MEDICAL PRACTICE

Contemporary Themes

The randomised controlled trial in the evaluation of new technology: a case study

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The 1983 report of the Council for Science and Society calling for evaluation of all expensive new medical technology[1] was welcomed in the *British Medical Journal*[2] and the *Lancet*.[3] An appraisal of the benefits and costs of the heart transplant programme is among encouraging developments which have followed.[4] Nevertheless, there is still resistance to the use of randomised controlled trials in evaluation not only of new medical technology but also of innovations in clinical practice.[5,6] There appear to be two standards for innovations in medicine: one which demands rigorous assessment of new drugs by proper trials; and a second which allows the introduction of expensive technology and new techniques on the strength of descriptive reports. A protocol for a randomised trial of the extracorporeal shock wave lithotripter was recently rejected.

The pros and cons of randomised trials in evaluation have been extensively discussed elsewhere. The purpose of this paper is not to add to this debate but rather, using the experience with the lithotripter trial, to seek to understand the barriers which exist to proper evaluation of new techniques, and in particular to the use of randomised controlled trials.

Lithotripter trial

The extracorporeal shock wave lithotripter is a device for fragmenting stones in the upper urinary tract without open surgery. The United Kingdom has two lithotripters—one at a private hospital and a second at St Thomas's Hospital, London, purchased as a result of a collaboration between the British United Provident Association (BUPA) and the National Health Service. The running costs of the St Thomas's machine were paid for by the Department of Health and Social Security so that an evaluation could be carried out. The Health Services Research Unit of the United Medical and Dental Schools at St Thomas's was commissioned to design and undertake this evaluation.

The only information available on extracorporeal shock wave lithotripsy consisted of descriptive reports of case series[7,8] and impressions from British urologists who had visited lithotripter centres in West Germany. Since then large series of cases have been reported from Germany[9,10] together with one small British series.[11] The results are encouraging, but none of the reports contains information on the selection of patients or a detailed description of complications. In a review of 7000 patients treated by lithotripsy in German centres Alken and his colleagues commented in 1985: "Unfortunately there are currently no objective data to determine the success or complications after shock wave lithotripsy. . . ."[12]

There has been no contemporaneous comparison of extracorporeal shock wave lithotripsy with existing methods for removing urinary calculi, and it would be misleading to make the comparison with historical results from open or percutaneous surgery. No long term follow up of patients treated by the lithotripter has been attempted, and reports on the cost of the new treatment are conflicting.[13,14]

Given the limited information which was available and the circumstances in which extracorporeal shock wave lithotripsy was introduced to Britain the Health Services Research Unit recommended a randomised controlled trial as the most appropriate method of evaluation. Accordingly, a protocol was submitted to the DHSS for a trial to compare lithotripsy with both conventional open and percutaneous renal surgery. It was proposed to assess the treatments in terms of effectiveness of stone removal, morbidity, including recurrence of stones, mortality, patient acceptability, and cost.

Randomisation offered several advantages. Firstly, it was necessary to have equivalent groups of patients in order to compare the different forms of treatment for urinary calculus. Randomisation was the simplest method of controlling for factors known to influence outcome and the only method of controlling for factors whose prognostic importance was unknown or unrecognised. Secondly, the long term side effects of lithotripsy, if any, were unknown, and a randomised trial was the surest method of identifying these; provision was made to detect damage to bone and renal tissue and any increase in stone recurrence, among other complications.

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The conditions under which the lithotripter was introduced favoured a randomised study. There would be only one or at most one and a half machines available to the NHS (if the invitation to the health service to buy time on the private machine in London was taken up), and these could not cope with all the stone surgery in Britain. Rationing was inevitable and randomisation seemed an ethical means of deciding who did and did not receive treatment on the new device. A randomised controlled trial would give any patient an equal chance of treatment on the lithotripter irrespective of age, sex, social class, and place of residence. It was estimated that about 800 patients would be required for the study and that these could be recruited in 12 months, long before another machine could be introduced and the shortage alleviated.

Other study methods were considered because it was recognised that clinicians might find difficulties in administering the randomised trial. The rapid evolution of stone surgery in recent years, with the introduction of percutaneous treatment, made the use of historical controls even more dangerous than usual. A large descriptive study was a second possibility: conventional and percutaneous surgery would continue as long as the lithotripter was in short supply, and it would be possible to follow this natural experiment. There were important disadvantages to this approach. Firstly, a very large sample would be required to control for variables such as stone history which might influence the comparison. Secondly, there might be unrecognised confounding factors unevenly distributed among the groups which would bias the outcome. Finally, open access to a limited service would almost certainly favour patients living in London and the south east. A randomised trial circumvented these problems.

