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Selective reduction in multiple pregnancy

Legal confusion and ethical dilemmas

Contrary to the happy image in the media of multiple births the reality is often starkly different. Data on multiple pregnancy are limited, but a study of registered multiple births in England and Wales between 1975 and 1983 reported a 21% perinatal mortality and a 22% infant mortality.[1] (These figures do not include early loss of pregnancy, and the total fetal wastage is even higher.) Although numbers are small, perinatal mortality among sextuplets rose to 41% and infant mortality to 50%. Many surviving infants after multiple birth are extremely premature, and a third of babies born before 28 weeks' gestation are likely to be seriously handicapped.[2] Hobbins described one case of quintuplets delivered at 27 weeks in which one baby died after two days, one had necrotising enterocolitis and was blind, one had post-haemorrhagic hydrocephalus, one had chronic lung disease, and the fifth had neonatal seizures because of perinatal ischaemia.[3] The cost of neonatal care was $300 000. Over and above the depressing statistics for the babies mothers with multiple pregnancies have very high risks of pre-eclampsia, postpartum haemorrhage, and thrombophlebitis and often face great misery from hyperemesis and polyhydramnios. Furthermore, the social, financial, and emotional strains consequent on multiple births may be devastating, especially if one or more of the children are handicapped. In addition, multiple births may cause overcrowding in special care baby units, hindering the units' ability to provide an optimum service.[4]

High order multiple pregnancies have risen sharply in recent years, partly because of induction of ovulation but occasionally because of multiple embryo or oocyte replacements during in vitro fertilisation or gamete intrafallopian transfer.[1,4] Doctors participating in assisted reproduction have a responsibility to ensure that they limit high order multiple pregnancy to an absolute minimum. Nevertheless, a few high order multiple pregnancies will inevitably occur, and the doctor has to help the couple to decide on the best course of action. Many couples will accept the risks and continue with the pregnancy, but they may have to face disappointment and distress. Others may opt to terminate the entire pregnancy, but this too is an unhappy prospect, especially for infertile couples who desperately want children. A third option is selective reduction of pregnancy, a choice which may be supported by several pragmatic obstetric arguments.[5] Selective reduction was first used when one twin had a fetal abnormality, allowing the normal twin to continue to term.[6]

Berkowitz *et al* have recently described their experience of selective reduction in 12 cases of multiple pregnancy, ranging from triplets to sextuplets, that all occurred after induction of ovulation.[7] A cardiotoxic injection of potassium chloride by the transabdominal route between nine and 13 weeks' gestation was used to reduce the fetuses, usually to two. Four mothers lost their complete pregnancies, one after the now discontinued operation of transcervical fetal aspiration and one in association with cervical incompetence; the two others aborted spontaneously four and eight weeks after the transabdominal procedure. On the positive side, eight mothers had 15 live births; all delivered after 34 weeks in healthy condition. Berkowitz *et al* claim that the survival of 15 out of 49 pregnancies is comparable with what would have occurred with non-interference but with the advantage of substantially lower morbidity.

Selective reduction of pregnancy does, however, raise difficult legal and ethical problems. In its third report the Voluntary Licensing Authority warned doctors that selective reduction could result in criminal proceedings.[8] The problem lies in the different wordings of the 1861 Offences Against the Person Act, which states that it is an offence "to procure a miscarriage," and the 1967 Abortion Act, which defines when it is lawful "to terminate a pregnancy." One literal interpretation holds that because selective reduction does not "terminate a pregnancy" the Abortion Act would not apply and doctors might be liable to prosecution under the 1861 act. It is clear, however, that doctors who perform selective reduction to protect the physical and mental health of the mother and prevent serious handicap in the baby would be acting in the spirit, if not the letter, of the 1967 act. The Voluntary Licensing Authority advises doctors to comply with the requirements of the Abortion Act while warning that the act might be ineffective for fetal reduction. This is one of the many medical topics in which the law is far from clear, and it is a matter of justice that doctors should know where they stand.

In some respects the ethics of selective reduction overlap with those of therapeutic abortion, and people who oppose abortion on principle will find selective reduction equally abhorrent.[9] On the other hand, many people who otherwise support abortion may regard the creation of pregnancy followed by its immediate destruction as exhibiting an

unacceptable disrespect for early human life. Perhaps a distinction has to be drawn between deliberately risking the induction of multiple pregnancy with the full intention of using fetal reduction and resorting to fetal reduction only when high order multiple pregnancy occurs inadvertently.

