinal paralysis period (Kehlet \textit{et al.}, 2003). The pathogenesis of postoperative ileus (POI) is thought to be multi-factorial and has not yet been completely clarified. Also, methods to treat POI have yet to be fully investigated. Recent studies of the relationship between epidural analgesia and gastrointestinal motility have indicated the need for further investigation in this field (Shibata \textit{et al.}, 1994; Park \textit{et al.}, 2001; Moraca \textit{et al.}, 2003; Delaney \textit{et al.}, 2004).

Clinical studies on post-surgical gastrointestinal motility have used indicators such as the occurrence of the first flatus, the time required to resume oral intake, or the recovery of bowel sounds (Saito \textit{et al.}, 1994; Kanazi \textit{et al.}, 1996; Carli \textit{et al.}, 2001). However, the significance of these indices as a parameter of gastrointestinal function remains controversial. In basic studies on laboratory animals, strain gauge force transducers (SGTs) are frequently used. Yet a direct correlation between the recovery of IMC and the resumption of normal gastrointestinal motility is still to be confirmed.

\textbf{Gastrointestinal motility patterns with SGT}

The use of strain gauge force transducers (SGT) is a well known method to investigate gastrointestinal motility in animal models (Stemper \textit{et al.}, 1975; Nakamura \textit{et al.}, 1995; Ohashi \textit{et al.}, 2001). Contractile activity of the digestive tract is known to show a cyclic and propagating action under normal conditions. Reflecting intestinal paralysis, IMCs disappear during abnormal conditions such as open abdominal surgery. A previous report demonstrated that the appearance of IMC in the stomach (gastric IMC) correlated with the recovery of digestive transport (Tsukamoto \textit{et al.}, 1999; Shibata \textit{et al.}, 2002; Tanaka \textit{et al.}, 2004).

\textbf{Normal gastrointestinal motility patterns (Fig. 1)}

Normal gastrointestinal motility is classified into two states: the interdigestive state and the digestive state. The IMC of the gastrointestinal tract in the interdigestive state show a strong cyclic and propagating action under normal conditions (Szurszewski, 1969), and have four different phases. These phases occur almost simultaneously in the stomach and the duodenum, which migrate distally in sequence along the entire small bowel. While phase I is a period of
quiescence, phase II is a period in which intermittent low amplitude random irregular contractions occur. This is followed by phase III which is a brief burst of irregular high amplitude contractions, after which in phase IV there is a brief transition back to the quiescence of phase I (Code, 1975). Phase III appears cyclically at intervals of 90–120 minutes in the stomach, and propagates to the distal intestine.

**Gastrointestinal motility patterns after open abdominal surgery**

Interdigestive contractile activity disappears during abnormal conditions such as in open abdominal surgery, reflecting temporary intestinal paralysis. Eventually phase III-like contractions appear first in the ileum, followed by the jejunum, duodenum, and finally in the stomach (Tsukamoto et al., 1999; Nakayoshi et al., 2007).

**Postoperative ileus**

Motility of the gastrointestinal tract is temporarily impaired after major abdominal surgery. This state may cause accumulation of secretions and gas (Mirza et al., 2004). Clinically it is characterized by abdominal distension, lack of bowel sounds, latency in the passage of flatus or stools, and symptoms of nausea, vomiting as well as stomach cramps (Behm et al., 2003). Postoperative ileus is a major contributing factor to postoperative discomfort (Table 1). With prolongation of this state, resumption of the intake of a regular diet and mobilization is delayed and the hospital stay is thereby prolonged. Facilitating postoperative recovery is an old but constantly evolving challenge for the surgical team.
Pathogenesis of postoperative ileus

The duration of postoperative ileus is thought to be multi-factorial. Contributing factors for such a complication consists of 1) the degree of surgical trauma, most intensive after colonic surgery, 2) the presence of inhibitory neural reflexes of the extrinsic, intrinsic and autonomic nerve systems, 3) changes in the levels of local and systemic neurotransmitters and inflammatory mediators as well as other exacerbating influences including exogenous and endogenous opiates, and 4) electrolyte abnormalities.

Treatment of postoperative ileus

Treatment of postoperative ileus is currently largely supportive and historically has consisted of routine naso-gastric intubation, intravenous hydration, and bowel rest, while early mobilization, less invasive surgical techniques, and epidural analgesia have been found to decrease the incidence of postoperative complications, including postoperative ileus (Shibata et al., 1994; Park et al., 2001; Moraca et al., 2003; Delaney 2004).

