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THE EFFECTIVENESS OF TRICLOSAN COATED POLYGLACTIN 910 IN REDUCING SURGICAL SITE INFECTION IN CLEAN WOUNDS
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THE EFFECTIVENESS OF TRICLOSAN COATED POLYGLACTIN 910 IN REDUCING SURGICAL SITE INFECTION IN CLEAN WOUNDS

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ABSTRACT

***Background*: Surgical site infection(SSI) is a major cause of morbidity, mortality and financial burden in healthcare. Worldwide it accounts for as much as USD 10 billion annually in direct and indirect medical cost.Many strategies have been developed to try and reduce SSI.**

***Objective*:To determine the effectiveness of triclosan coated polyglactin 910 sutures in reduction of superficial surgical site infection in clean wounds as well as infection rates in clean wounds**

***Design*: A non-blinded randomised controlled trial.**

***Setting*: Kenyatta National Hospital (KNH), the minor theatre in clinic 24.**

***Subjects*: A total of 157patients underwent excision of breast lump.**

***Results*:The prevalence rate of SSI in the study group was 5%(4 of 79 patients) while in the control group it was 4%(3 of 78 patients). The difference between the two groups was not statistically significant(P-value 0.507).**

***Conclusion*: This study did not demonstrate a reduction of superficial surgical site when triclosan coated polyglactin 910 suture was used in clean wounds. Currently, the clinical role and indication for use of triclosan coated polyglactin 910 is yet to be fully defined.**

INTRODUCTION

About a century ago most wounds got infected, with high morbidity and mortality 70-90% (1). Infection in modern surgery continues to be a significant problem for healthcare providers across the globe. Surgical site infection is the third most commonly reported infection and accounts for 14-16% of all nosocomial infections among hospital inpatients (2).It is a major cause of prolonged hospital stay, morbidity and mortality in healthcare (3). Worldwide it accounts for as much as USD 10 billion annually in direct and indirect medical cost (3,4).

Surgical site infection is an infection that develops within 30 days after an operation or within one year if an implant was placed and the infection appears to be related to the surgery (5).The new Center for disease control (CDC) -definition for surveillance of surgical site infection (1992) devised by Horan and his colleagues takes into account 3 classes of surgical site infections (SSI):Superficial SSI, deep incisional SSI,organ/space SSI (6).

The scope of the problem: Before the use of prophylactic antibiotics, infection rates were 1-2% for clean wounds, 6-9% for clean contaminated wounds, 13-20% for contaminated wounds, and about 40% for dirty wounds (3,4). With the introduction of antibiotics the infection rates have drastically dropped to clean 2.1%, clean contaminated 3.3%, contaminated 6.4% and dirty 7.1 %(7). A local prospective study by Bhatt (8) in KNH in 2003,looked at early clinical post operative infection in 292 patients who underwent surgical operations in the general surgical firms, three broad variables were studied-endogenous contamination, exogenous contamination and patient factors. Endogenous contamination was found to be of great significance in predicting wound infection ($p<0.001$). Exogenous contamination and patient factors that were found to be significant included prolonged pre-op stay, shaving, comorbidities, anaemia among others The infection rates were found to be - clean wounds 3.1%, clean contaminated 7.4%, contaminated 22.2% and dirty wounds 38.8% (8), overall wound infection rates was 17.4%. In the same study it was found that patients with SSI spent more money in hospital bills as well as time in hospital in treatment of SSI. They concluded that SSI remained

a major cause of morbidity and financial burden and so more efforts should be put in reducing it.

Risk factors: The development of SSI is the result of a complex interaction between the local and systemic defence mechanisms of the patient and the contaminating organisms(9). The risk factors can be divided into 2 main groups: -

- Patient related factors like obesity, diabetes, smoking, malnutritionetc
- Perioperative factors e.g. preoperative hair removal, skin, length of surgery, use of drains etc

These factors increase the risk of a patient acquiring a SSI. The risk factors are generally related to the patient's capacity to fight against an infectious threat, the infectious challenge itself as represented by the number and pathogenicty of the bacteria, the extent of the associated injury, and environmental factors such as the hospital bacterial flora(9). Surgical wounds can thus be classified based on the presumed magnitude of the bacterial load at the time of surgery.

