Using antimicrobial Surgihoney to prevent caesarean wound infection

Abstract

Caesarean section (CS) wound infection rates are unacceptably high (around 10% according to figures from the Health Protection Agency (2012)). This service evaluation assessed the effects of Surgihoney on surgical site infection rates in women undergoing caesarean section. All women presenting for CS were offered Surgihoney as a single application wound dressing at the end of the procedure. All women were followed up and examined for surgical site infection for 30 days after CS. A single application of Surgihoney dressing reduced surgical site infection (SSI) by 60.33% from a rate of 5.42% (*n*=590) to 2.15% (*n*=186) (*p*-value=0.042). The potential saving to the NHS of using Surgihoney as a single-application achieving this level of wound infection reduction is considerable. Surgihoney offers a simple, cost-effective intervention to reduce SSI in women undergoing CS. It is applicable to practice in all health economies and could potentially save considerable surgical infective morbidity in patients undergoing surgical delivery.

Caesarean section (CS) is a common operation in obstetric practice. There has been a national increase in Caesarean wound infection (8–24.6%) (National Institute for Health and Care Excellence (NICE), 2011; Paranjothy et al, 2005; NHS Information Centre for Health and Social Care , 2009) and a wide variation across NHS hospitals (ranging from 13.6 to 31.9%) associated with the 147 726 cases of CS each year in the UK (Bragg et al, 2010). A recent survey showed a national average wound infection rate of 9.6% (Wloch et al, 2012a). Caesarean wound infection is a major cause of prolonged hospital stay, resource consumption, as well as other morbidities and mortality. Recovery from CS is more difficult for women who develop post-operative wound infection (Wloch et al, 2012a). In terms of the burden on health-care resources, the cost of each case of CS infection has been estimated to be between £300 and more than £17 000, depending on severity (Wloch et al, 2012b)

Surgihoney™ (Healing Honey International, UK) is a licensed sterile product which has been developed for wound care and as a prophylactic dressing for wounds. It consists of honey which has been modified to produce different potencies of antimicrobial activity. Its potency is comparable to chemical antisepsis but it retains the wound healing properties of natural honey (Armstrong, 2009; Jull et al, 2013). Surgihoney is highly active against gram-positive and gram-negative bacterial wound isolates (Dryden et al, 2013). Minimum inhibitory and bactericidal concentrations are well below the concentration of Surgihoney in the wound (Dryden et al, 2013).

This paper reports a service evaluation developed because of concern around the national reporting of rising CS infection. Its aim was to establish whether Surgihoney, applied to the wound at operation, had any effect on promoting wound healing and reducing post-CS wound infection. A cost-effectiveness analysis was modelled around the clinical data in line with international consensus (Husereau et al, 2013).

Methods

Clinical Evaluation

The evaluation was an observational study with temporal comparison of CS surgical site infection (SSI) rates. It was primarily a service evaluation for the use of Surgihoney antimicrobial dressing. The Hampshire Hospitals NHS Foundation Trust's research and development committee was consulted in the preparation of this evaluation. The project was classified as a service evaluation, using a licensed product for its approved indication as part of routine clinical care. The study involved collecting anonymised data in relation to the intervention.

All women giving birth by CS at the Royal Hampshire County Hospital in Winchester between October 2012 and January 2013 were offered Surgihoney as a single application wound dressing at the end of the procedure. Consent was obtained from every participant. Each 10g sachet of Surgihoney was for single patient use. Using an aseptic technique, a 'non-sterile' operative assistant opened the Surgihoney sachet and carefully applied the sterile contents onto the sterile dressing. The dressing was then applied to the surgical wound by the obstetrician or theatre midwife. Women were also given routine single dose antibiotic prophylaxis around the

Matthew Dryden
Consultant in Infection and Microbiology
Hampshire Hospitals NHS Foundation Trust

Clare Goddard
Midwife
Hampshire Hospitals NHS Foundation Trust

Aznvik Madadi
Midwife
Hampshire Hospitals NHS Foundation Trust

Michael Heard
Consultant Obstetrician
Hampshire Hospitals NHS Foundation Trust

Kordo Saeed
Consultant Microbiologist
Hampshire Hospitals NHS Foundation Trust

Jonathan Cooke
Professor
Centre for Infection Prevention and Management, Imperial College London

CS. The timing of the antibiotic prophylaxis was not uniform—some were administered at skin incision, some after cord clamping.

