Therapy for intra-abdominal adhesions

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Therapy for adhesions encompasses their prevention and treatment. They are reduced in number and severity by good surgical technique but antiadhesion agents are useful adjuncts. Small bowel obstruction secondary to adhesions requires surgery following resuscitation if signs of peritonism develop. Otherwise a trial of conservative therapy is advocated.

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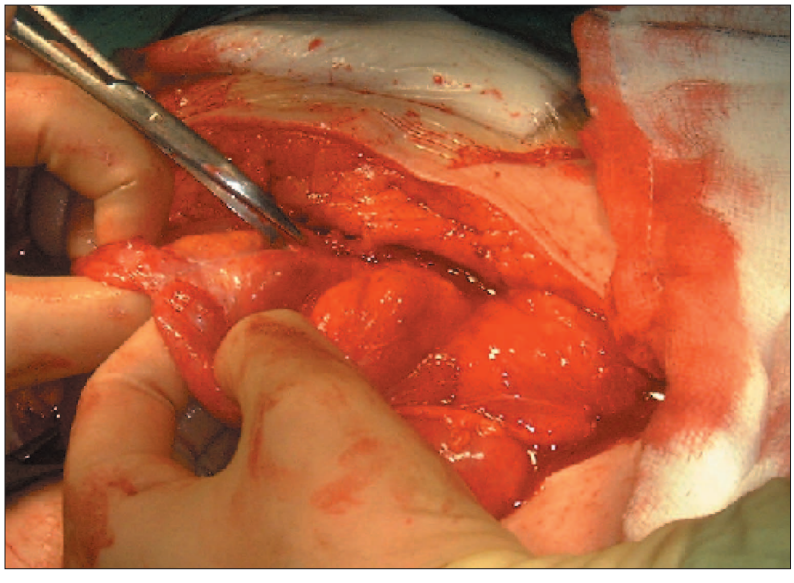
Adhesions may be congenital or follow radiotherapy but are invariably more common following surgery, occurring after 67–93% of operations (*Figure 1*) (Risberg, 1997). These occur in the abdomen following the release of plasma proteins from injured peritoneum, which results in the adhesion of adjacent viscera (Holmdahl, 1999). Adhesions are reversible in the first few days but once fibroblasts replace the fibrin with collagen the adhesions become irreversible (Holmdahl, 1999).

Abdominal adhesions are most prevalent following appendiceal and colonic surgery (Matter et al, 1997) and result in small bowel obstruction, infertility or pelvic pain (Risberg, 1997). Ellis et al (1999) reported that over a period of 10 years following surgery 5.7% of patients were readmitted for complications directly related to adhesions and a further 34.6% readmitted for symptoms possibly related to adhesions with a mean of 2.1 admissions per patient. In addition up to 20% of first episodes of small bowel obstruction resulting from adhesions occur two decades after the initiating procedure (Holmdahl, 1999).

There is a 21% risk of adhesion-related bowel perforation in re-operated patients (Ellis et al, 1999). The time taken to make the initial incision and to divide adhesions present is longer in patients with previous surgery (Coleman et al, 2000). The cost of adhesions incurred from episodes of small bowel obstruction is estimated at £2 077 796 for the whole of Finland (Kössi et al, 2003) and in the UK at £1606.15 per conservatively treated patient and £4677.41 per surgically treated admission (Menzies et al, 2001).

Therapy for adhesions covers two broad areas, prevention of adhesions and treatment of those already formed. The best method of preventing adhesions is to avoid surgery, however, this is not always possible. Research has focused on the reduction of inflammation intra- and postoperatively (reducing fibrin deposition), enhancing fibrin degradation and keeping tissues physically separated following surgery.

Figure 1. Adhesions.



CONTRAST STUDIES

Two studies (Assalia et al, 1997; Choi et al, 2002) of a 100 ml gastrografin small bowel meal introduced via a nasogastric tube in simple partial small bowel obstruction found it to be safe and possibly therapeutic, as it may resolve the obstruction. One prospective randomized controlled trial of 127 patients with 157 episodes of adhesive obstruction reported faster resolution, fewer operations and shorter total length of stay in those patients who were given a small bowel meal (Assalia et al, 1997). A second prospective study of 124 patients experiencing 139 episodes of obstruction found 101 episodes improved after 48 hours of conservative management (one patient from this group required

surgery after 6 days) and the remainder were randomized to either gastrografin meal (19 patients) or surgery (16 patients). The gastrografin meal group detected partial obstruction in 14 patients, all of whom settled with conservative management and the remainder (5 patients) required surgery (Choi et al, 2002).

SURGERY

The incidence of adhesions may be reduced by observing well-established surgical principles. These include gentle dissection, careful haemostasis, prophylaxis against infection, irrigation, putting little tension on tissues, and avoiding ischaemia, thermal injury or the introduction of foreign bodies where possible. It has been suggested that laparoscopic surgery may reduce the incidence of adhesions (Holmdahl, 1999). However, the Surgical and Clinical Adhesions Research (SCAR) 2 study demonstrated that laparoscopic gynaecological surgery (excluding laparoscopic sterilization) does not reduce the incidence of adhesions compared with open surgery (Lower et al, 2003).