Epidural analgesia

Severe pain occurs after major abdominal operations, and epidural analgesia exerts an excellent effect on the relief of pain. By targeting sympathetic nerves around the spinal cord and the sensory fields of the central nervous system, epidural administration of analgesics allows analgesia at very low dosages compared to intravenous infusion (Hansen, 2004). This results in decreased adverse systemic effects of the analgesics. Local analgesics and opioidergic agents are often used together when epidural analgesia is performed.

Epidural analgesia and gastrointestinal motility

The correlation between epidural analgesia and the recovery of gastrointestinal motility is being investigated. Morphine, a major opioid agent frequently used in clinical practice, is known to induce excessive and abberant contractions in the small intestine and the colon, leading to disturbance of the intestinal motility rhythm with subsequent constipation (Murthy et al., 1998). In contrast, the epidural administration of morphine plus bupivacaine has been reported to facilitate recovery from paralytic ileus following surgery (Barzoi et al., 2000),

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<th>Table 1. The Problems of postoperative ileus</th>
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<tr>
<td>Nausea and vomiting</td>
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<td>Abdominal discomfort/pain</td>
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<td>Delay in resuming oral nutrition</td>
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<td>Increased risk of other postoperative complica-tions</td>
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<td>Delay in return to normal activity</td>
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<td>Longer hospital stay</td>
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suggesting the existence of differing effects of epidural morphine and intravenous morphine on the recovery process of gut motility from paralytic ileus after open abdominal surgery. Moreover, local anesthesia is often used together with opioids for epidural analgesia to provide an effective blockade of the sympathetic nerves, which are also considered to play a role in the recovery of gut motility (Blumenthal et al., 2005). Because local anesthesia is usually not separated from epidural analgesia, the role of sympathetic nerve blockage in early recovery of gut motility remains uncertain.

However, evidence of the usefulness of epidural analgesia in the recovery of gut motility is based on clinical observations such as reduced time intervals before the first flatus and the first bowel movement, reduced time elapse before the first oral intake, and a reduction in the frequency of nausea and abdominal symptoms (Saito, 1994; Kanazi et al., 1996; Carli et al., 2001). These widely used clinical determinants of the resumption of gastrointestinal motility are very subjective. Confirmation of first flatus passage is highly dependent on a report from the patient, and the correlation between passage of flatus and propulsive bowel movements is unpredictable. Evacuation of stools, although a clinical manifestation, is not specific, as it may only indicate the distal bowel emptying and not necessarily the function of the entire gastrointestinal tract. The time elapse before the first oral intake is highly influenced by the surgeon’s policy. Furthermore, bowel sounds are not specific because the origin of the sound is not specified and also requires frequent auscultation for assessment. Therefore the clinical effects of epidural analgesia on the speed of recovery from postoperative ileus have yet to be confirmed by experiments in animal models.

Morphine is known to delay gastric emptying and intestinal transit, to suppress the intestinal secretion of water and electrolytes, and to inhibit the transport of bile into the duodenum (Wood, 2004); however, epidural morphine can shorten postoperative ileus (Morimoto et al., 1995; Delaney, 2004). Low doses of morphine have been reported to induce premature phase III-like activity in dogs (Konturek et al., 1980, Sarna et al., 1984; Lewis et al., 1999) and humans (Waterfall, 1983), whereas a supramaximal dose of morphine did not initiate premature phase III contractions and alter the migration of migrating myoelectric complexes (Sarna et al., 1982).

Intravenous morphine facilitates the appearance of phase II-like contractions (Sarr et al., 1988). Intravenous morphine did not significantly facilitate the first appearance of IMC which is consistent with the finding that morphine administration has no effect on gastric motility, while it markedly increases duodenal contractility (Ingram et al., 1981). Moreover a previous review noted that the primary sites of action of morphine with respect to inhibition of gastrointestinal function are in the peripheral nervous system, whereas analgesic activity resides primarily in the central nervous system (Greenwood-Van Meerveld et al., 2004). Thus the additive effect of epidural morphine may occur indirectly through analgesic or other actions on the central nervous system.

After major open abdominal surgery, severe pain persists for the first 48 hours (Bonica, 1990). Opioids have remarkable effects in the reduction of this unbearable pain. With sufficient analgesia early mobilization is possible which may decrease the incidence of complications including postoperative ileus. As morphine is widely known to reduce gastro-intestinal motility,
there is often hesitation to use morphine for analgesia. Nevertheless, epidural analgesia requires a much lower dose compared to intravenous analgesia, more aggressive use of opioids may take place in clinical practice. Further investigations to clarify correlation of gastrointestinal motility such as gastric emptying, small intestine transit time and colonic transfer with the results of SGT may be useful in reinforcing the clinical assessment of gastrointestinal motility.

References


