STUDY PLAN / SCIENTIFIC PROTOCOL

Title of Research Project:

Surgical Wound Infection Prevention by Early Intervention using Topical negative pressure therapy – the "SWIPE IT" Trial

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Overview / Synopsis:

Surgical site infection (SSI) is the most common cause for health care associated infections (HCAIs) in patients undergoing surgery and is one of the best available surrogate measures of quality in surgery. SSI contribute to increased morbidity, mortality, scarring, delayed return to activities, impaired quality of life, increased health care costs, challenges in media, affects key performance indicators (KPI) and augments litigation.

Abdominal surgery, especially colorectal procedures are known to have higher risk of developing SSI compared with other operations, and therefore preventive measures are desirable. Incidence of incisional SSI in colorectal surgery is estimated to be between 5 – 45%. Laparoscopic surgery has been shown to significantly reduce wound infections in colorectal surgery but may not be applicable to all patients.

Over the last decade, there has been emerging evidence in success of topical negative pressure (TNP) dressings in prevention of SSIs. **However, there has been no randomised study to date to address its effectiveness in reducing SSI in abdominal surgery**.

The primary objective of this study is to assess the effectiveness of incisional TNP in reducing SSI following abdominal surgery. We also aim to ascertain rate of SSI in obese patients (BMI>30) and assess the effect of TNP in this subgroup, overall cost effectiveness of the intervention and effect of TNP on length of hospital stay. (TNP used in study will be **Prevena™ Peel & Place™ Therapy**, KCI Inc., USA)

We propose to set the study up as a prospective randomised control trial.

Background (incl reference to relevant literature) / rationale:

Surgical site infection (SSI) is the most common cause for health care associated infections (HCAIs) in patients undergoing surgery. It is now considered by policy makers to be one of the best available surrogate measures of quality in surgery.

Abdominal surgery especially colorectal procedures are known to have higher risk of developing SSI compared with other operations, and therefore preventive measures are desirable. Incidence of incisional SSI in colorectal surgery is estimated to be between 5 – 30%, though some series have reported as high as 45% [1, 2].

Laparoscopic surgery has been shown to significantly reduce wound infections in colorectal surgery but this approach is not applicable to all patients.

Consequences of SSI [3-5],

- ✓ Patient – increased morbidity, poor scarring, delayed return to work / normal activities, impaired quality of life, increases risk of sepsis & mortality
- ✓ Hospital – prolonged hospital stay, increased health care costs, challenges in media
- ✓ Surgeon – affects key performance indicators (KPI), litigation

Obesity has been now recognised as a global health problem and its epidemic in increasingly taxing the health care systems worldwide. A recent article in JAMA Surgery identified obesity (body mass index, BMI ≥ 30) as an independant risk factor for SSI and reported an overwhelming 60% increase in wound infections after colectomy in this sub-group [6].

Negative-pressure wound therapy (NPWT) was introduced in 1994-95 by Kinetics Concepts Inc, KCI, USA as a form of therapeutic technique using a vacuum dressing to promote healing in acute or chronic wounds and enhance healing of first and second degree burns. It involves use of a vacuum device set at sub-atmospheric pressure over a specialised sealed polyurethane foam dressing [7]. Vacuum assisted therapy VAC® therapy works by increasing tissue perfusion, reduces oedema and exudation, and promotes granulation tissue formation by facilitating cell migration and proliferation, thereby facilitating faster wound healing [8].

Over the last decade, there has been emerging evidence in success of topical negative pressure (TNP) dressings in prevention of SSIs [9]. Retrospective comparative studies have demonstrated the superiority of incisional TNP over standard dressings in reducing incidence of SSI, seroma & hernia rates and wound dehiscence in high risk abdominal and reconstructive surgery [10, 11]. The NPWT theory is further supported by a recent multicenter prospective randomized clinical trial studying its use in high-risk wounds after severe skeletal trauma [12].

TNP used in study will be **Prevena™ Peel & Place™ Therapy**, KCI Inc., Australia. The first prospective RCT studying *Prevena™ Incision Management System* was published in 2011 by Pachowsky et al. This prospective, randomised study demonstrated decreased development of postoperative seromas in the wound and improved wound healing in surgical incisions for total hip arthroplasty [13]. Two other recent comparative studies have shown the effectiveness of 'Prevena™' in reducing SSI in groin and post-sternotomy and following vascular and cardiac surgery respectively [14, 15].

However, there has been no randomised study to date to address effectiveness of TNP or in specific 'Prevena™' in reducing incisional SSI in abdominal surgery.

Study aims / objectives:

Our study is aimed to observe the effect of incisional topical negative pressure (TNP) dressing on surgical site infection (SSI) in patients undergoing open abdominal surgery.