The protocol was recommended for support by the external referees of the Department of Health and was approved by the ethical committee of the BMA. The reception from urologists was mixed. On the advice of selected urologists the DHSS decided not to proceed with the trial and asked the Health Services Research Unit to consider alternative approaches to evaluation. A descriptive study comparing lithotripsy with the alternatives is now under way. It is understood that a randomised trial to evaluate extracorporeal shock wave lithotripsy is planned in Sweden.

Objections to the trial

The following factors may have contributed to the failure to mount a randomised trial.

Ethical resistance has been described elsewhere as non-intellectual resistance.[15] A randomised controlled trial implies that there is no preference for one treatment over others, and in the view of many urologists this was clearly not so with lithotripsy. Even those who recognised that descriptions of case series were not proof of the superiority of extracorporeal shock wave lithotriptor was in short supply, and it would be possible to follow this superficially unequal forms of treatment. The emotional adherence to new technology is one of the most important obstacles to evaluation and becomes insurmountable once it has spread to the general public. In the case of the lithotripter it was hoped that the circumstances surrounding its introduction would temper anxiety about "an unethical trial." The service would be available in very limited supply for at least 12 months and randomisation offered a fair means of deciding who received the new treatment.

Interference with the doctor-patient relationship—A randomised trial requires the clinician to suspend judgment in advising or choosing treatment for the patient.[16 17] This interference with the doctor-patient relationship is particularly difficult when the choices of treatment seem unequal, as with lithotripsy and surgery. Prerandomisation has been suggested as a means of dealing with this problem.[15]

Effect on dissemination—A randomised trial may have been seen as a mechanism for deferring the decision on buying additional lithotripters. Until the results of the evaluation were available bids for further machines could quite legitimately be rejected. Although definitive results on the medical effects of extracorporeal shock wave lithotripsy would not be available for some years, this need not have held back the spread of the technology. At most the trial would have produced a 12 month delay, during which time data for an informed introduction of the technique would have been collected. Conceivably an evaluation might have been used to defer a decision on more machines beyond this period.

Medical-industrial complex—The dissemination of medical technology owes a great deal to the pursuit of profit by commercial interests.[18] Though this is a more important influence in the United States than in the United Kingdom, prestige rather than profit may influence the British clinician in the bid for acquisition of new technologies.

Influence of the private sector—The existence of a lithotripter in the private sector may have influenced the response to a randomised trial. A study in which patients would be required to run the gauntlet of randomisation in order to gain access to a machine in the health service, when there was already one in a private hospital available to any individual or health authority prepared to meet the cost of treatment, may have been seen as a source of embarrassment. This ignores the important distinction between private health care and the NHS. Considerations which motivate acquisition of technology in the private sector should not be allowed to influence behaviour in the health service and to constrain the drive for evaluation.

Role of champions—The assumption that those most closely concerned with an innovation must be right has underpinned the dissemination of technology for years. As a result substandard and even harmful techniques have been introduced.[19] If doctors are to be given a free hand in seeding technologies they have a responsibility to sanction only those drugs and techniques whose value has been established beyond reasonable doubt.

Source of the evaluation—The authors of the evaluation of extracorporeal shock wave lithotripsy were from a non-clinical medical department and might have been regarded as out of touch with the front line problems of administering a randomised study. The trial would perhaps have stood a better chance if it had emanated from among the urologists. Nevertheless, past experience—for example, with CT scanners—has shown that those most closely concerned with new technologies are unwilling to moderate their enthusiasm and evaluate.[20] There may be a case for asking specialists in the same discipline to take this responsibility but there is a risk of conflict of interest. Checks and balances could be provided by specialists in evaluation, who would advise on protocols produced by clinicians. This reverses the situation which existed with the evaluation of the lithotripter.

Recommendations for the future

Gastric freezing, high concentration oxygen for neonates, the use of hyperbaric oxygen in intensive care, and insulin coma for the treatment of schizophrenia are all examples of innovations introduced without evaluation and subsequently abandoned because they proved ineffective or unsafe. If mistakes are to be avoided a more rigorous attitude towards evaluation is required, with a wider acceptance of the randomised controlled trial. The following are suggestions for how this might be achieved.

Better education of physicians, patients, and the public—There is a growing awareness that resources for health care are limited, and the time is right for the simple message that evaluation avoids waste. It must be understood that evaluators are not opposed to new technology, only to those examples which are dangerous or wasteful.

Greater central control—There is a need for regulation of the introduction of new technology to ensure safety, assess social and economic implications, and advise on dissemination. This task could be undertaken either directly by the Department of Health or by an independent body established for the assessment of new technology, responsible to the new NHS Management Board.

