Novel approach to antibiotic prophylaxis in percutaneous endoscopic gastrostomy (PEG): randomised controlled trial

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EDITORIAL by Kurien and Sanders

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STUDY QUESTION Could sulfamethoxazole and trimethoprim (also known as co-trimoxazole or Bactrim) administered as an oral solution in the catheter replace intravenous cefuroxime (Zinacef) for antibiotic prophylaxis in percutaneous endoscopic gastrostomy (PEG)?

SUMMARY ANSWER A single dose of co-trimoxazole (20 ml of oral solution) given via the PEG catheter as part of the catheter insertion procedure is at least as effective at preventing peristomal infections as a single dose (1.5 g) of cefuroxime given intravenously one hour before the PEG procedure.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Infection at the wound site is common after insertion of a PEG catheter; however, antibiotic prophylaxis during the PEG procedure has been shown to be of benefit. This study indicates that antibiotic prophylaxis during insertion of the PEG catheter could be given in a new and more efficient way than the current standard treatment.

Design

We conducted a single centre, randomised, controlled, double blind, non-inferiority clinical trial to compare 20 ml co-trimoxazole (Bactrim; F Hoffmann-La Roche Ltd, Basel, Switzerland) deposited in the PEG catheter immediately after insertion and 1.5 g of cefuroxime (Zinacef; GlaxoSmithKline, London) administered intravenously one hour before insertion of the PEG catheter (standard treatment) for the prevention of acute wound infections. We chose co-trimoxazole rather than an oral cephalosporin as the test drug because co-trimoxazole is absorbed more rapidly in the upper gastrointestinal tract; has a longer half life; doesn't need to be mixed with food intake; is associated with a lower risk of infection with *Clostridium difficile*; and costs less.

Participants and setting

A total of 234 patients with an indication for PEG who were referred to the endoscopy unit of the Karolinska University Hospital in Stockholm, Sweden, between 3 June 2005 to 31 October 2009 and were able to give informed consent were included in this study.

COMPLICATIONS AFTER INSERTION OF THE PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) CATHETER

	Co-trimoxazole group (n=116)	Cefuroxime group (n=118)
No complications	66 (57)	63 (53)
Abdominal pain	13 (11)	17 (14)
Leakage around the catheter	10 (9)	16 (14)
Infection	10 (9)	14 (12)
PEG procedure failed	12 (10)	12 (10)
Constipation	7 (6)	11 (9)
Diarrhoea	5 (4)	4 (3)
Patient died before follow-up	3 (3)	2 (2)
Fever	0 (0)	3 (3)
Patient pulled out PEG catheter before follow-up	0 (0)	1 (1)

Values are number (%). Each individual patient could have more than one complication.

Primary outcome

The primary outcome was occurrence of a clinically identifiable wound infection at follow-up 7-14 days after insertion of the PEG catheter.

Main results and the role of chance

Of the 234 patients included in this study, 116 were randomly assigned to co-trimoxazole and 118 to cefuroxime. At follow-up, wound infection was found in 10 (8.6%) patients in the co-trimoxazole group and 14 (11.9%) in the cefuroxime group, which corresponds to a percentage point difference of −3.3% (95% confidence interval −10.9% to 4.5%). The per protocol analysis, which comprised 100 patients in each group, gave similar results—10% and 13% infection in the co-trimoxazole and cefuroxime groups, respectively (percentage point difference −3.0%, 95% CI −11.8% to 5.8%). Both these analyses indicate the non-inferiority of co-trimoxazole compared with cefuroxime because the upper bounds of the confidence intervals are lower than the pre-determined non-inferiority margin of 15%.

Harms

No adverse reactions to the antibiotics used were recorded.

Bias, confounding, and other reasons for caution

The included patients had to be well enough to be able to give informed consent, and, therefore, they might have been healthier than those who were not included. The potential for problems with the subjectivity of infection diagnosis was counteracted by the strict blinding of patients and the experienced nurses who evaluated the patients at follow-up, as well as the additional use of objective markers of infection (blood tests and bacterial cultures).

Generalisability to other populations

The validity of the study and the rapidness of administration, safety, and low cost of co-trimoxazole antibiotic prophylaxis, as well as the fact that with this technique prophylaxis will not be given needlessly when insertion of a PEG catheter proves impossible, could make this new approach suitable wherever the PEG procedure is done.

Study funding/potential competing interests

This study was funded by the Swedish Cancer Society and the Swedish Research Council. The authors have no competing interests.

