

THE ROLE OF ANTIBIOTIC PROPHYLAXIS IN CLEAN INCISED HAND INJURIES: A PROSPECTIVE RANDOMIZED PLACEBO CONTROLLED DOUBLE BLIND TRIAL

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A prospective, randomized, double blind, placebo controlled trial was designed to investigate the effect of prophylactic flucloxacillin on the infection rate in clean incised hand injuries, which included trauma to skin, tendon and nerve in adults. Using strict exclusion criteria, a total of 170 patients were recruited into one of three trial groups; Group A – intravenous flucloxacillin on induction followed by an oral placebo; Group B – intravenous flucloxacillin on induction followed by an oral flucloxacillin course or Group C – oral placebo. Thirteen of the patients were subsequently withdrawn, leaving 92% available to complete the trial. Infection was diagnosed using clinical criteria. The infection rates in the three groups were Group A – 13%, Group B – 4% and Group C – 15%. Strictly, the results demonstrate no statistically significant difference in the infection rates between the groups.

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INTRODUCTION

The role of antibiotic prophylaxis in clean incised injuries of the hand remains unclear. Attempts to define this role are hampered by studies with low patient numbers, varying definitions of infection and different out-patient wound surveillance protocols (Hoffman and Adams, 1998). There is good evidence to support the use of prophylactic antibiotics in the treatment of hand injuries involving open fractures (Platt and Page, 1995; Sloan et al., 1987), contaminated wounds, crush injuries (Hoffman and Adams, 1998; Shapiro, 1998) and both animal (Callahan, 1988; Cummings, 1994; Elenbaas et al., 1984) and human (Zubowicz and Gravier, 1991) bites. Conversely, there is good evidence that prophylactic antibiotics are not indicated in simple, “skin only”, lacerations of the hand (Grossman et al., 1981; Roberts and Teddy, 1977). Controversy remains over the role of prophylactic antibiotics in clean complex injuries of the hand involving skin, tendon and neurovascular structures (Hoffman and Adams, 1998).

Data from surveys of plastic surgeons (Drew and Titley, 1995), orthopaedic surgeons (Brown, 1994) and the British Society for Surgery of the Hand (Platt and Page, 1995) has shown little uniformity in the use of antibiotic prophylaxis in the management of acute hand injuries. The survey of plastic surgeons revealed that when dealing with a clean injury (a group which would include most incised injuries) the majority of respondents did not use antibiotics; only 12% to 22% reported their use depending on the structures damaged by the injury. A variety of antibiotic administration routes was employed including oral, intravenous or intravenous followed by oral.

The consequences of a postoperative wound infection vary. Infection can result in significantly increased

fibrosis and stiffness which may cause marked impairment of subsequent function. The literature corroborates this, suggesting that most operative hand infections resolve without sequelae (Platt and Page, 1995; Shapiro, 1998). The reported incidence of post-operative hand infections in clean procedures varies between studies from 1% to 10%, with rates for dirty procedures as high as 40% (Shapiro, 1998).

The aim of this study was to investigate the role of prophylactic antibiotics in clean incised hand injuries.

PATIENTS AND METHODS

A prospective, randomized, placebo-controlled, double-blinded trial was designed, with patients allocated to one of three groups. Group A received intravenous flucloxacillin 1g on induction followed by an oral placebo course (1 tablet qds) for 5 days. Group B had flucloxacillin on induction in an identical manner to group A, but this was followed by an oral course of flucloxacillin (500 mg qds) for 5 days. Finally, Group C had oral placebo for 5 days (1 tablet qds).

At the design stage of the study, advice from an independent medical statistician was sought. Assuming an infection rate of 5% without antibiotics and 3% with antibiotic prophylaxis it was calculated that each group should contain 50 patients to provide sufficient power to demonstrate statistical significance. Ethical approval was granted from the local ethical committee.