The classification was devised by National Research Council(NRC) of the National Academy of science (5). This classification is useful in estimating the risk of SSI, predicting the potential pathogens and determining the need of antimicrobial prophylaxis. It divides wounds into 4 classes namely - Clean/class I wounds, Clean-contaminated/ class II wounds, Contaminated/class III wounds and Dirty wounds.

The clean wound infection rates is purported to be the most valuable measure of surgical care in any hospital (10) and is used in surveillance audit and quality assurance(10). And so it can be a useful tool in assessing the quality of infection control we offer to our patients.

Prevention: Preventive strategies for reducing SSI can be divided into(5,9)- Pre-operative period, Intra-operative period, Post-operative period and Intrinsic patient-related factors

Some of the risk factors are modifiable, while others are not. Lots of efforts have been put into reducing SSI by optimising the modifiable risk factors. Some example of preventive strategies include (5,9)- Control of glucose in diabetic patients, Use of prophylactic anti-biotics where indicated, anti-septic skin preparation and others. None of the preventive strategies can guarantee total elimination of SSI.

Suture material is commonly used in modern surgery for wound closure, ligature and others, however they are foreign material. The presence of a foreign body like suture in a wound is known to lower the size of bacterial inoculi necessary to produce infection (11, 12). It is postulated that using anti-microbial coated sutures for wound closure might reduce SSI by preventing bacterial adherence to the suture and create overlapping zones of inhibition radiating outward from the suture (13, 14).

Pharmacology of Triclosan: Triclosan 5-chloro-2 (2,4-dichlorophenoxyphenol) is a broad spectrum anti-microbial agent developed 40 years ago(15). It was first introduced in the healthcare industry in a surgical scrub of 1% concentration in 1972 and for oral care in toothpaste in Europe in 1985(16). Triclosan has been used in over the counter health products for more than 30 years, being non toxic, non irritating, non carcinogenic, non teratogenic and non pyogenic(16). Triclosan acts at multiple cytoplasmic and membrane targets(15, 17). At lower concentration, it appears bacteriostatic and is seen to target bacteria mainly by inhibiting fatty acid synthesis(17), but at higher concentrations it is bacteriocidal. Triclosan binds to bacterial enoyl-acyl carrier protein reductase enzyme (ENR), which is encoded by the gene Fabl. This binding increases the enzyme's affinity for nicotinamideadenine dinucleotide (NAD+). This results in the formation of a stable complex of ENR-NAD+ -triclosan, which is unable to take part in fatty acid synthesis(17). Fatty acids are necessary for building cell membranes. Humans do not have ENR enzyme, so are not affected.Triclosan has a broad range of activity that encompasses many, but not all, types of Gram-positive and Gram-negative non-sporulating bacteria, some fungi(18) and protozoa(19). The organisms most sensitive to triclosan are *staphylococci*, some *streptococci*, some *mycobacteria*, *Escherichia coli* and *Proteus spp*. The tissue reaction, healing response, and absorption profile of triclosan-coated polyglactin 910 anti-microbial suture has not been found to be affected by the presence of triclosan(20).

Study justification: A single centre prospective double blinded randomised control trial(21) done in the United States of America looked at the use of triclosan coated sutures (polyglactin 910) in the closure of galea and fascia in cerebrospinal fluid(CSF) shunts surgery and the resultant infection rates. The results were: the incidence of infection in the study group was 2 out of 46 (4.3%) while in the control 8 out of 38 (21%). The study was halted prematurely because they realised significantly higher infection rates in the control group. The conclusion drawn from that study was that anti-microbial sutures was associated with a reduced risk of post-operative shunt infection. Although the CSF shunt surgery study (21) showed benefits, generalisation cannot be made because of population differences that included; paediatric age group, anti-biotics use pre-operatively, use of iodine impregnated adhesive drapes, anti-biotic wound irrigation before closure, presence of a foreign material- VP shunt and follow up for six months.