After the procedure, the attending midwife completed an evaluation record. Data collected were MRSA status, history of diabetes, medications, and body mass index (BMI). For 14 days after the procedure, the attending midwife in the community also recorded any wound healing problems, specifically the presence of oozing, pain and inflammation. If there was any inflammation, a wound culture swab was requested and microbiological results were recorded. The women were given a postal questionnaire or were telephoned for follow-up at 30 days after the CS.

SSI was defined as the presence of clinical signs and/or antibiotics prescribed. Clinical signs had to comprise at least two of pain, erythema, swelling and pus discharge at the operative site.

The SSI rate during the 3 months of the evaluation using the Surgihoney dressing was compared with the infection rate in the 9 months prior to the evaluation, based on data also collected by the obstetric team with the infection control department using the same clinical criteria. Infection rate data was collected for a full year, with the Surgihoney intervention occurring in the final 3 months, hence the first 9 months data were compared with the final 3 months after the Surgihoney intervention. The rate of SSI was calculated as a percentage of all CS procedures carried out.

Economic evaluation was modelled on published average rates of CS SSI (Wloch et al, 2012a), of costs associated with CS SSI (Wloch et al, 2012b) and the observed differences in CS SSI rates in the study. An average estimated cost for each CS SSI was determined to be £600 (range £300 to more than £17,000) (Wlochet al, 2012b).

Results

In the 3-month period, October 2012 to January 2013, there were 186 CS procedures carried out at the hospital, of which 102 (55%) were emergencies.

No women were colonised with MRSA. Four (2.23%) had diabetes mellitus and 42 (27.3%) had a BMI of more than 25.

Single dose antibiotic prophylaxis was given at every CS procedure in addition to the Surgihoney dressing. However, timing of the antibiotic dose was not uniform throughout the year during the two study periods of 9 months pre intervention and 3 months post intervention. This may therefore have been a confounding factor. The timing depended on the anesthetist; some women were given antibiotic prophylaxis prior to skin incision and some at clamping of the cord. An analysis of women with CS wound infection in both cohorts showed no significant association between antibiotic prophylactic dose timing and CS SSI.

Post-operatively, wound characteristics were recorded by the attending midwife in the clinical questionnaire (*Table 1*). Four women out of 186 were reported to have a CS SSI during the evaluation (*Table 2*). This represented an infection rate of 2.15 %. A single patient reported an adverse event related to Surgihoney treatment in the form of wound irritation which resolved without further intervention in 3 days.

In the preceding 9 months, there were 590 CS procedures (234 elective and 356 emergency) carried out at the hospital and obstetric infection control surveillance recorded 32 CS SSI, representing an infection rate of 5.42% (*Table 3*). The 60% reduction in infection rates is significant (p-value=0.042; χ^2 test).

Economic evaluation

In the calendar year of 2008 in the UK, among 620 604 singleton births, there were 147 726 (23.8%) infants delivered by CS (Bragg et al, 2010). A prospective multi-centre cohort study in 2009 found that 9.6% of CS women developed a post-surgical infection (Wloch et al, 2012a). Extrapolation of these rates nationally would predict an expected number of 14 182 cases of SSI. As the reported estimated average individual cost of CS SSI is £600 (range £300 to more than £17,000) (Wloch et al, 2012b) then the corresponding national annual economic burden in the UK is therefore £8 509 017.

Sensitivity analysis

The wound infection rates fell by 60% when Surgihoney was used. If this level of reduction could be repeated nationally then there would be a reduction in the number of CS SSI from 14 182 to 5672. This would mean that there would be a potential national annual cost saving to the NHS of £5 105 400.

Using the SSI data from the two arms of the evaluation (the first 9 months pre-intervention and the 3 months post-intervention), CS SSI rates (expected) were 5.42% before Surgihoney and (observed) 2.15% after. At these levels, which are lower than the rates of infection previously reported at 9.6% (Wloch et al, 2012a), the extrapolated CS SSI infections rates for UK would be (expected) 8007 cases per year and (observed) 3176 cases per year. The difference is 4831 cases of CS SSI that

could potentially be reduced and therefore the potential total cost that could be saved by the NHS by using Surgihoney as a CS wound dressing would be £2 898 600 per annum. The cost of Surgihoney is not known, but it is a simple, low-technology intervention. If the cost per application was an additional £5 to the dressing, then the cost of every CS receiving Surgihoney would be £738 630 per annum.

