The role of arthoscopic lavage in the management of knee osteoarthritis: the KORAL study

KORAL
KNEE OSTEOARTHRITIS:
ROLE OF ARTHROSCOPIC LAVAGE

Osteoarthritis of the knee is a disabling condition affecting around 10% of people aged over 55. Surgeons have used arthroscopic lavage, a technique which involves washing out the joint space and sometimes the removal of debris from the area (debridement), for the management of osteoarthritis of the knee for many years. The research evidence to support its claimed benefits to patients is, however, weak. Systematic reviews of previously conducted trials provide little evidence to support the routine use of the technique and a recent study, conducted in the US, suggested that the procedure was no better than placebo.

Against this background the NHS Health Technology Assessment Programme wish to mount a new trial of arthroscopic lavage. Ideally this would be a placebo-controlled trial. They recognise, however, that there may be concerns about the use of a placebo-surgical procedure and, as such, have commissioned the KORAL (Knee Osteoarthritis: Role of Arthroscopic Lavage) study group to investigate the acceptability of mounting such a trial in the UK. The KORAL study group is led from the Unit and involves a large multidisciplinary team of researchers from across the UK.
During the feasibility phase, the research team will ask prospective patients, as well as surgeons, anaesthetists and members of research ethics committees whether they would find the inclusion of any form of placebo surgery acceptable and, if so, what a placebo procedure might consist of. If, and only if, all these parties agree that the inclusion of a pre-specified surgical placebo is acceptable will the study proceed to a full trial.

The full study is likely to compare arthroscopic lavage (with debridement if necessary) with some form of placebo surgery and non-operative management. Patients who are allocated to surgery or placebo-surgery would not know which procedure had been undertaken. Patients would be followed-up for two years and asked about the pain in their knee, general health and any visits they have had to the GP or hospital about their knee arthritis. This will allow the research team to draw conclusions about which intervention resulted in the greatest improvement in patients' quality of life.

The KORAL study commenced in July 2005. Ethics approval has been granted and initial consultations with stakeholder groups are underway. Findings from the feasibility phase are expected to be available in June 2006, with progression to a formal trial pilot (assuming the inclusion of a placebo procedure is found to be acceptable) scheduled for June to December 2006. Results from any formal randomised controlled trial are not expected to be available until 2010.

For more information contact Marion Campbell
(email m.k.campbell@abdn.ac.uk or telephone 01224 554480).

Selected Unit publications

Campbell MK, Fayers P, Grimshaw JM. Determinants of the intracluster correlation coefficient in cluster randomised trials: the case of implementation research. Clin Trials 2005;**2**:99-107.

Cuthbertson B, Scott J, Strachan M, Kilonzo M, Vale L. Quality of life before and after intensive care. Anaesthesia 2005;**60**:332-339.

Cuthbertson B, McKeown A, Croal BL, Mutch WJ, Hillis G. Utility of B-type natriuretic peptide in predicting the level of peri and post-operative cardiovascular support required after coronary artery bypass grafting. Crit Care Med 2005;**33**:437-442.

Grimshaw JM, Eccles M, Campbell MK, Elbourne DR. Cluster randomised trials of professional and organisational behaviour change interventions in health care settings. Annals of the American Academy of Political and Social Sciences 2005;**599**:71-93.

Langston AL, Campbell MK, Entwistle V, Skea Z. A centralised public information resource for randomised trials: desirability and feasibility. BMC Health Serv Res 2005;**5**(39).

McCormack K, Wake B, Perez J, Fraser C, Cook JA, Vale L et al. Systematic review of the clinical effectiveness and cost-effectiveness of laparoscopic surgery for inguinal hernia repair. Health Technol Assess 2005;**9**(14):1-218.

Staff news

We bid a fond farewell to Vikki Entwistle who has moved to a new position within the Social Dimensions of Health Institute at the University of Dundee. Following Vikki's departure, Lorna McKee has become Director of the Unit's Delivery of Care Programme.

We welcome Diane Collins, Angela Coutts, Niina Kolehmainen and Euan Wiseman to the Unit.

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Editorial team: Jonathan Cook and Kathleen McIntosh.
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Health Services Research Unit

Newsletter
Autumn 2005

The MAVIS trial points to no protective effect against infections of vitamin and mineral supplementation amongst elderly people

The results of the Mineral and Vitamin Intervention Study (MAVIS trial) were reported recently in the British Medical Journal. Members of the Health Services Research Unit coordinated the trial which examined whether multivitamin and multimineral supplements taken by older people, mostly living at home, influence infections.[1] Infections are common reasons for older people to contact primary care, and can precipitate hospital admission. Dysregulation of the immune system has been linked with both ageing and poor nutrition. The UK National Diet and Nutrition Survey found evidence of multiple nutritional deficiencies in older people. Deficiencies were greater in Scotland than in Southern England, and in people over 75 or in long term care. At least a quarter of older people in the UK take nutritional supplements, but it is unclear whether these supplements influence infections among older people who live at home.