Secondary objectives are, to evaluate the effect on

- Length of stay
- Cost-effectiveness
- Cosmetic outcomes
- Incisional hernias

Hypotheses to be tested:

Null hypothesis

Early intervention with topical negative pressure dressing(s) does not reduce incidence of incisional surgical site infections in patients undergoing open abdominal surgery.

Population / setting (anticipated number / ages / where / by whom):

Setting

Patients admitted to the Department of Surgery in Westmead (Public), Blacktown (Public), Norwest Private and Westmead Private Hospitals. Surgeons from the above hospitals, including those participating in Acute Surgical Roster will be invited to participate in our study.

Inclusion Criteria

1. Patients (over age of 16 years) undergoing elective and emergency laparotomy
2. Type of wounds - clean contaminated, contaminated and dirty

[Note: Patients who have had previous laparotomy including those who may have mesh implants in the site of proposed surgical incision and those patients with pre-existing stoma will also be considered for our study]

Exclusion Criteria

1. Patients who have hypersensitive allergy to silver
2. Patients who lack capacity to give / sign their own consent
3. Pregnancy
4. Patients with pre-existing 'open abdomen / laparostomy'

Anticipated number **178** patients

Trial design / methods / power calculations / data analysis / statistical considerations:

Type of study

Prospective, non-blinded, randomised controlled study (RCT)

Methodology

Informed consent will be taken from eligible patients participating in our study. Data will be collected prospectively on a standardised proforma (see *appendix i*) and then entered into a MS Excel database. A computer assisted randomisation will be used to assign patients to either the control (standard dressing) or interventional arm (TNP dressing). This will be made available to the operating surgeon only upon completion of skin closure to avoid performance bias. Wound closure will be by sutures or skin staples as per surgeon's preference. Stoma nurse(s) attached to our department will be independent assessor of the wounds. Wounds will be assessed on post-operative day 5-7 and again in 1 month's time. We propose to use SPSS for statistical analysis. We also aim to perform an intention to treat analysis in event of violation of research protocol.

Type of standard dressing (control arm)	Standard Hospital Dressings (**Comfeel / Cutiplast / Post-op Visible**)
Type of TNP dressing (interventional arm)	**Prevena™ Peel & Place™ Therapy**, (KCI, Australia)

Confounding variables

Diabetes mellitus, immunosuppression, comorbidities, surgeon, degree of contamination, elective vs. Emergency surgery, length of surgery, intra-operative blood loss, wound protectors, mesh, 'take-backs / re-operations', antibiotics (other than for prophylaxis).

Definition of SSI (as per CDC Criteria) [16]

An infection is defined by the CDC as being the presence of at least one of the following:

1. Purulent drainage, with or without laboratory confirmation, from within the wound
2. Organisms isolated from an aseptically obtained culture of fluid from the incision
3. At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness and superficial incision deliberately opened by the surgeon, unless incision is culture-negative
4. Diagnosis of superficial incisional SSI by the independent assessor

Power and sample size estimation

SSI is highest in colorectal surgery with a reported cumulative incidence of 9.5% [17]. Over the last decade, there has been emerging evidence in success of wound management devices in reduction of the burden of post-operative wound infections to as low as 0 % [9, 18]. Two recent studies using Prevena™ for incisional negative pressure therapy have reported significant reduction in wound

infection rates from 30% to 6% for groin vascular surgery and from 16% to 4% for sternotomy incisions in cardiac surgery respectively [14, 15].

Assuming an overall incidence of SSI is about 15% for the range of abdominal surgery, and a rate of 3% for clean cases, we have calculated that we will need 89 patients in each arm of the study group, to provide a significant difference with a power of 80%. We have estimated this to provide a relative risk reduction of about 80% in keeping with existing evidence on Prevena™.

A two group $\chi 2$ test with a 0.050 two-sided significance level will have 80% power to detect the difference between the control arm, of **0.150** and intervention arm of **0.030** (odds ratio of 0.1752) when the sample size in each group is **89**. (NB: We have obtained expert statistical help from our hospital statistician regarding sample size calculation).

Study procedures:

This is an investigator-initiated study and the devices will be funded by Kinetics Concepts Inc, KCI, Australia. Prevena™ is a licensed product entered onto the Australian Register of Therapeutic Goods (TGA ARTG certificate: **2156636**). Patients enrolled into the study will be counselled and a patient information brochure about the research project provided as part of informed consent. Risks associated with use of the device / dressing is expected to be negligible. Any grievances / complaints will be referred to the hospital Patient Representative Department and the study doctor(s) will aim to resolve the same within an acceptable period of time.

Expected outcomes:

We anticipate our study will provide high quality evidence regarding usage of topical negative pressure therapy as a primary incisional therapy for abdominal surgery. It could potentially identify specific target groups where benefits will be maximal and cost-effective.