A double blinded randomised control trial done in Thammasat university Thailand(22), evaluated the

efficacy and safety of triclosan coated polyglactin 910 compared to polyglactin 910 in reducing surgical site infection in appendectomy operation.In the study either triclosan coated polyglactin 910 or plain polyglactin 910 was used to close the abdominal sheath and the patients were followed up for one year. The preliminary results showed that there was no statistical difference in the surgical site infection between polyglactin 910 and triclosan coated polyglactin 910 (8 and 10 %, p= 0.05)

Another study done in Japan(23) looked at the use of triclosan coated sutures in colorectal surgery. All the patients received intravenous anti-biotics pre and post-operatively. In the study they also included patients with diabetes mellitus, smokers and those on steroids.The infection rate was 4.3% for the triclosan coated polyglactin group while 9.3% for the control. There was a statistically significant difference in the two groups. The conclusion from the study was that triclosan coated sutures can reduce the incidence of wound infection in colorectal surgery.

In the other two studies (22, 23)there was also use of antibiotics peri-operatively thereby introducing a confounding factor. The other difference is that they were not Class 1 wounds and so it is not possible to extrapolate these results for clean wounds.The role of anti-microbial coated suture in reducing SSI has not been fully studied and lots of grey areas still exist as to their effectiveness. This study endeavoured to answers these questions as well being a foundation for more detailed and comprehensive studies.

Null hypothesis: There is no difference in infection rate in clean wound when anti-microbial coated suture (triclosan coated polyglactin 910) is used compared to plainpolyglactin 910 suture.

MATERIALS AND METHODS

Study location: The study was conducted in Kenyatta National Hospital, the national referral and teaching hospital of the University of Nairobi.

Study design: This was a non blinded randomised control study.

Study population: Patients with breast lump for excision in minor theatre day care surgery.

Inclusion criteria: Adult patients 18-50 years of age with Class I wounds.

Exclusion criteria patients with wounds requiring a drain, known immune-compromised patients for example AIDS, diabetes mellitus, if anti-biotic was administered peri-operatively and if shaving of operative site was done.

Sample size estimation: Formulae for sample size calculations for comparisons between proportions in a randomised control trial when the outcome is dichotomous.

$$N = c\left[\frac{\mu_1(1-\mu_1)+\mu_2(1-\mu_2)}{(\mu_1-\mu_2)^2}\right]$$

N = is the sample size for each group = 82 (i.e. 164 patients in total for the 2 arms)
C = 7.9 for a power of 80%
μ_1 = Successrate in the control group (0.79) usedpolyglactin 910 suture
μ_2 = Success rate in the study group (0.937) after a 30% improvement from the control group

The control figure is from the VP shunt study with infection rates of 21%.
There is no local study available.

Ethical Consideration Ethical approval was obtained from the KNH/UON ethic and research committee.

Recruitment and enrolment: The patients selected for the study were those due to undergo excision of breast lump at the minor theatre. A total of 157 patients were enrolled for the study. They were expected to come to KNH, on the 3rd, 7th, and 30th day for review visits by principal investigator (PI).

Intervention: Patients were randomly divided into two groups, each with 82 patients, by use of random permuted blocks. In one group,triclosan coated polyglactin 910 suture was used while in the second group, plain polyglactin 910 suture was used, in wound closure. The surgeons for the study were senior house officers, who were not be blinded. The skin preparation was standardised, there was no shaving done and skin cleaned with three swabs with a povidine mixed with methylated spirit and lastly painted with aqueous povidine.Meticulous haemostatic control was encouraged and no suturing was done inside the wound.All wounds were closed by subcutaneous suturing. There was no use of antibiotics pre and post operatively. In cases where there was a break of aseptic technique, the patients were excluded from the study so as to reduce confounding factors. Patients were then discharged on adequate analgesia. Wound exposure was done by the PI on the third post operative day as well as examination for SSI. The data was entered into a questionnaire. Post operative wound care entailed Op site spray (from smith & nephew) as a form of dressing for all the patients. Subsequently the patients were examined by the PI on day 7 and 30 post operatively for signs of SSI, however they were also instructed to come back to hospital immediately and contact the PI in case they developed wound infection. The criteria for making the diagnosis of superficial SSI