Trial registration number

Current Controlled Trials ISRCTN18677736.

Efficacy of standardised manual therapy and home exercise programme for chronic rotator cuff disease: randomised placebo controlled trial

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STUDY QUESTION Is manual therapy and exercise treatment over 10 weeks more efficacious than placebo treatment for middle aged to older adults with chronic shoulder rotator cuff disease?

SUMMARY ANSWER Manual therapy and home exercise did not immediately improve pain and function compared with a realistic placebo; however, with active treatment shoulder function and strength were significantly better at 22 weeks.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Conservative non-drug interventions are commonly used in this disease, but evidence has been sparse. The beneficial effects of a standardised manual therapy and home exercise programme may accrue over time and may be of more value for function and strength than pain.

Design

This was a randomised, participant and single assessor blinded, placebo controlled trial. Participants were randomised in permuted blocks, stratified according to the treating physiotherapist, to receive either active treatment (manual therapy and home exercises) or placebo treatment (inactive ultrasound and inert gel). Both groups received 10 sessions of standardised treatment over 10 weeks. For the next 12 weeks, the active group continued the exercise.

Participants and setting

We recruited 120 participants with chronic (more than 3 months) rotator cuff disease through medical practitioners and from the community in metropolitan Melbourne, Australia.

Primary outcomes

Primary outcomes measured at baseline, 11 weeks, and 22 weeks included pain and function measured by the shoulder pain and disability index, average pain on movement measured on an 11 point numerical rating scale, and participants' perceived global rating of overall change.

Main results and the role of chance

At 11 weeks, we found no difference between groups for change in the shoulder pain and disability index or in pain; both groups showed significant improvements. A similar percentage of participants in both groups reported a successful outcome (defined as "much better"): 42% (24/57) of active participants and 30% (18/61) of placebo participants (relative risk 1.43, 95% confidence interval 0.87 to 2.34). At the 22 week follow-up, the active treatment group showed a significantly greater improvement in the shoulder pain and disability index than did the placebo group, although the groups did not differ significantly for change in pain or for the percentage of participants reporting a successful treatment outcome (relative risk 1.39, 0.94 to 2.03). Several secondary outcomes favoured the active group, including shoulder pain and disability index function score, muscle strength, interference with activity, and quality of life.

Harms

Minor adverse effects, mostly short term increased shoulder pain, were reported by 17/55 (31%) active participants and 5/61 (8%) placebo participants during the treatment phase and 7/49 (14%) active participants during the follow-up phase.

Bias, confounding, and other reasons for caution

Therapists were not blinded to treatment group and participants' blinding may have been incomplete. Some participants failed to complete more than half of the prescribed home exercises, although results did not differ in a compliers' analysis.

Generalisability to other populations

Results cannot necessarily be generalised to other manual therapy and exercise programmes, given differences in type and dosage, or to other populations of patients with different clinical features including younger patients and those with more severe disease.

Study funding/potential competing interests

All researchers are independent of the funding body, the National Health and Medical Research Council. RB and KB are partly supported by fellowships from the National Health and Medical Research Council and the Australian Research Council respectively.

Trial registration number

Clinical trials NCT00415441.

MEAN (SD) DIFFERENCE* WITHIN GROUPS AND MEAN (95% CI) DIFFERENCE* BETWEEN GROUPS FOR PRIMARY OUTCOMES WITH CONTINUOUS DATA

Outcomes	Shoulder pain and disability index (0-100)†	Pain on movement (0-10)†
Within group difference (week 0-11):		
Active	16.1 (17.7)	2.1 (2.6)
Placebo	12.7 (16.3)	1.3 (2.2)
Within group difference (week 0-22):		
Active	22.4 (22.0)	2.6 (2.9)
Placebo	15.6 (17.8)	1.6 (2.4)
Between group difference (week 0-11)	3.6 (−2.1 to 9.4)	0.7 (−0.1 to 1.5)
Between group difference (week 0-22)	7.1 (0.3 to 13.9)	0.9 (−0.03 to 1.7)

*Adjusted for baseline scores.
†Higher scores=greater pain and disability.

Transdermal and oral hormone replacement therapy and the risk of stroke: a nested case-control study

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STUDY QUESTION Do oral and transdermal administration of hormone replacement therapy (HRT) increase the risk of stroke in postmenopausal women?

