Brain, Behavior, and Immunity 26 (2012) 212–217

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

A brief relaxation intervention reduces stress and improves surgical wound healing response: A randomised trial ☆

Elizabeth Broadbent [a,*], Arman Kahokehr [b], Roger J. Booth [a], Janine Thomas [c], John A. Windsor [b], Christina M. Buchanan [d], Benjamin R.L. Wheeler [b], Tarik Sammour [b], Andrew G. Hill [b]

[a] Department of Psychological Medicine, The University of Auckland, New Zealand
[b] Department of Surgery, The University of Auckland, New Zealand
[c] Inner Zest Ltd., Auckland, New Zealand
[d] Maurice Wilkins Centre for Molecular Biodiscovery, Department of Molecular Medicine and Pathology, The University of Auckland, New Zealand

ARTICLE INFO

Article history:
Received 9 March 2011
Received in revised form 21 June 2011
Accepted 24 June 2011
Available online 28 June 2011

Keywords:
Surgery
Wound healing
Relaxation
Intervention
Stress
Hydroxyproline
ePTFE

ABSTRACT

Psychological stress has been shown to impair wound healing, but experimental research in surgical patients is lacking. This study investigated whether a brief psychological intervention could reduce stress and improve wound healing in surgical patients. This randomised controlled trial was conducted at a surgical centre. Inclusion criteria were English-speaking patients over 18 years booked to undergo elective laparoscopic cholecystectomy; exclusion criteria were cancellation of surgery, medical complications, and refusal of consent. Seventy five patients were randomised and 15 patients were excluded; 60 patients completed the study (15 male, 45 female). Participants were randomised to receive standard care or standard care plus a 45-min psychological intervention that included relaxation and guided imagery with take-home relaxation CDs for listening to for 3 days before and 7 days after surgery. In both groups ePTFE tubes were inserted during surgery and removed at 7 days after surgery and analysed for hydroxyproline as a measure of collagen deposition and wound healing. Change in perceived stress from before surgery to 7-day follow-up was assessed using questionnaires. Intervention group patients showed a reduction in perceived stress compared with the control group, controlling for age. Patients in the intervention group had higher hydroxyproline deposition in the wound than did control group patients (difference in means 0.35, 95% CI 0.66–0.03; $t(43) = 2.23$, $p = 0.03$). Changes in perceived stress were not associated with hydroxyproline deposition. A brief relaxation intervention prior to surgery can reduce stress and improve the wound healing response in surgical patients. The intervention may have particular clinical application for those at risk of poor healing following surgery.

1. Introduction

A systematic review has shown that psychological stress impairs wound healing across a variety of laboratory and clinical settings (Walburn et al., 2009). Dermal punch biopsy wounds heal more slowly in women caring for relatives with Alzheimer's disease than in matched control subjects, and mucosal punch biopsy wounds heal more slowly in students during exams than during vacation time (Kiecolt-Glaser et al., 1995; Marucha et al., 1998). Diabetic foot ulcers heal more slowly in depressed patients, and surgical wounds show impaired healing in patients with higher stress levels in the month prior to surgery (Broadbent et al., 2003; Cole-King and Harding, 2001; Monami et al., 2008; Vedhara et al., 2010). Higher cortisol levels may play a role in the relationship between stress and slower healing by down-regulating the immune system (Ebrecht et al., 2004). Local inflammatory cells, and pro-inflammatory cytokines including interleukin-1, have been shown to be lower in the wounds of highly stressed individuals (Glaser et al., 1999).

This evidence points to the potential for psychological interventions to improve wound healing. A recent study has shown that emotional disclosure improves the healing of punch biopsy wounds in healthy males, although no changes in depression or stress were achieved (Weinman et al., 2008). Psychological interventions may be particularly applicable for surgical patients, where poor wound healing can have serious consequences (Galat et al., 2009). Meta-analysis has shown psychological preparation for medical procedures can reduce distress, pain, and length of hospital stay (Devine, 1992). In terms of physiological indices, relaxation and guided imagery have improved anxiety, and reduced urinary cortisol and wound erythema amongst cholecystectomy

☆ Please see Brief commentary by Kavita Vedhara on page 210 of this issue.

* Corresponding author. Address: Department of Psychological Medicine, Faculty of Medical and Health Sciences, The University of Auckland, Private Bag 92109, Auckland 1142, New Zealand. Fax: +64 9 3737013.
E-mail address: e.broadbent@auckland.ac.nz (E. Broadbent).

0889-1591/$ - see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.bbi.2011.06.014

patients, but the effect on physiological indices of wound healing has not been assessed (Holden-Lund, 1988).