The West Midlands Regional Plastic Surgery Unit receives referrals from various Accident and Emergency departments throughout the region. All patients referred to us with an injury to the upper limb distal to the proximal wrist crease were considered for participation

in the trial. The exclusion criteria for trial entry were diabetes, immunosuppressant medication, prior antibiotic administration, a delay of more than 24 hours to presentation, penicillin allergy, age less than 16 years and wounds involving bites, crush injuries, bone and joint or gross contamination. Patients gave informed, written consent for participation in the trial before going to theatre. The surgeon informed the anaesthetist of the patient's recruitment and the anaesthetist then randomly allocated the patient to one of the three groups by selection of a sealed envelope bearing a unique trial number. The surgeon had no knowledge as to which group the patient had been allocated to.

Once under anaesthetic, but prior to any skin preparation or intravenous antibiotics, the patients' wound was swabbed for bacteriological analysis. This swab was transported in a container with Stuarts medium to the microbiology department. The swabs were cultured on primary plates of Blood agar, McConkey and Canamycin at 37°C. Aerobic plates were cultured for 48 hours and anaerobic plates for 5 days. Wounds were managed under tourniquet control in a standard fashion with surgical debridement, followed by thorough irrigation with 1 L of normal saline, prior to exploration and any repair. Both registrar and SHO grade surgeons performed the surgery.

Immediately following surgery, the patient details, time and mechanism of injury, time of surgery, structures damaged and treatment were entered into the computer database in theatre.

Upon discharge the patient was given a letter for their general practitioner detailing the trial and containing a contact number for emergency codebreaking.

At 1 week postoperatively, a member of the plastic surgery team formally assessed the patients' wounds and further wound swabs were taken for bacteriological analysis. All assessors remained blinded with respect to

the trial group. Wounds were categorized into three groups:

- *Wound infections*: defined as frank purulence, greater erythema or swelling than expected or any wound dehiscence in the presence of a healthy blood supply (Shapiro, 1998), or a wound problem with a pathogenic bacterial growth on microbiological swab results.
- *Wound problems*: defined as mild erythema or serous discharge without pathogenic bacterial growth on microbiology swabs.
- *Healthy wounds*.

Patient assessment was repeated at 2 and 4 weeks post surgery, although routine wound swabs were not collected at these visits.

RESULTS

Between November 1996 and December 1998, 1920 patients presented to our unit with hand injuries. Only 10% to 15% of adult patients with hand injuries had clean incised injuries with no contamination and no indication for antibiotics, but very few of these declined to give their consent for inclusion into the study.

One hundred and seventy patients met the strict entry criteria, were willing to be recruited into the trial, and were randomly allocated to the three groups. Thirteen patients were subsequently withdrawn from the trial for the following reasons; three patients withdrew consent postoperatively, two patients were withdrawn peri-operatively due to gross contamination and proximal interphalangeal joint involvement; one patient grew both *Staphylococcus aureus* and β *Haemolytic Streptococci* on the pre-operative swabs; two patients had a time from injury to theatre which was well in excess of 24 hours; and five patients failed to attend out-patient follow-up appointments. Thus data from 157 patients

Table 1—Demographic comparison of the three groups

Group	IV flucloxacillin + placebo	IV + PO flucloxacillin	Placebo
Number	56	46	55
Sex ratio (M:F)	45:11	38:8	46:9
Right dominance	53	44	50
Alcohol involvement	18 (32%)	10 (21%)	11 (20%)
Age (range)	30 (16–51)	33 (17–64)	32 (17–65)
Waiting time (hours) (range)	15 (2–24)	14 (1–24)	13 (2–23)
Number attending assessments			
1 week assessment	48	44	55
2 week assessment	46	23	25
4 week assessment	31	18	32
Number with wound swabs			
Preop microbiology swab	28	21	18
1 week microbiology swab	45	44	52
2 week microbiology swab	13	12	23
4 week microbiology swab	2	6	9

were analysed, though not all were seen for the week 1, 2 and 4 assessments (Table 1).

The groups were well matched for all factors, including general patient factors (Table 1), side, injurious agent (Table 2), structures injured (Fig 1)

and anatomical site of injury (Table 3). Most injuries were largely accidental (86%), with smaller numbers being the result of an assault (9%) or self-inflicted (5%). The most common scene of injury was the home (43%), followed by the workplace (34%) and leisure centres/sites (23%).