Patients presenting with small bowel obstruction secondary to adhesions may be managed conservatively for up to 5 days (but more commonly 48 hours) unless signs of strangulation or peritonitis develop, in which case they require surgery following an initial period of resuscitation (Seror et al, 1993). Approximately one third of patients require surgery for small bowel obstruction (Menzies et al, 2001). In cases of obstruction immediately following surgery, the patient is more likely to resolve with conservative management (80–90% recover within 14 days) except in patients whose obstruction follows abdominoperineal resection of the rectum, when immediate surgery is necessary (Wilson et al, 1999).

INTESTINAL TUBES

Nasogastric tubes are routinely used in the management of small bowel obstruction to decompress the proximal bowel. Longer tubes have been used to splint the bowel following adhesiolysis but there are only anecdotal reports of benefit (Wittens et al, 1990).

PHARMACOLOGICAL

A variety of pharmacological agents have been assessed for prevention of adhesions but have not demonstrated definite effects. The prevention of fibrin formation by inhibition of prostaglandin synthesis with non-steroidal anti-inflammatory drugs showed promise in animal studies (Monk et al, 1994) but has shown questionable efficacy in human studies, possibly as a result of difficulties in drug delivery (Risberg, 1997). Corticosteroids with and without antihistamines have equivocal results but have side effects of immunosuppression and delayed wound healing (Risberg, 1997). Enzymatic degradation with recombinant tissue plasminogen activator has been shown to be effective in an animal study but is precluded from clinical use because of the need for intraperitoneal administration and its expense (Monk et al, 1994).

BARRIER AGENTS

Barrier agents are compounds which are used to block bowel loops from coming into contact and hence adhesions forming. Agents studied include:

- Polyglycolic acid mesh, which actually increased adhesion formation
- Polytetrafluoroethylene (Gortex, W.L. Gore and Associates, Inc., Flagstaff, Ariz), which does not degrade and requires suturing in place
- Oxidized cellulose (Interceed, Johnson & Johnson Medical Inc., New Brunswick, NJ), which increased adhesions unless complete haemostasis was achieved (Monk et al, 1994)
- Hyaluronic acid and carboxymethylcellulose (Seprafilm, Genzyme Corporation, Cambridge, MA). This is a bioresorbable translucent adhesions barrier (*Figure 2*). It is the most promising barrier agent and has demonstrated a significant reduction in the severity of adhesions, however, its effect on their incidence is uncertain (Vrijland et al, 2002; Becker et al, 2003). The sheets are placed over any area that sustains direct surgical trauma. This may require between 1 and 10 sheets (average 4.4 sheets) (Beck et al, 2003) which are absorbed over a period of approximately 1 week. Use of the material is safe, but there is a slightly higher incidence of anastomotic leaks if the anastomosis is covered with the barrier agent. Consequently it is suggested that the anastomosis should be left uncovered (Beck et al, 2003).

Figure 2. Hyaluronic acid and carboxymethylcellulose film.

HYDROFLOATATION SOLUTIONS

Hydrofloatation solutions work by floating loops of bowel away from each other and have shown great promise for the prevention of adhesions. They are administered during surgery after the abdomen has been closed.

Adept

Adept (Shire Pharmaceuticals Limited, Basingstoke, Hampshire) is a 4% solution of icodextrin (an α 1,4 glucose polymer) and has been shown to be safe in humans. Historically the solution has been used for peritoneal dialysis for many years. It was noted that these patients developed fewer adhesions and this led to investigation of its antiadhesion properties. A minimum of 500 ml of the solution is used to irrigate the operative field at the conclusion of surgery. The abdomen is closed in the usual fashion but before placement of the final sutures a further 1000 ml is instilled into the abdomen via a giving set (*Figure 3*). The solution is absorbed over the following week.

Drains do not pose a problem with the use of Adept: it has been demonstrated that they allow only one third of the instillate to escape and that the product is still effective. The product is currently the cheapest agent on the market, costing £44 for a 1.5 litre bag.

Figure 3. Instillation of hydrofloatation solution.

KEY POINTS

- The majority of abdominal adhesions occur as a result of surgery.
- Adhesions result in repeat admissions plus increased length and difficulty of further surgery.
- Laparoscopic surgery probably does not protect against adhesions.
- The severity of adhesions may be reduced by good surgical technique and the use of hydrofloatation or barrier therapies.

CONCLUSION

Adhesions occur even without surgery but develop in up to 93% of patients following surgery. As long as a surgeon uses good surgical technique, the technique of surgery (open or laparoscopic) probably does not affect the incidence of adhesion formation. There are a variety of innovative adjuncts available which help reduce the incidence of adhesion formation. Hydrofloatation methods show great promise. **HM**

Conflict of interest: Mr TF Bullen is being sponsored for a higher degree by Shire Pharmaceuticals Group plc.

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