was, purulent discharge from the incision site, pain or tenderness, localised swelling, redness or heat. All the patients who developed SSI were referred to a consultant for treatment.

Outcome: The primary outcome was the development of superficial surgical site infection in class1 wounds. Wound infection was identified by the presence of erythema, localised swelling,raised local temperature, tenderness/pain, or purulent discharge

Data analysis: Data were collected by use of a questionnaire and strict confidentiality was exercised in the handling and storage of the patient's information. The data were analysed using SPSS version 12 data analysis package. Statistical significance was determined using Chi square, fisher's exact test, and a P-value of <0.05 was considered to be significant. Kruskal walls test was used to test the median size of the lump between the groups.

RESULTS

A total of 157 individuals were enrolled into the study, of these 79 patients had their wound closed with triclosan coated polyglactin 910 while in 78 patients plain polyglactin 910 was used. From the study population a total of seven patients developed superficial SSI, giving an overall infection rate of Superficial SSI of 4.5%.

Characteristic of patients: Most of the patients who went underwent excision for benign breast lesions were females 156 (99%) and there was 1 male (1%). The median age of the patients was 25 years, with 111 patients(71%) being 18-29 years, 27 patients (17%) were 30-39 years, while 19 patients (12%) were between 40-50 years old. There was no significant statistical difference between the age groups and developing SSI (P-value 0.761)

Diagnosis: The most common diagnosis found in the study was fibroadenoma seen in 122 patients (77.7%), followed by undefined benign breast lump in 19 patients (12%), 9 patients (5.7%) had galactocele (5.7%), 6 patients (3.8%) had fibrocystic disease and 1 patient (0.6%) had a wart. There was no statistically significant difference between age groups and developing SSI (P-value 0.536)

Location of the pathology: In 146 patients (93%) out of the study population of 157,the disease was unilateral (involving only one breast), while bilateral in 11 patients (7%). In the unilateral cases the left breast disease had 72 patients (46%) while the right side had 74 patients (47%). There was no statistical difference with regard to developing SSI and the location (P- value 0.290)

The most frequently affected quadrant of the breast was the outer upper quadrant with 63 patients (40%),24 patients (15%) upper inner quadrant, 25 patients (16%) lower outer quadrant, 24 patients (15%) lower inner quadrant and in 21 patients (14%) the peri areolaarea.There was no significant statistical difference between the locations and developing SSI (P-value 0.214)

There was no statistically significant difference among the quadrants and developing SSI (P value 0.214).

Summary of the study population: A total of 157 patients underwent surgery for minor breast lesions at the surgical outpatient minor theatre. 156 were female, 1 was male. The median age of the study population was 25 years. The most common diagnosis was fibroadenoma with 122 patients (78%), followed by the diagnosis of breast lump 19 (12%) who also had excisional biopsy done. The most common quadrant affected was the upper outer quadrant with 63 patients (40%). The mean diameter of the excised lesion was 3cm.

Summary of patients with SSI: Out of the 7 patients who developed SSI, 4 patients were in the triclosan coated polyglactin 910 group while 3 patients in the plain polyglactin 910 group.Most of patients who developed SSI had a diagnosis of fibroadenoma 86%, with a mean age of 24 years, the youngest being 21 years, while the oldest was 35 years. The upper outer quadrant was the commonest involved site on the breast.