Discussion

This evaluation demonstrated that Surgihoney, a highly effective antimicrobial wound dressing (Dryden et al, 2013), can be employed as a wound dressing of primary CS wounds to prevent infection. As a 'natural' product with established wound healing properties, Surgihoney is likely to promote wound healing in addition to providing potent antimicrobial activity to prevent wound colonisation and infection. Some halogen-based chemical antiseptics may provide the same degree of antimicrobial activity but may delay wound healing (Jan et al, 2012). However, iodine wound dressings are contraindicated in CS (Joint Formulary Committee, 2013) and a range of toxicities are associated with their use (Pietsch and Meakins, 1976; Scoggin et al, 1977; Zec et al, 1992; Colpaert et al, 2009; Ramaswamykanive et al, 2011; Lakhal et al, 2011). Similarly, a Cochrane Systematic Review showed there was insufficient evidence to establish whether silver-containing dressings or topical agents promote wound healing, prevent wound infection (Storm-Versloot et al, 2010) or are effective treatments of infected or contaminated chronic wounds (Vermeulen et al, 2010).

In a comparison of wound infection rates over two time periods, the evaluation has shown a 60% reduction in infection rates from 5.42% prior to the intervention ,to 2.15% using Surgihoney.

Strengths and limitations

Caesarean wounds were chosen in this evaluation because the patients are by and large healthy with no, or very few, co-morbidities, and CS infection rates are reported to be increasing (NICE, 2011; Paranjothy et al, 2005; NHS Information Centre for Health and Social Care, 2009). Possible reasons for this rise have been increases in older mothers, mothers with co-morbidities, particularly diabetes, and mothers with higher BMIs (National Institute for Health and Care Excellence, 2011; Health Protection Agency, 2012). While it has not previously been routine to use an antimicrobial agent in the primary wound dressing, this evaluation has shown an interesting and effective role for Surgihoney in the prevention of CS wound infections.

The limitation of this evaluation is that it was not a randomised controlled study and used retrospective comparisons. However, a recent well-controlled study of a variety of surgical techniques in CS showed little difference in a composite of death, maternal infectious morbidity, further operative procedures or blood transfusion up to the 6-week follow-up visit (CORONIS Collaborative Group, 2013). Further randomised controlled studies of the use of Surgihoney to prevent SSI in different surgical

Table 1. Adverse events in wound healing in Surgihoney patients

Wound characteristic	Number	%
Oozing	5	2.68
Pain	7	3.76
Inflammation	5	2.68
Positive microbiology	4	2.15
Antibiotics required	4	2.15
Wound healing delay after 10 days	1	0.53
Wound infection (met the case definition of infection	4	2.15

Table 2. Microbiology of infected caesarean section wounds in the Surgihoney group

Patient	Microbiology	Clinical comments
1	Heavy growth *Enterococcus* sp. and mixed anaerobes, scanty *Candida albicans*	Erythema, oozing wound, oral antibiotics, body mass index (BMI) 31
2	Moderate growth *Streptococcus milleri* and anaerobes	Pain, Purulent Dx, oral antibiotics, BMI 32
3	Culture not done	Redness and some oozing, antibiotics prescribed, BMI 22.4
4	Moderate growth of *Staphylococcus aureus*, + anaerobes	Erythema, oozing wound, pain, oral antibiotics

Table 3. Caesarean section numbers and infection rates

Period	Total number of caesarean sections	Elective (%)	Emergency (%)	Number of surgical site infections	Infection rate
Jan 2012–Sept 2012	590	234 (39.7%)	356 (60.3%)	32	5.42%
Oct 2012–Jan 2013	186	84 (45.2%)	102 (54.8%)	4	2.15%

procedures are warranted. A further limitation is the variability in timing of antibiotic prophylaxis around the CS. Analysis of CS SSI cases in both arms, showed no significant difference in antibiotic prophylaxis timing and so this variation is not believed to be a confounding factor.