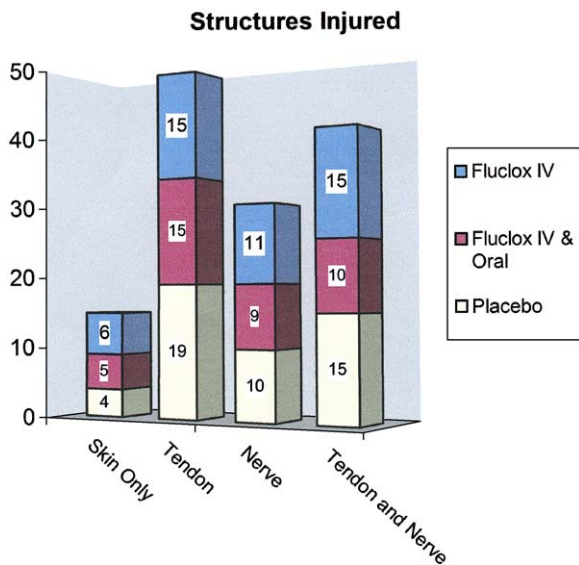


Fig 1 Structures injured by group.

Table 2—Summary of injurious agents

Injurious agent	A	B	C	Total (%)
Glass	26	21	31	50
Knife	13	9	10	20
Tool	7	7	5	12
Metal	10	9	9	18

Table 3—Anatomical regions of the hand injury

Anatomic region	Group A	Group B	Group C	Total injured
Thumb	13	7	14	34
Fingers	25	19	26	70
Palm	5	8	7	20
Wrist	8	10	2	20

Table 4—Wound infections

Number infected patients	Group	Postoperative pathogenic wound swab results	Pre-operative pathogenic wound swab results
7	A	<i>Staph. aureus</i>	4
		Coliforms	1
2	B	<i>Staph. aureus</i>	1
		No growth	2
8	C	<i>Staph. aureus</i>	7
		Coliforms	1

Infection rates

The overall rate of infection for all three groups was 10%. The infection rates were 15% with placebo (Group C), 13% with i/v flucloxacillin alone (Group A) and only 4% with i/v followed by oral flucloxacillin (Group B). Analysis of these rates did not reveal a statistically significant difference between the groups (two sided *P*-value ~mid-*P*, *P* = 0.19; Fishers exact test). The organisms involved were identified in most cases (Table 4).

The mean time from injury to operation for those patients with an infective complication was 11 (range 2–24) hours, for those patients with a wound problem it was 17 (range 3–24) hours and for those patients with no wound problems it was 13 (range 2–24) hours. Individually the groups had similar mean delays. The average time for wound infection to be diagnosed was 8 (3–17) days.

Aside from infection, wound problems were classified as serous discharge or erythema/swelling (Table 5). The group receiving intravenous and oral antibiotics had fewer wound problems (7%) than both the single dose intravenous antibiotic (14%) and the placebo groups (20%). Applying statistical analysis using a 3 × 2 contingency table did not reveal any significant differences between the groups (two sided *P*-value mid-*P*, *P* = 0.14; Fishers exact test). The average time taken to diagnose a wound problem of this nature was 10 (5–24) days.

Analysis of all wound complications together (i.e. wound problems and wound infections), did not reveal a statistically significant difference between the groups (*P* = 0.28; Fishers exact test).

Injured structures and infection

The proportions of structures injured were evenly distributed in each group (Fig 1). From the placebo

Group C, one wound infection came from the skin only group, two from isolated nerve injuries and three from tendon injuries. Isolated tendon injuries in Group A subsequently developed a wound infection in two patients. Finally two patients, one each from Group A and B, had combined tendon and nerve injuries.

Tendon ruptures

These occurred in five patients (one with an extensor and four with flexor tendon repairs). One patient had wound problems with *Staphylococcus aureus* on wound swab culture. The grade of surgeon was a specialist registrar in four patients and an SHO in one.

Grade of surgeon

The operating surgeons were similar in each group, and a specialist registrar was the operating surgeon on 60% of occasions. A specialist registrar operated on seven of the wound infection patients and 80% of patients with wound problems.