There is no information on the emotional consequences of selective reduction on the mother or the surviving children. In a short time mothers go from the emotional problems of prolonged infertility to high order multiple pregnancy and fetal reduction. Initially, they may experience relief after selective reduction, but they may later have feelings of guilt or bereavement. Careful follow up is required.

Fetal reduction is an example of technical advance moving ahead of public opinion, and open discussion of the obstetric, legal, and ethical issues is required before the practice can be fully accepted. Clearly, prevention is better than cure, and everything should be done to prevent the dilemma for parents in the first place. It may well come to be recognised, however, that selective fetal reduction is the humane option for some couples faced with the horrifying potential consequences of multiple births.

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Intra-arterial hepatic chemotherapy for liver malignancy

Not yet proved to prolong survival

The rationale for giving patients with tumours of the liver intra-arterial hepatic chemotherapy is anatomical, pharmacological, and toxicological. The blood supply to liver tumours derives mainly from the hepatic arterial bed, and consequently more drug should reach the tumour if given by this route rather than either systemically or into the portal circulation.[1-3] Using drugs with short plasma half lives that can be efficiently extracted by the liver should diminish systemic toxicity, and the ability to deliver high local concentrations of drug may increase the regression of tumours.[4] Giving drugs by infusion and decreasing hepatic arterial flow may further enhance toxicity.[5] Concomitant injection of inert particulate matter—for example, biodegradable starch microspheres—may not only decrease blood flow but also infarct the tumour.[6] A recent advance has been to show the prolonged retention in sites of metastatic tumour of lipophilic cytotoxic drugs injected in lipid contrast medium.[7]

Numerous non-randomised studies of intra-arterial hepatic chemotherapy in primary and secondary liver cancer have been conducted since the technique was described in the early 1950s.[8,9] Higher rates of response than for systemic chemotherapy have been seen in patients with hepatoma,[10] metastatic ocular melanoma,[11] and metastatic colorectal carcinoma.[12] But randomised studies are needed to determine toxicity, rates of response, and the benefits to survival. So far randomised studies have been reported only for metastatic colorectal carcinoma.

The California Oncology Group compared systemic and intra-arterial fluorouracil in 61 patients with liver metastases of colorectal carcinoma and found no difference in rate of response or survival.[13] Two separate trials—from the Memorial Sloan Kettering Cancer Research Centre and the Northern California Oncology Group—have used floxuridine and shown a higher rate of response (50-59%) with intra-arterial hepatic chemotherapy than with systemic chemotherapy (10-17%).[14,15] Patients failing to respond to systemic chemotherapy were crossed over to intra-arterial hepatic chemotherapy, and up to a quarter responded further. The crossover made true assessment of survival impossible, but this was not the primary aim of the trials. In the trial at the Sloan Kettering the median survival of the patients starting treatment with intra-arterial hepatic chemotherapy was 17 months compared with 12 months for those starting treatment with systemic chemotherapy. This difference was not significant but may show some survival benefit in certain subgroups of patients—for example, those not prone to developing extrahepatic disease. The main toxicity of intra-arterial hepatic chemotherapy was chemical hepatitis, biliary sclerosis, and gastroduodenal ulceration. Some patients had liver pain, but abdominal pain was more common and was caused by misperfusion of the gastrointestinal tract. Indeed, systemic infusional chemotherapy was associated with greater toxicity, especially diarrhoea, and the overall quality of life of patients given intra-arterial hepatic chemotherapy was judged to be better than that of those given systemic chemotherapy.[14] An important problem, however, has been the higher rate of extrahepatic metastases in those given intra-arterial hepatic chemotherapy.

The morbidity caused by intra-arterial hepatic chemotherapy has decreased with experience of the technique.[16] Ambulatory patients may be treated with internally or externally placed pumps.[17] One important factor limiting the use of intra-arterial hepatic chemotherapy is the lack of effective drugs to treat tumours such as hepatoma and colorectal carcinoma; other factors include cost and the continued growth of disease in other sites.

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