Logistics:

Enrolled patients will be assigned unique study number for purpose of data protection and confidentiality. Randomisation will be securely kept in a sealed envelope tagged onto consent form and be made available to surgeon upon completion of wound closure. The same will be made available by the study doctor(s) in the event of accidental loss of the sealed envelope (using the unique number). Patients who satisfy the entry criteria and consent to the study will be randomised in blocks of 8 to either control or intervention arm.

Anticipated start / finish dates:

Anticipated start date	December 2014
Anticipated finish date	April 2016

Monitoring / reporting:

A data monitoring steering committee led by is being set up to review progress every 3 months, and updates will be discussed in our 'Westmead Colorectal Research Forum'. We proposed to register the project upon ethics approval for a post-graduate research degree (MS) with University of Sydney Medical School. We aim to disseminate the results as peer reviewed publication(s) in scientific journals and also present in Royal Australasian College of Surgeons (RACS) annual scientific meeting.

Data Monitoring Steering Committee:

Dr. Peter Loder, *VMO in Colorectal Surgery, Westmead Hospital, NSW 2145*

Dr. Toufic El-Khoury, *Staff Specialist in Colorectal Surgery, Westmead Hospital, NSW 2145*

Ms. Kerry Hitos, Executive Director, *Westmead Research Centre, Westmead Hospital, NSW 2145*

Ms. Lucy Davies, *Biostatistician NHMRC Clinical Trial Centre, University of Sydney*

Statement of ethical issues:

We aim to commence recruitment for the research project upon Westmead HREC ethics approval. Suitable measures will be taken for providing adequate interpreters for non-English speaking participants for informed consent. Conduct of research will be according to strict hospital and NSW health regulations.

Acknowledgements:

RN Fiona Lee Gavegan & RN Karen Shedden - *Westmead Hospital Stoma Therapy Unit.*

Mr. Anant Kasbekar - *KCI PTY Ltd Australia, Sydney, NSW 2066*

References:

1. Murray B et al. Surgical site infection in colorectal surgery: A review of the non-pharmacologic tools of prevention. J Am Coll Surg. Dec 2010. 211(6). 812-822

2. Bonds A et al. *Incisional negative pressure wound therapy significantly reduces surgical site infection in open colorectal surgery*. Dis Colon Rectum 2013; 56: 1403–1408

3. CG74. *Surgical Site Infection.* NICE Clinical Guidelines. UK. October 2008

4. Pinkney T et al. *Impact of wound edge protection devices on surgical site infection after laparotomy: multicentre randomised controlled trial (ROSSINI Trial).* BMJ. 2013 Jul 31;347:f4305.

5. Pear S et al. *Patient risk factors and best practices for surgical site infection prevention. Managing Infection Control*. March 2007

6. Wick E et al. *Surgical site infections and costs in obese patients undergoing colorectal surgery*. Arch Surg. 2011; 146(9): 1068-1072

7. Morykwas M et al. *Vacuum-assisted closure: a new method for wound control and treatment: animal studies and basic foundation.* Ann Plast Surg. 1997 Jun; 38(6):553-62.

8. Science behind wound therapy (VAC®). http://www.kci1.com/KCI1/sciencebehindwoundtherapy#howworks

9. Ingariola M et al. *Does the application of incisional negative pressure therapy to high-risk wounds prevent surgical site complications? A systematic review*. Vol 13, Sep 2013. www.eplasty.com

10. Blackham A et al. *Prevention of surgical site infections in high-risk patients with laparotomy incisions using negative-pressure therapy*. Am J Surg. 2013 Jun;205(6):647-5

11. Conde-Green A et al. *Incisional negative-pressure wound therapy versus conventional dressings following abdominal wall reconstruction: a comparative study*. Ann Plast Surg. 2013 Oct;71(4):394-7

12. Stannard J et al. *Incisional negative pressure wound therapy after high-risk lower extremity fractures*. J Orthop Trauma. 2012 Jan;26(1):37-42.

13. Pachowsky M et al. *Negative pressure wound therapy to prevent seromas and treat surgical incisions after total hip arthroplasty*. Int Orthop. 2012 Apr;36(4):719-22.

14. Matatov T et al. *Experience with a new negative pressure incision management system in prevention of groin wound infection in vascular surgery patients*. J Vasc Surg. 2013 Mar;57(3):791-5.

15. Grauhan O et al. *Prevention of poststernotomy wound infections in obese patients by negative pressure wound therapy*. J Thorac Cardiovasc Surg. 2013 May;145(5):1387-92

16. Procedure-associated Module SSI – CDC. http://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf

17. European Centre for Disease Prevention and Control. *Surveillance of surgical site infections in Europe 2010-2011*. Stockholm: ECDC; 2013.

18. Cheng KP et al. *ALEXIS O-Ring wound retractor vs conventional wound protection for the prevention of surgical site infections in colorectal resections*. Colorectal Dis. 2012 Jun; 14(6):e346-51.