The MAVIS trial group examined whether taking vitamin and mineral supplements affected self-reported infections, general practice consultations and quality of life in 910 people aged 65 and over. Participants were recruited from six GP practices in the Grampian region of Scotland and randomised to take one daily multivitamin and multimineral supplement or a matching placebo for one year. Participants were asked to keep a diary of when they had an infection and when they had contacted their general practice for an infection (practice records were also examined). Questionnaires were returned on quality of life, e.g. physical and social functioning, mental health, vitality, pain and perception of general health.

Supplementation made no significant difference to participants' contacts with primary care, participants' infections or quality of life. However, it remains to be seen whether higher-risk populations, such as older people living in nursing home care, who generally have poorer nutritional status, benefit from supplementation in terms of infections.

For more information contact Alison Avenell
(email a.avenell@abdn.ac.uk or telephone 01224 554336).

Reference

1. Effect of multivitamin and multimineral supplements on morbidity from infections in older people (MAVIS trial): pragmatic, randomised, double blind, placebo controlled trial. Avenell A, Campbell MK, Cook JA, Hannaford PC, Kilonzo MM, McNeill G et al. BMJ 2005;**331**:324-329.

Audrey Stephens (MAVIS Research Assistant) with one of the trial participants

Staff Profile: Brian Cuthbertson

Brian Cuthbertson joined the Unit in December 2004. He is Clinical Senior Lecturer within the University of Aberdeen and Honorary Consultant in Anaesthetics and Intensive Care at Aberdeen Royal Infirmary. His research interests are broadly around critical care. This includes randomised trials of critical care interventions (such as alternative levels of care after major surgery). He is also leading a programme of work on predicting outcome from critical illness especially with regard to biochemical factors such as B type natriuretic peptide.

Contents

Pros and cons of open rather than placebo-controlled trial designs

It can be hard to decide whether or not to have a placebo in a randomised controlled trial. Advantages and disadvantages were recently examined in research performed by members of the Health Services Research Unit and reported in the journal, 'Clinical Trials'.[1]

538 people aged over 70 years who were eligible for a trial of secondary fracture prevention were randomised to either an open trial design (no placebo tablets and people were told what kind of tablets they were given) or a blinded, placebo-controlled design.

Significantly more people (9%), agreed to join the trial with an open design. Reluctance to take a placebo and the desire to know tablet allocation were common reasons given for not taking part in the blinded, placebo-controlled design. Compliance with tablet taking was similar with the two trial designs. Overall, open trial participants were more likely to remain in the trial for one year. But (unlike in the placebo design) this reflected differing rates of dropout: in particular, there was a very low dropout rate amongst people who received no tablets in the open trial.

Using an open trial design may therefore enhance participant recruitment and retention and thus could improve generalisability and statistical power of randomised trials. However, withdrawal rates may differ in an open trial design which may introduce bias and threaten the internal validity of the trial itself.

For more information contact Alison Avenell
(email a.avenell@abdn.ac.uk or telephone 01224 554336).

Reference

1. Avenell A, Grant AM, McGee M, McPherson G, Campbell MK, McGee MA, for the RECORD Trial Management Group. The effects of an open design on trial participant recruitment, compliance and retention - a randomised controlled trial comparison with a blinded, placebo-controlled design. Clin Trials 2004;**1**:490-498.

Postnatal incontinence trial: six year follow up

In the mid-1990's, 747 women who reported urinary incontinence three months after delivery were recruited to a multi-centre (Aberdeen, Birmingham and Dunedin), randomised controlled trial that evaluated nurse-led conservative interventions. One year data showed fewer women in the intervention group with urinary incontinence (60% v 69%) and fewer with faecal incontinence (4% v 11%).

Follow-up of the cohort at six years has recently been reported in the British Medical Journal.[1] The differences in the number performing exercises and the number of daily contractions (which had been present at one year) had disappeared. The difference in urinary incontinence between the groups seen at one year had also disappeared (76% v 79%). Furthermore, there was no evidence that the effect at one year was more likely to persist among women with more severe incontinence at baseline, or according to type of incontinence, or whether or not they had had further deliveries. Similarly, the lower prevalence of faecal incontinence in the intervention group at one year was not sustained at six years (12% v 13%).

These findings were disappointing because pelvic floor muscle training and bladder training are simple to teach and perform and have few if any adverse effects. There is a need to identify conservative strategies for both urinary and faecal incontinence that have longer-term effects.

For more information contact Charis Glazener
(email c.glazener@abdn.ac.uk or telephone 01224 553732).

Reference

1. Glazener CM, Herbison GP, MacArthur C, Grant AM, Wilson PD. Randomised controlled trial of conservative management of postnatal urinary and faecal incontinence: six year follow-up. BMJ 2005;**330**:337-339.