SUMMARY ANSWER Use of transdermal HRT containing low doses of oestrogen was not associated with increased risk of stroke. Conversely, high dose transdermal HRT and the oral route of oestrogen, alone or combined with a progestogen, were associated with increased risk.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Oestrogen replacement therapy with or without progestogen is associated with an increased risk of stroke in postmenopausal women. This study shows that the use of low dose transdermal HRT is not associated with an increased risk of stroke, in contrast to oral HRT.

Participants and setting

The cohort of all women in the UK General Practice Research Database aged 50-79 years between 1 January 1987 and 31 October 2006 without a prior diagnosis of stroke.

Design, size, and duration

We conducted a nested case-control analysis within this cohort of 870 286 women. Mean duration of follow-up was 6.7 years. For each incident case of stroke occurring during cohort follow-up, up to four controls, randomly selected from the risk set defined by the case, were matched on age, general practice attended, and year of start in the practice.

Primary outcome, risks, exposures

We assessed the risk of stroke by estimating the rate ratio of stroke associated with current use of oral and transdermal HRT compared with no use.

Main results and the role of chance

There were 15 710 cases of stroke matched to 59 958 controls. The overall rate of stroke in the cohort was 2.85 per 1000 per year. The adjusted rate ratio of stroke associated with current use of transdermal HRT was 0.95 (95% CI 0.75 to 1.20) relative to no use. The risk of stroke was not increased with current use of low oestrogen dose patches as compared with no use, whereas the risk was increased with high dose patches (table). Current users of oral HRT (oestrogen alone or with a progestogen) had a higher rate of stroke compared with non-users (adjusted rate ratio 1.28 (1.15 to 1.42)) with both low dose and high dose. This 28% increase in risk represents an additional 0.8 strokes per 1000 person years of use. The direct comparison between transdermal and oral HRT showed that the risk of stroke was lower with transdermal use (rate ratio 0.74 (0.58 to 0.95)).

Bias, confounding, and other reasons for caution

We were able to adjust for many potential confounder variables, including some lifestyle risk factors. One unmeasured potential confounder was age at menopause, but this confounding is most likely to be non-differential between the two routes of administration. Also, we could not adjust for our cohort subjects' socioeconomic status or educational level, but matching on the general practice attended represents an indirect attempt to adjust for such potential confounders. We cannot, however, exclude the possibility that users of transdermal and oral HRT differed for such characteristics, resulting in some residual confounding.

Generalisability to other populations

We expect these results to apply to postmenopausal women in other primary care settings.

Study funding/potential competing interests

This research was funded by grants from the Canadian Institutes of Health Research (CIHR), the Canadian Foundation for Innovation and Organon. CR is the recipient of a postdoctoral fellowship from the Multiple Sclerosis Society of Canada. SS received research funding from Organon, Schering, and Wyeth, makers of hormone replacement therapy products. EG received research funding and acted as a consultant to Schering AG. All authors were independent from all sources of funding.

RISK OF STROKE ASSOCIATED WITH CURRENT USE OF HRT BY DRUG DOSE AND ROUTE OF ADMINISTRATION

	Percentage (number) of subjects		Rate ratio (95% CI)	
Type of HRT	Cases (with stroke) (n=15 710)	Controls (no stroke) (n=59 958)	Crude	Adjusted*
None	92.27 (14 496)	93.12 (55 834)	1.00	1.00
Transdermal route:	0.66 (103)	0.74 (441)	0.92	0.95 (0.75 to 1.20)
Low dose (≤50 µg)	0.48 (76)	0.64 (384)	0.78	0.81 (0.62 to 1.05)
High dose (>50 µg)	0.17 (27)	0.10 (57)	1.87	1.89 (1.15 to 3.11)
Oral route†:	3.93 (618)	3.38 (2025)	1.20	1.28 (1.15 to 1.42)
Low dose	3.28 (515)	2.92 (1753)	1.16	1.25 (1.12 to 1.40)
High dose	0.66 (103)	0.45 (272)	1.51	1.48 (1.16 to 1.90)

*Adjusted for age, body mass index, smoking status, alcohol misuse, diabetes, hyperlipidaemia, hypertension, atrial fibrillation, cardiovascular disease, transient ischaemic attack, aspirin or other NSAID use, and history of hysterectomy or oophorectomy.
†Low dose oral HRT ≤0.625 mg equine oestrogen or ≤2 mg estradiol; high dose >0.625 mg equine oestrogen or >2mg estradiol. Categories for oral and transdermal route represent roughly bioequivalent doses of oestrogens.

