Should anaesthetic technique be modified for cancer surgery?

Following surgical resection of cancer, morbidity often results from recurrence and metastatic disease. The neuroendocrine response to surgery and choice of surgical technique can influence metastatic spread, but perioperative factors may also be important. Should we modify anaesthetic technique during cancer surgery to reduce metastatic disease and recurrence?

Arguments for changing anaesthetic technique

Natural killer cell activity protects against metastasis, but in animal models thiopentone and ketamine suppress this. In vitro, volatile agents decrease cell-mediated immunity and increase the possibility of metastatic spread (Snyder and Greenberg, 2010; Heaney and Buggy, 2012). In contrast propofol's effects on prostaglandins and preserving NK function may be anti-neoplastic, so propofol total intravenous anaesthesia may confer benefits over volatile agents.

Effective analgesia attenuates the pro-metastatic effect of surgery. However, opioids, the mainstay of postoperative analgesia, may promote tumour progression through suppressing cell-mediated and humoral immunity. μ-opioid receptor activation is also associated with prometastatic processes including angiogenesis and oncogenic signalling. Using regional anaesthesia, non-steroidal anti-inflammatory drugs and gabapentin as part of a multimodal analgesia strategy could reduce both opioid requirements and metastatic spread. In vitro, local anaesthetic agents have antiproliferative and cytotoxic effects on tumour cells and help maintain NK cell function. Regional anaesthesia reduces anaesthetic and analgesic requirements, helping to preserve immune function and possibly decrease the incidence of cancer recurrence (Heaney and Buggy, 2012). COX-2 facilitates cancer progression, yet is inhibited by non-steroidal anti-inflammatory drugs. In epidemiological studies, long-term non-steroidal anti-inflammatory drug use is associated with a reduced incidence of cancer (Heaney and Buggy, 2012). Finally gabapentin reduces metastases at low doses in animal models (Bugan et al, 2015).

Allogeneic blood transfusions increase the risk of cancer recurrence via immunomodulation, so a high threshold for blood transfusion could be beneficial (Heaney and Buggy, 2012). Psychological stress activates the physiological stress response, increasing the risk of metastasis (Heaney and Buggy, 2012), so minimizing patient anxiety could reduce this effect. Ensuring normothermia could reduce the risk of metastasis as perioperative hypothermia increases sympathetic stimulation, increases the risk of blood loss and suppresses cell-mediated and humoral immunity (Heaney and Buggy, 2012).

Arguments against changing anaesthetic technique

Interpreting evidence regarding the use of volatile anaesthetic agents in cancer surgery is difficult. Some agents, particularly sevoflurane and desflurane, reduce cancer cell migration in vitro but most studies are preclinical or investigate use in specific cancers, so there is not enough evidence to support a change of anaesthetic technique (Buggy et al, 2015).

The same is true regarding opioid use in cancer. Opioids can decrease migration and proliferation of cancerous cells. The degree of immunomodulation varies depending upon the opioid used and the route and duration of administration (Heaney and Buggy, 2012). While regional anaesthesia in general improves analgesia, a Cochrane review concluded that 'evidence for the benefit of regional anaesthesia techniques on tumour recurrence is inadequate' (Cakmakkaya et al, 2014). Non-steroidal anti-inflammatory drugs are important analgesics, but potential renal and cardiovascular effects preclude their use in some patients. Similarly, gabapentin is only indicated for neuropathic pain and its role in the acute postoperative setting is unclear.

Strategies for restrictive blood transfusion lack generalizability as much of the evidence for an association with cancer recurrence was obtained in patients with colorectal cancer. Anaemia, a frequent complication of both cancer and chemotherapy, can reduce survival, so the benefits of a normal haemoglobin may outweigh the risk of transfusion.

Conclusions

Translation of in-vitro findings into the clinical setting is lacking and there is insufficient evidence to support adapting perioperative care for patients undergoing cancer surgery (Buggy et al, 2015). Patient outcomes are most likely improved by ensuring a meticulous anaesthetic with effective postoperative analgesia, irrespective of how this is achieved. **BJHM**

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