Interpretation

If this CS SSI rate reduction of 60% could be delivered throughout the NHS by this simple intervention, considerable health quality improvements could be achieved: a reduction in antibiotic use and substantial cost savings.

Health-care-associated infections are a significant and costly health-care complication, accounting for around 8% of patients in hospital with 14% of these infection attributed to SSIs (Smyth et al, 2008). Nearly 5% of patients who had undergone a surgical procedure were found to have developed an SSI (Smyth et al, 2008). SSIs are associated with considerable morbidity and over a third of post-operative deaths are related, at least in part, to SSI (Astagneau et al, 2001). Antimicrobial prophylaxis is routinely employed in many surgical procedures to reduce surgical wound infection. While skin disinfection is also routinely used by surgeons to reduce the skin bacterial load prior to skin incision, it has not been routine practice to use antimicrobial dressings (National Institute for Health and Care Excellence (NICE), 2008). A reason for this may be that most topical antiseptics have a deleterious effect on tissue healing (Baghel et al, 2009; Storm-Versloot et al, 2010; Hoon et al, 2013). Surgihoney is a product with potent antimicrobial activity, which also appears non-toxic and may indeed promote tissue healing (Dryden et al, 2013). It is tempting to speculate whether an antimicrobial, non-toxic, tissue healing agent applied topically to 'clean' surgical wounds could actually replace systemic antibiotic prophylaxis in certain types of surgery. Such an advance would assist the reduction of antibiotic volume use and the selection pressure on colonising bacteria. Further studies would clearly be needed to support this approach.

Key points

- Caesarean section wound infection rates are unacceptably high
- Surgihoney is a novel honey preparation with unique action which should not be confused with other medicinal honeys
- Surgihoney has potent antimicrobial activity and can be used as a wound dressing
- In this evaluation, Surgihoney was used as a single dose at dressing of the caesarean section wound
- This intervention was associated with a reduction in caesarean section wound infection rate by 60%

Conclusion

Prevention of infection of wounds with Surgihoney, an agent which is not toxic to healing tissue and also promotes the healing process, is a novel and potentially important finding which may change the way that surgical wounds are managed. The findings in this study strongly support the need for further studies on the effects of Surgihoney on surgical wounds. **BJM**

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Armstrong DG (2009) Manuka honey improved wound healing in patients with sloughy venous leg ulcers. *Evidence-based Medicine* **14**(5): 148

Astagneau P, Rioux C, Golliot F, Brücker G; INCISO Network Study Group (2001) Morbidity and mortality associated with surgical site infections: results from the 1997–1999 INCISO surveillance. *Journal of Hospital Infection* **48**(4): 267–74

Baghel PS, Shukla S, Mathur RK, Randa R (2009) A comparative study to evaluate the effect of honey dressing and silver sulfadiazene dressing on wound healing in burn patients. *Indian Journal of Plastic Surgery* **42**(2): 176–81

Bragg F, Cromwell DA, Edozien LC, Gurol-Urganci I, Mahmood TA, Templeton A, van der Meulen JH (2010) Variation in rates of caesarean section among English NHS trusts after accounting for maternal and clinical risk: Cross sectional study. *BMJ* **341**: c5065

Colpaert K, Tromp F, Vandecasteele E, Dhondt A, De Waele J, Hoste E, Decruyenaere J, Monstrey S (2009) Iodine toxicity as a cause of total atrioventricular block in burn patients. *Burns* **35**(Supplement 1): S45-S46.

CORONIS Collaborative Group, Abalos E, Addo V, Brocklehurst P, El Sheikh M, Farrell B, Gray S, Hardy P, Juszczak E, Mathews JE, Masood SN, Oyarzun E, Oyieke J, Sharma JB, Spark P (2013) Caesarean section surgical techniques (CORONIS): A fractional, factorial, unmasked, randomised controlled trial. *Lancet* **382**(9888): 234–48

Dryden M, Hudgell L, Saeed K, Dryden AWS, Brooks J, Cooke J (2013) *Surgihoney - Engineered honey wound*

treatment: First report of in vitro activity and early clinical evaluation. Abstracts of the Federation of Infection Society Conference, ICC, Birmingham

Health Protection Agency (2012) *Risk of infection from caesaereans at nearly 10 percent*. www.hpa.org.uk/NewsCentre/ationalPressReleases/2012PressReleases/120801Infectionriskfromcsection/ (accessed 27 January 2014)

Hoon R, Rani A, Najafi R, Wang L. Debabov D (2013) Antimicrobial activity comparison of pure hypochlorous acid (0.01%) with other wound and skin cleansers at nontoxic concentrations. *Wound Repair and Regeneration* **21**: A27.

Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, Augustovski F, Briggs AH, Mauskopf J, Loder E; CHEERS Task Force (2013) Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. *BMC Medicine* **11**: 80

NHS Information Centre for Health and Social Care (2009) *NHS maternity statistics, England 2008–9*. data.gov.uk/dataset/nhs_maternity_statistics_england (accessed 22 January 2014)

Jan WA, Shah H, Khan M, Fayaz M, Ullah N (2012) Comparison of conventional pyodine dressing with honey dressing for the treatment of diabetic foot ulcers. *Journal of Postgraduate Medical Institute* **26**(4): 402–7

Joint Formulary Committee (2013) *British National Formulary 66*. The Pharmaceutical Press, London

Jull AB, Walker N, Deshpande S (2013) Honey as a topical treatment for wounds. *Cochrane Database of Systematic Reviews* **2**: CD005083

Lakhal K, Faidherbe J, Choukhi R, Boissier E, Capdevila X (2011) Povidone iodine: Features of critical systemic absorption. *Annales Françaises d'Anesthésie et de Réanimation* **30**(7-8): e1–3

National Institute for Health and Care Excellence (2008) *Surgical site infection: Prevention and treatment of surgical site infection. NICE Clinical Guideline 74*. www.nice.org.uk/CG74 (accessed 22 January 2014)

National Institute for Health and Care Excellence (2011) *Caesarean Section. NICE Clinical Guideline 132*. www.nice.org.uk/cg132

Paranjothy S, Frost C, Thomas J (2005) How much variation in CS rates can be explained by case mix differences? *BJOG* **112**(5): 658–66

Pietsch J, Meakins JL (1976) Complications of povidone-iodine absorption in topically treated burn patients. *Lancet* **1**(7954): 280–2

Ramaswamykanive H, Nanavati Z, Mackie J, Linderman R, Lavee O (2011) Cardiovascular collapse following povidone-iodine wash. *Anaesthesia and Intensive Care* **39**(1): 127–30

Scoggin C, McClellan JR, Cary JM (1977) Hypernatraemia and acidosis in association with topical treatment of burns. *Lancet* **1**(8018): 959

Smyth ET, McIlvenny G, Enstone JE, Emmerson AM, Humphreys H, Fitzpatrick F, Davies E, Newcombe RG, Spencer RC; Hospital Infection Society Prevalence Survey Steering Group (2008) Four Country Healthcare Associated Infection Prevalence Survey: Overview of the results. *Journal of Hospital Infection* **69**(3): 230–48

Storm-Versloot MN, Vos CG, Ubbink DT, Vermeulen H (2010) Topical silver for preventing wound infection. *Cochrane Database of Systematic Reviews* (3): CD006478

Vermeulen H. Van Hattem JM. Storm-Versloot MN. Ubbink DT, Westerbos SJ (2010) *Topical silver for treating infected wounds (Review)*. tinyurl.com/k83xcej (accessed 22 January 2014)

Wloch C, Wilson J, Lamagni T, Harrington P, Charlett A, Sheridan E (2012a) Risk factors for surgical site infection following caesarean section in England: Results from a multicentre cohort study. *BJOG* **119**(11): 1324–33

Wloch C, Lamagni T, Conneely J, Harrington P, Elgohari S, Jan Van Hoek A, Wilson J, Sheridan E (2012b) *Estimating the healthcare costs of post-surgical infection in patients undergoing caesarean section in England*. Health Protection Agency, Colindale

Zec N, Donovan JW, Aufiero TX, Kincaid RL, Demers LM (1992) Seizures in a patient treated with continuous povidone-iodine mediastinal irrigation. *New England Journal of Medicine* **326**(26): 1784