The prevalence rate of superficial SSI in thetriclosan coated polyglactin 910 group was 5%, while in the plain polyglactin 910 groupit was 4.5%, therefore there was no statistically significant difference between the two groups (P-value 0.507)

Table 1
Summary of outcome

	Number of patients	Number of patients infected in each group
Polyglactin 910	78	3
Triclosan coated polyglactin 910	79	4
Total	157	7

Table 2
Diagnosis

Diagnosis	polyglactin 910 N (%)	Triclosan coated polyglactin 910	P-value
		N(%)	
Fibroadenoma	61(50)	61(50)	
Breast lump	8(42)	11(58)	
Galactocele	6(67)	3(33)	0.536
Fibrocystic breast disease	2(33)	4(67)	
Wart	0(0)	1(100)	

Table 3
Location of pathology on the various breast quadrants

The breast quadrant involved	Number of patients	P-value
Upper outer	63 (40%)	
Upper inner	24 (15%)	
Lower outer	25 (16%)	0.214
Lower inner	24 (15%)	
Periareola	21 (14%)	

DISCUSSION

The age of the patient was not found to be a contributing risk factor in the development of SSI. There was no age group associated with an increased risk of developing SSI (P value 0.761).

The diagnosis and size of the lesion were not found to be contributing factors to developing SSI, however taking into accounts that the operations were done under local anaesthesia this limited the surgery to relatively small lesions i.e. mean diameter of 3 cm, so it's not possible to infer whether size would be a risk factor in developing SSI.

From this study we failed to demonstrate a reduction of superficial SSI when triclosan coated polyglactin 910 was used as compared to plain polyglactin 910. There was no significant statistically difference (P-value 0.507) demonstrated between the two sutures. This is in line with some previous studies (22, 28) that also did not demonstrate any significant difference between the two sutures. It is important to note that the mechanisms leading to surgical site infections are not fully understood,however the presence of a foreign material like a suture is known to lower the size of bacterial inoculi necessary to develop infection (11, 12), hence creating an anti-bacterial environment within the wound is supposed to reduce the risk of SSI (13). This was the thinking behind the creation of anti-microbial coated sutures (13, 14). Although triclosan coated polyglactin 910 has been demonstrated to reduce SSI in some areas like abdominal surgery (23), it has not been found to be effective in others (22, 28). This therefore begs the question- why? One possibility is that, like all good innovations it may be overused and misused. The widespread use of triclosan for many years in topical personal hygiene products (16) like toothpaste, soap etc may lead to diminished anti-microbial activity. This can lead to the development of drug resistance,as demonstrated in some studies (29,30).

The other issue of concern is safety when using triclosan coated sutures, although several studies have demonstrated triclosan to be relatively safe in classic toxicological terms (16, 20), negative effects (31) such as dermatitis,skin irritation and allergic reactions have been described. Currently in the United States, the Food and Drug Administration (FDA) is reviewing the safety and efficacy of triclosan (32). It would therefore be prudent to exercise caution when using triclosan coated sutures (33).

Study limitation: Follow up of the patients was a challenge, because it was on outpatient basis and ascertaining whether the patients were compliant

with the instruction given e.g not taking antibiotics, was difficult. Screening for immunosuppression for example Diabetes Mellitus, HIV-AIDS, was not done, so it's not possible to tell whether they could have been a contributing factor in patients who developed SSI.

In conclusion therewas no significant difference in the rate of SSI in clean wound between plain polyglactin 910 and triclosan coated polyglactin 910 so there is no proven benefit of using triclosan coated sutures in closure of clean wounds

The prevalence rate of SSI for clean wound at KNH is 4.5% which is significantly higher than the expected rate of 1-2%.

More studies should be done to evaluate the effectiveness of antimicrobial coated sutures in other areas like dirty wounds, implants etc.Microbiological testing for local patterns of resistance to triclosan should also be done.Prudent use of antimicrobial so as to reduce the development of drug resistance should be encouraged. Finally healthcare providers should be educated on the various strategies available in prevention of SSI.

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