New million pound grant from the MRC: the SIGNET trial

A collaborative group whose development was led by the Unit was recently successful in securing a £1 million grant from the Medical Research Council for a Scottish multicentre randomised trial of glutamine and selenium supplemented parenteral nutrition for critically ill patients (SIGNET trial). This work is a continuation of a successful pilot study based at the Western General Hospital in Edinburgh and Aberdeen Royal Infirmary.

Mortality and infective complications in Intensive Care Units (ICUs) are high, and infections in ICUs are associated with a 2-3 times increased risk of death. The amino acid glutamine and the trace element selenium both have the potential to enhance the immune system and may reduce infection. Glutamine and selenium are either absent or only present in low amounts in standard parenteral nutrition. Beginning later this year, the SIGNET trial will run for 42 months and will test whether the addition of glutamine and/or selenium to parenteral nutrition, improves patient outcome and reduces the use of ICU and hospital resources. The aim is to eventually recruit 500 patients to the trial. Nearly 10% have already been recruited. Nine ICUs in Scotland have agreed to take part, and up to 15 are likely to eventually participate.

For more information contact Anne Milne
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Consumer representation in a multicentre randomised controlled trial

The drive for consumer involvement in clinical trials has increased over recent years but there is often little guidance about how to actually do this. The PRISM trial adopted an integrated approach to consumer representation in clinical trials.[1]

Paget's disease of bone (PDB) is a chronic bone disease that is often painful and can have very disabling long-term complications such as deformity, fracture and deafness. The PRISM trial is a UK-based, multicentre, randomised controlled trial, studying its treatment.

Within the UK there is one formal support group for sufferers of PDB; the National Association for the Relief of Paget's Disease (NARPD). The NARPD aims to offer support and information to Paget's disease sufferers, to sponsor research into causes and treatment, and to raise awareness among the medical profession and the public.

Partnership between the PRISM team and NARPD aided the design, conduct and delivery of the trial. For PRISM, the primary advantage has been the harnessing of a well-informed and interested population. In addition, PRISM has received a sizeable number of requests from patients asking to take part and our active partnership has led to unsolicited patient advocacy of the trial.

There have been benefits to the NARPD and its membership as well. The trial has promoted awareness of the NARPD and Paget's disease, to sufferers, the general public and health professionals. Although it has been very demanding for both parties, this relationship has been very rewarding, on both professional and personal levels.

For more information contact Anne Langston
(email a.langston@abdn.ac.uk or telephone 01224 551126).

Reference

1. Langston A, McCallum M, Campbell MK, Robertson C, Ralston SH. An integrated approach to consumer involvement representation and involvement in a multicentre randomized controlled trial. Clin Trials 2005;**2**:80-87

Joyce Cupitt (NARPD Trustee) and Anne Langston (HSRU PRISM trial co-ordinator)

CHaRT receives major funding boost – the Scottish Collaboration of Triallists (SCoT)

We were delighted to get confirmation in July of our success in landing £1.2 million of funding to create a Scottish Collaboration of Triallists (SCoT) through a Strategic Research Development Grant from the Scottish Higher Education Funding Council. The four-year funding (with Aberdeen's share amounting to £0.85m) will support excellence and build capacity for multicentre randomised controlled trials of healthcare interventions led from Scotland. The collaboration will be led from Aberdeen by John Norrie, Adrian Grant Marion Campbell and Phil Hannaford. The SCoT project has two components.

The first is the creation of a collaboration of experienced triallists from clinical trials units at the four Scottish universities with medical schools – in addition to Aberdeen, this comprises the Health Informatics Consortium (Prof Frank Sullivan, University of Dundee): the Neurosciences Trials Unit (Prof Peter Sandercock, University of Edinburgh), and the Robertson Centre for Biostatistics (Prof Ian Ford, University of Glasgow) and the Clinical Trials Unit (Dr Allan Gaw, University of Glasgow). Together, we will deliver a range of workplans to improve expertise, efficiency and capacity to mount landmark trials which address important health issues.

The second component of SCoT will enhance Aberdeen's Centre for Healthcare Randomised trials (CHaRT) to meet the demand for trials infrastructure from groups of clinicians who wish to evaluate an aspect of health care. Clinical research is changing, so much so that now many questions can now only be addressed through multicentre collaboration, mediated through clinical networks – this is the philosophy behind the UK Clinical Research Collaboration (www.ukcrc.org). Clinical trials units such as CHaRT will support the trials sponsored by these networks, and this new funding will be crucial to allow CHaRT to expand its capacity to meet this demand, in particular from clinical networks that currently have limited trial infrastructure support. We are grateful for the backing that we received from a number of existing networks.

We expect that within the four years of the grant, the SCoT will develop into a national resource, and an enhanced CHaRT will be operating at full capacity. A national approach to problem solving within randomised clinical trials, coupled with integrated joint working will provide the confidence, momentum and commitment for further collaboration, which will ensure that Scotland remains competitive in leading international-standard multicentre trials.

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