Royal colleges—A set of standards needs to be established to guide the introduction of new technologies. These standards would set down the minimum extent of evaluation required for any innovation. A group appointed by the royal colleges would be an ideal source for such guidelines.

Voluntary agreement with industry—A voluntary code of practice should be agreed with manufacturers of medical equipment to guide the introduction of new technology.

The aim of these recommendations is to obtain a consensus on the need for evaluation and to win a proper place for randomised trials in this process.

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Comparison of treatment of renal calculi by open surgery, percutaneous nephrolithotomy, and extracorporeal shockwave lithotripsy

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Abstract

This study was designed to compare different methods of treating renal calculi in order to establish which was the most cost effective and successful. Of 1052 patients with renal calculi, 350 underwent open surgery, 350 percutaneous nephrolithotomy, 328 extracorporeal shockwave lithotripsy (ESWL), and 24 both percutaneous nephrolithotomy and ESWL. Treatment was defined as successful if stones were eliminated or reduced to less than 2 mm after three months. Success was achieved in 273 (78%) patients after open surgery, 289 (83%) after percutaneous nephrolithotomy, 301 (92%) after ESWL, and 15 (62%) after percutaneous nephrolithotomy and ESWL. Comparative total costs to the NHS were estimated as £3500 for open surgery, £1861 for percutaneous nephrolithotomy, £1789 for ESWL, and £3210 for both ESWL and nephrolithotomy. ESWL caused no blood loss and little morbidity and is the cheapest and quickest way of returning patients to normal life.

Introduction

Throughout the 1970s research and skill improved the success rates of open renal surgery for the large staghorn and smaller renal calculi and allowed all stones to be removed with minimal loss of function. The morbidity associated with such procedures was also reduced. In 1980 percutaneous nephrolithotomy was introduced, whereby a radiologically guided track was made through the skin into the renal collecting system, permitting the stones to be extracted under direct vision with an endoscope.[1] This technique reduces mortality and morbidity and entails a short stay in hospital at low cost to the National Health Service.[2]

In November 1984 the first extracorporeal shockwave lithotripter in the United Kingdom was installed by the St Martin's group of hospitals at the London Stone Centre. This apparatus enables kidney stones to be broken up in situ by using focused shock waves generated by an ultrashort, high tension underwater electrical discharge; it obviates the need for invasive surgery, although an anaesthetic is still required.[3] In all, 750 treatments have now been performed at the London Stone Centre and over 80 000 have been performed world wide (Dornier Systems, West Germany).

With any new and capitally expensive treatment three questions need to be answered: What is the difference in mortality? What is the difference in morbidity? Which mode of treatment is the most cost effective? We tried to define the current place of extracorporeal shockwave lithotripsy (ESWL) in the management of renal calculi by comparing 350 cases of open stone removal, 350 cases of percutaneous nephrolithotomy, and 352 cases of ESWL. All patients were treated by the same team of surgeons under the direct supervision of one consultant. Patients in all groups were unselected and treated consecutively over 14 years (open surgery from 1972 to 1980, percutaneous nephrolithotomy from 1980 to 1985, and ESWL in 1985).

Methods

Open surgery—All renal and ureteric calculi were treated by nephrolithotomy, pyelolithotomy, ureterolithotomy, or a combination of these procedures. Many patients had complicated conditions and had been operated on previously. Some complex renal calculi were removed with the aid of regional hypothermia,[4] in some cases intravenous inosine was used to protect function during controlled ischaemia, and in some cases minimal ischaemia or no clamping of the renal pedicle was used. Intraoperative radiography was commonly used, antibiotics were given routinely, and all patients required general anaesthesia.

Percutaneous nephrolithotomy—The techniques of one and two stage nephrolithotomy used have been extensively described.[5] This study comprised 150 two stage and 200 one stage nephrolithotomies. All types of stone were treated. In the one stage procedure the tracks were kept patent with an Amplatz sheath and the stones were removed whole or broken up with electrohydraulic lithotripsy or ultrasound.[6,7] All patients were given prophylactic antibiotics and general anaesthesia.

ESWL—The technique of ESWL used was based on the German experience of the Dornier lithotripter.[8] The number of shocks was limited to that required to render the stones into particles that could be passed spontaneously (roughly 2 mm in diameter)[7] (G W Drach *et al*, tapes presented at meeting of American Urological Association, 1984). Patients underwent either general or epidural anaesthesia, and all received prophylactic antibiotics. All patients were screened for clotting defects and renal impairment, and urine samples were cultured. Follow up consisted of a plain abdominal *x* ray examination on the second postoperative day; renal ultrasonography, if clinically indicated by fever or pain; and a plain abdominal *x* ray examination on the 10th postoperative day and at three

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