

Intra-operative autologous transfusion in cancer patients

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The surgical treatment of cancer may require blood transfusion. Twenty years ago, 25% of all banked blood was used in cancer patients. Although surgery is now generally less haemorrhagic than in the past, surgeons do not hesitate to perform more aggressive, haemorrhagic procedures such as hepatectomy, extensive tumour resection, and peritonectomy (often associated with intraperitoneal hyperthermic chemotherapy) etc. Homologous transfusion results in immunosuppression, and consequently may increase the risk of postoperative infections and negatively affect the malignant disease itself (more tumour recurrences and reduced survival) (1, 2). Thus, autologous transfusion methods developed to reduce or avoid allogenic blood transfusion in non-tumour surgery would be of particular interest in cancer patients.

PREOPERATIVE DONATION OF BLOOD

Preoperative blood donation is feasible and might be recommended for these patients. However, several limiting factors preclude its systematic use (3, 4). Tumour anaemia excludes some patients from blood pre-deposition. Furthermore, erythropoiesis is frequently impaired, partly because of iron depletion and inability to use iron reserves. The relative urgency in scheduling surgery often does not provide enough time for a sufficient number of donations. Transfusion of autologous banked blood does not eliminate all risks associated with transfusion, such as bacterial infection and incompatibility. Recently, blood storage at low temperature has been reported to result in immunosuppression; growth factors released under these conditions could enhance tumour growth (4). However, experimental studies suggest a continuous decline in the metastatic potential of tumour cells in pre-donated blood during storage. Finally, the viability of banked red blood cells is impaired.

INTRA-OPERATIVE BLOOD SALVAGE

Intra-operative blood salvage would appear to be a more favourable strategy, since its efficacy is

blood loss dependent and it provides fresh autologous red blood cells. However, blood salvage may be contraindicated in cancer surgery because of the risk of systemic dissemination of tumour cells.

Blood shed from the surgical field during cancer surgery contains tumour cells (3-5). The invasiveness of these cells when injected intravenously, and the consequent risk of metastasis have been questioned by some authors (3, 5). Moreover, they claim that the number of tumour cells remaining after processing the blood shed from the surgical field is small compared to the spontaneous and continuous dissemination of cancer cells. Accordingly, certain clinical studies did not report increased risk of tumour dissemination after autotransfusion of such blood (5). Therefore, these authors accept use of intra-operative autotransfusion techniques in case of unexpected life-threatening haemorrhage, or even in case of scheduled surgery with a high risk of massive haemorrhage (3).

However, other investigators, using highly sensitive methods, have demonstrated that tumour cells in the surgical field are viable, proliferating, tumourigenic and potentially invasive (4, 6). Tumour cells can be isolated even in cases with small tumours and after resections with clean margins. Indeed, blood shed from veins and lymphatic vessels draining these tumours carries tumour cells (7, 8). Filtration, centrifugation and cell washing during blood processing in the autotransfusion device remove insufficient numbers of tumour cells. Although some clinical studies have not reported shortened survival after intra-operative autotransfusion (5), the statistical power of these studies does not allow, however, firm conclusions with regard to the safety of transfusion of shed blood during cancer surgery. These authors conclude that intra-operative blood salvage is unacceptable for cancer surgery unless efficient methods are used for tumour cell elimination (4).

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Two methods were proposed to eliminate tumour cells from red blood cells concentrates before transfusion : the use of leucocyte depletion filters and irradiation.

LEUCOCYTE-DEPLETION FILTERS

Leucocyte-depletion with new generation filters results from mechanical filtration and electrostatic properties of cell membranes. Filtration of 400 ml of blood requires 40 minutes. Several in vitro studies using blood enriched with different tumour cell lines conclude that these filters are capable of eliminating tumour cells (3, 5). In one clinical study of patients undergoing lung resection for cancer no tumour cells were detected after filtration ; on the other hand, blood from the Cell Saver® from 9 out of 16 patients contained cancer cells before filtration (9). Two other studies found tumour cells after filtration (6, 10). HANSEN *et al.* estimated that filtration provided a 5 log reduction in numbers of tumour cells (4, 6). Whereas ELIAS *et al.* consider these filters to be efficient in substantially reducing the risk of dissemination (3), HANSEN *et al.* claim leucocyte depletion filters are not safe enough to allow retransfusion of blood shed during cancer surgery (4, 6).

BLOOD IRRADIATION

HANSEN *et al.* propose blood irradiation to eliminate tumour cells contaminating blood salvaged during cancer surgery (6). Radiosensitivity is improved and is quite similar across tumour cell lines when they are oxygenated and in suspension. An irradiation of 50 Gy was shown to provide a 12 log reduction in proliferating cells (6). With a tumour burden of 10^9 cells in the salvaged blood (which is more than is observed clinically or expected in wound blood), this 12 log reduction would leave less than 1 cell. In fact, irradiation does not destroy all cells ; but those that are not physically killed are incapable of proliferation or DNA metabolism. Since gamma irradiation exerts its effect primarily on DNA, non-nucleated red blood cells are unaffected. No significant haemolysis occurs. Blood salvage with cell washing and irradiation provides red blood cells of high quality with normal function and viability (11). Therefore, blood irradiation allows safe retransfusion of shed blood in cancer surgery since the recommended dose of 50 Gy can kill or sterilise cells from all

types of malignant tumours and with any conceivable level of tumour cell contamination during cancer surgery and does not damage the red blood cells. Intra-operative blood salvage with blood irradiation has been used in several cancer centres in Europe. This technique has been shown to be effective in saving blood in cancer patients and in reducing allogenic transfusions (3).

CONCLUSIONS

There is evidence that the rate of postoperative infection is reduced in cancer surgery if autologous blood is used, but any beneficial effect on malignant recurrence is less clear. It is unlikely that a definitive trial could be carried-out. However, it appears that the use leucocyte-depletion filters and, better, blood irradiation produces a product as safe, if not safer, than allogenic blood. Intra-operative blood salvage with filtration or irradiation should be used in case of unexpected life-threatening haemorrhage and of scheduled surgery with a high risk of massive haemorrhage.

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