Microbiology results

In the 67 patients who had pre-operative microbiology swabs (Table 1), a number of each group subsequently

developed either an infection or a wound problem (Table 6). Although not all patients had pre-operative swab results available at the first postoperative out-patient assessment, 97% of these patients had a clean wound. At the first out-patient assessment, one patient had a frank infection due to *Staphylococcus aureus* and one had a wound problem, but nothing was grown from a postoperative wound swab.

In Group A, seven pre-operative swabs revealed pathogenic bacteria, with three of these patients developing a wound complication. Two patients with *Staphylococcus aureus* present in their pre-operative swabs developed erythema and serous discharge post-operatively. When reswabbed postoperatively skin flora and *Staphylococcus aureus* were cultured, respectively. One patient grew Coliforms on the pre-operative swab and developed postoperative erythema. Postoperative swabs grew *Staphylococcus aureus* initially and later Coliforms. In Group B two patients had pre-operative *Bacillus cereus* growths, which caused no postoperative problems. In Group C, five patients had positive pre-operative wound cultures, all showing *Staphylococcus aureus*. Four patients developed wound complications postoperatively. Two developed infections and one had erythema, with all continuing to demonstrate *Staphylococcus aureus* on their postoperative swabs. One patient developed serous discharge and postoperative swabs isolated skin flora.

Microbiology swabs taken pre-operatively revealed pathogenic bacterial results in 21% of patients, with 10% (n = 14) subsequently developing either a wound infection or a wound problem. The patients with non-pathogenic pre-operative results (79%) contained a similar proportion of patients with wound complications (n = 28).

Wound problems

A total of 22 patients developed a wound problem (Table 5). *Staphylococcus aureus* was present in post-operative wound swabs (Table 7) in four of eight

Table 5—All wound problems

Group	Erythema	Serous discharge	Total
A	7 (12%)	1 (2%)	8/56 ¹ (14%)
B	2 (4%)	2 (4%)	3/46 ² (7%)
C	8 (15%)	3 (5%)	11/55 ³ (20%)

¹Four patients had *Staphylococcus aureus* on swabs, hence infected.

²One patient had serous discharge which progressed to erythema, swab revealed *Staphylococcus aureus*. This was counted as one patient.

³Four patients subsequently developed infection, two with *Staphylococcus aureus*, one Coliforms and one frank infection with no growth.

Table 6—Pre-operative microbiology swab results

Group	Pre-operative swabs	Outcome		
		Wound problem	Wound problem and positive swab	Wound infection
A	<i>Staph. aureus</i>	3	1	1
	Coliforms	2		1
	<i>Streptococcus</i>	1		
	<i>Bacillus cereus</i>	1		
	Skin flora	21	1	1
B	<i>Bacillus cereus</i>	2		
	Skin flora	19	2	1
C	<i>Staph. aureus</i>	5	1	2
	Skin flora	13	6	1

patients with a wound problem receiving bolus intravenous antibiotics only (Group A) and one of three wound problems in the group receiving oral and intravenous antibiotics (Group B). Postoperative wound swabs were not available in a number of patients who had clean wounds on assessment at their initial out-patient visit. The 11 patients in the placebo group with wound problems had positive postoperative swabs in three cases, with *Staphylococcus aureus* grown on two cases and Coliforms in one. From the remaining placebo wound problem patients, one further developed wound infection although no pathogenic bacteria were grown on postoperative swabs. Hence from the initial 22 patients with a wound problem nine patients developed an infection on our criteria.

Clean wounds on the first clinical assessment postoperatively also revealed pathogenic bacterial growth on postoperative wound swabs in eight cases.

DISCUSSION

North American studies suggest that a second generation cephalosporin is the commonest antibiotic used for prophylaxis of clean hand trauma. However, in the UK, the majority of plastic surgeons surveyed indicated that flucloxacillin was their first choice. Platt and Page (1995) recommend flucloxacillin as the antibiotic of choice, on the grounds that the majority of infections were caused by *Staphylococcus aureus* which is sensitive to flucloxacillin.