Response on bmj.com

"The results . . . on transdermal replacement versus oral replacement, showing that the risk differs according to the route of administration and dose, is likened to a light at the end of the tunnel. The reductions in the risks associated with different routes of administration have all but eliminated the increased risk of heart disease."
Denese A McFarlane, lecturer, Ministry of Health, Jamaica
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Sexuality and obesity, a gender perspective: results from French national random probability survey of sexual behaviours

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EDITORIAL by Goldbeck-Wood

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STUDY QUESTION What is the association between body mass index (BMI) and sexual activity, sexual satisfaction, unintended pregnancies, and abortions in obese people?

SUMMARY ANSWER There is a link between BMI and sexual behaviour and adverse sexual health outcomes, with obese women being less likely to access contraceptive healthcare services and have more unplanned pregnancies.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS There is a relation between obesity and erectile dysfunction, but the evidence in relation to other sexual health outcomes has been equivocal. Our results show a link between BMI and both sexual behaviours and adverse sexual health outcomes, especially among young obese women (age 18-29), who are four times as likely to report unintended pregnancies.

Participants and setting

National population based survey of 5535 women and 4635 men aged 18-69 living in France in 2006.

Design

Random probability survey of sexual behaviours, with interviews carried out by telephone. To categorise weight we used the WHO classification of BMI and distinguished four groups: underweight (BMI <18.5), normal weight (18.5-<25), overweight (25-<30), and obese (≥30).

Primary outcomes

Sexual partners, sexual dysfunctions, sexual satisfaction, contraceptive practices, abortion.

BMI AND SEXUAL AND REPRODUCTIVE HEALTH IN WOMEN (%) BY AGE

Age (years)	Normal (n=3651)	Obese (n=411)	Adjusted odds ratio* for obese *v* normal
Unintended pregnancy over lifetime			
18-29	13	44	4.26 (2.21 to 8.23)
30-49	34	36	1.03 (0.67 to 1.59)
Abortion in past five years			
18-29	6	22	3.72 (1.59 to 8.70)
30-49	4	6	2.01 (1.01 to 4.00)
Pill used at last sexual intercourse			
18-29	79	58	0.34 (0.15 to 0.78)
30-49	49	52	0.91 (0.53 to 1.55)
Saw doctor in past 12 months for contraceptive issues†			
18-29	86	69	0.37 (0.18 to 0.76)
30-49	79	57	0.37 (0.24 to 0.57)

*Adjusted for age, living as couple, chronic disease, education, limitation of activity, and number of lifetime sexual partners.
†Among those who have had sex in past 12 months and who did not want to get pregnant; also adjusted for health insurance and income.

Main results and the role of chance

Of those whom we initially selected, 10 170 (75%) agreed to complete the questionnaire. After adjustment for potential confounding factors (age, education level, chronic disease, and limitation of daily activity), obese women were 30% less likely than normal weight women to report a sexual partner in the past 12 months (odds ratio 0.71, 95% confidence interval 0.51 to 0.97). Two out of three (67%) obese women reported having an overweight or an obese sexual partner compared with 39% of obese men (P<0.001). Once with a sexual partner, obese and overweight women and men were no different from others in terms of sexual practices and sexual satisfaction.

Men with a higher BMI were more likely to report erectile dysfunction (2.58, 1.09 to 6.11, P<0.05). Overweight and obese women were no more likely to report sexual dysfunction than normal weight women. Obese women aged 18-49 were less likely to use effective methods of contraception, especially the pill, and were more likely to have had an unintended pregnancy or abortion, or both. They were also less likely to use contraceptive healthcare services.

The marked increase in unintended pregnancies was not due to differences in sexual behaviours but to lower rates of use of effective methods of contraception. This finding must be seen in tandem with the infrequent attendance of obese women at healthcare services for contraception and might, in part, reflect their negative feelings towards their bodies. It is also likely to reflect the reluctance of healthcare professionals to prescribe combined oral contraceptive pills because of the higher risks of cardiovascular complications among obese women, although obesity remains only in category 2 (caution) in WHO's medical eligibility criteria for combined oral contraceptives.

Doctors should not be tempted to think that obese women are less sexually active and therefore less in need of effective methods of contraceptive.

Bias, confounding, and other reasons for caution

Social stigma about weight, which is related to gender, might be compounded by other issues for people whose sexuality could also be socially stigmatised. Further research should include information on comorbidities that could act as mediators of the relation between obesity and sexual activity.

Generalisability to other populations

These results could apply to populations in which obesity among women is socially stigmatised.

Study funding/potential competing interests

The survey was funded by the French National Agency on AIDS Research (ANRS). The authors have no competing interests.