Wound healing proceeds as a cascade with the later stages involving the deposition of collagen, which restores strength and function to damaged tissue (Hunt and Hopf, 1997). The ePTFE model measures collagen synthesis as an index of healing through the assessment of hydroxyproline deposited in high porosity tubing (Goodson and Hunt, 1982). Hydroxyproline is an amino acid that gives stability to the triple helix structure of collagen (Prockop et al., 1979), and has been used as a marker of collagen synthesis, and therefore a marker of the proliferative phase of wound healing. Hydroxyproline levels have also been shown to correlate with the tensile strength of wounds, which is of clinical relevance (Wicke et al., 1995). Reduced hydroxyproline deposition occurs with corticosteroid therapy (Wicke et al., 1995), which provides further basis for suggesting that psychological stress and stress hormones might impair wound healing. The ePTFE method has been used previously in surgical studies to investigate the influence of anaemia (Jensen et al., 1986), pre-operative illness (Goodson et al., 1987), recent food intake (Windsor et al., 1988), and tissue oxygenation (Jonsson et al., 1991) on wound healing. It has also been used to test the effectiveness of peri-operative interventions on wound healing. For example, immunonutrition has been shown to increase levels of hydroxyproline in surgical patients (Farreras et al., 2005; Williams et al., 2002).

This study aimed to investigate whether a psychological intervention to reduce stress could improve the deposition of hydroxyproline in surgical wounds. Elective laparoscopic cholecystectomy patients were selected because the operation is common, of moderate magnitude, and the acute phase response is short lived and well characterised. The psychological intervention was based on the study by Holden-Lund (1988). We hypothesised that patients who received the psychological intervention would demonstrate higher concentrations of hydroxyproline at the wound site than would the control group.

2. Methods

Ethical approval was obtained from the Northern X ethics committee. The trial was registered at clinicaltrials.gov NCT00633737.

2.1. Sample characteristics and setting

Inclusion criteria were patients over the age of 18, able to read and write English, and undergoing elective laparoscopic cholecystectomy at Manukau Surgical Centre, South Auckland, New Zealand, between April 2008 and May 2010. Laparoscopic cholecystectomy is the preferred treatment for gallstone disease, where the gallbladder is removed through laparoscopic techniques (Soper et al., 1992). It involves the insertion of 4 ports through 4 wounds, all one centimetre or less in length.

2.2. Procedure

Eligible patients were informed about the study and invited to participate by the surgical research fellow. If patients agreed to take part in the study they were met by a health psychologist at least 3 days prior to their surgery (range 3–132 days), gave written informed consent and completed a pre-operative questionnaire. While 80% of participants had their surgery within 28 days of completing the first questionnaire, 20% of participants had their surgery delayed due to changes in hospital scheduling. Following informed consent, patients were randomised by the health psychologist, and received standard care or the intervention plus standard care. All patients completed further questionnaires at the 7-day follow-up. During surgery, two ePTFE tubes were implanted in the wound site and patients returned for a 7-day follow-up where the tubes were removed by a surgeon blind to group allocation.

2.3. Trial design

This was a parallel group randomised controlled study with a 1:1 allocation. Participants were randomised using a random sequence generator and allocation was sealed in consecutively numbered envelopes by EB. The surgeons and surgical research fellows conducting the surgical procedure and follow-up assessments, as well as the laboratory technician performing the hydroxyproline tests, were all blind to group allocation. Patients were asked not to reveal their group allocation.

2.4. The intervention

Patients individually met with a health psychologist for 45 min. They were informed that stress could influence surgical outcomes and relaxation could help reduce stress. The psychologist instructed the participants in deep breathing techniques and read a script that included deep breathing, progressive muscle relaxation, and guided imagery about the body being relaxed and prepared for surgery. Patients were provided with a 20-min recording of the script on a CD to take home and listen to each day prior to surgery, with quiet background music. The psychologist helped the patient plan a time in their day to listen to the CD, and telephoned them the next day to see how they were doing with the exercises. The CD contained a second recording of a similar script for patients to listen to each day after surgery for 7 days; the guided imagery focused on the body healing after surgery.

2.5. ePTFE tube implantation

All patients underwent a standard elective four-port laparoscopic cholecystectomy under general anaesthesia. At the end of the procedure prior to closure of the skin wounds, two 20 cm ePTFE tubes (High porosity PTFE tubing, International Polymer Engineering, Tempe, Az, USA) with an internal diameter of 1.2 mm and a 0.6 mm wall thickness and 90–120 μm pore size, were inserted in the subcutaneous layer of the abdominal wall using a guiding laparoscopic instrument. Each end was brought out through the right-sided abdominal port site (5 mm) wounds to the skin. The ends of the ePTFE tubes were trimmed and sutured to the skin to avoid accidental removal. A standard sterile dressing was applied. All patients were seen at a 7-day follow-up at the clinic by a surgical research fellow and the ePTFE tubes were removed under local anaesthetic. The subcutaneous portion was measured and sent to the laboratory in a sterile container to be stored at −80 °C prior to testing.

2.6. Measures

2.6.1. Hydroxyproline assessment

The ePTFE tubes were trimmed to a length of 5 cm and submerged in 1 ml 6 M HCl in a 10 ml screw-cap Pyrex glass tube (Kimax) to breakdown the embedded protein into composite amino acids by hydrolysis at 105 °C for 16 h (Contherm Series 5 digital oven). The samples were then freeze-dried for 24 h (Glass dessicator attached to a Thermo RVT4104 refrigerated vapour trap and a Thermo DC120A chemical trap). Once dry, 1 ml of milli Q water and 45 μl of 5 M NaOH was added to each tube and vortex mixed for hydroxyproline analysis. Acetate–citrate buffer, oxidant solution and Erlich's reagent were prepared for the hydroxyproline assay according to established methods (Chiariello et al., 1986). To