In our study the patients who developed an infection had *Staphylococcus aureus* on their postoperative swabs in 12 of the 17 infected cases. Coliforms were grown twice and no pathogenic growth was identified on three occasions (Table 7). Of all the pathological organisms cultured postoperatively, *Staphylococcus aureus* was identified on 18 occasions, and on 12 of these there was a frank infection. Coliforms were identified on five occasions and on two of these occasions there was a frank infection. *Bacillus cereus* was identified on three occasions but in none of these was a clinical infection

evident. Thus, *Staphylococcus aureus* was found four times more often than Coliforms and, when present, *Staphylococcus aureus* was twice as likely to cause a clinical infection. With a six to eightfold higher risk of *Staphylococcus aureus* infection, flucloxacillin can be considered to cover the majority of infections after hand injury. The choice of antibiotics can be changed according to microbiology results if necessary.

The overall infection rate in the study was 10%, which appears to be within the upper range published in other studies (Shapiro, 1998). The strict adherence to the study definition for identifying infection and the prospective method of recording of infections and wound problems may be responsible for this apparently high figure. The use of a looser definition of infection in other studies may have led to underreporting of this complication. Wound problems were found in 22 patients. Although these clinical signs did not meet the strict definition of frank infection, nine of these patients were found to have pathogenic bacteria on postoperative wound swabs and hence were classified as infected. Low grade infection may present with these signs, with progression to frank infection prevented by either host defences or antibiotic administration.

Definitions of a wound infection have been numerous, but unless relatively simple can be difficult to apply in the clinical setting. Many previous studies have not used clear and accepted definitions and hence there has been confusion in the reported results for infection. Quantitative culture methods are invasive and can produce false negative results. Infection scoring systems have been criticized for their impracticality given time constraints and do not assist in the detection of infection. Therefore, many studies use clinical methods of wound assessment. Several studies have suggested the most appropriate clinical criteria for the definition of wound infection, and it is those that we have used (Kleinert et al., 1997; Peel and Taylor, 1991; Platt and Page, 1995; Shapiro, 1998).

Prolonged antibiotic use is associated with risk to patients. Although uncommon, antibiotics can cause significant complications from allergic reactions includ-

Table 7—Postoperative microbiology swab results

Group	Post-operative swabs		Outcome		
			Wound problem	Wound problem and positive swab	Wound infection
A	<i>Staph. aureus</i>	6		4	
	Coliforms	3			1
	Skin flora	51	2		1
B	<i>Staph. aureus</i>	1			
	<i>Bacillus cereus</i>	1			
	Skin flora	60	2		1
C	<i>Staph. aureus</i>	11		2	6
	Coliforms	2		1	
	Skin flora	71	7		

ing anaphylaxis and pseudomembranous colitis from *Clostridium difficile*. Emergence of multiresistant organisms has occurred with prolonged, widespread use of broad spectrum antibiotics and use of prophylactic antibiotics for more than 4 days is associated with altered antimicrobial sensitivities of the infecting organisms (Conte et al., 1972). However, for surgical procedures involving implants and bone which last for more than 2 hours, the beneficial role of prophylactic antibiotics has been established and is recommended (Shapiro, 1998). The benefit of prophylactic antibiotics outside these circumstances is difficult to ascertain given low rates of infection and difficulties with trial design and patient numbers.

The pre-operative microbiology swabs were in total, positive for pathogenic bacteria on 21% of occasions. Although half of these patients developed a wound complication, this high proportion was also seen in the patients with non-pathogenic growth and hence preoperative swabs cannot be used to detect a group at higher risk of developing wound complications. Furthermore, in our study only three of the 10 patients who had a wound complication at their first out-patient assessment had a pathogenic bacterial growth on their pre-operative swabs. Hence prophylaxis given on pre-operative swab results would have missed 70% of patients' wound complications. A previous study which looked for pre-operative pathogenic bacteria in wound swabs found none in any of its 50 patients (Drew and Titley, 1995).

Although a convincing trend of decreasing rates of infection with antibiotics was seen, statistically there was no significant difference between our three groups. A further study using the definitions for wound infection used in this study would likely require greater patient numbers to delineate whether a true and significant difference exists.

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