Systematic review

Meta-analysis of antibiotics for simple hand injuries requiring surgery

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Background: **Simple hand trauma is very common, accounting for 1·8 million emergency department visits annually in the USA alone. Antibiotics are used widely as postinjury prophylaxis, but their efficacy is unclear. This meta-analysis assessed the effect of antibiotic prophylaxis *versus* placebo or no treatment on wound infection rates in hand injuries managed surgically.**

Methods: **Embase, MEDLINE, PubMed, Cochrane Central, ClinicalTrials.gov and the World Health Organization International Clinical Trials Portal were searched for published and unpublished studies in any language from inception to September 2015. The primary outcome was the effect of antibiotic prophylaxis on wound infection rates. Open fractures, crush injuries and bite wounds were excluded. Study quality was assessed using the Cochrane risk-of-bias tool. Data were pooled using random-effects meta-analysis, and risk ratios (RRs) and 95 per cent c.i. obtained.**

Results: **Thirteen studies (2578 patients) were included, comprising five double-blind randomized clinical trials, five prospective trials and three cohort studies. There was no significant difference in infection rate between the antibiotic and placebo/no antibiotic groups (RR 0·89, 95 per cent c.i. 0·65 to 1·23; $P = 0·49$). Subgroup analysis of the five double-blind randomized clinical trials (864 patients) again found no difference in infection rates (RR 0·66, 0·36 to 1·21; $P = 0·18$).**

Conclusion: **There was moderate-quality evidence that routine use of antibiotics does not reduce the infection rate in simple hand wounds that require surgery.**

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Introduction

Antibiotic resistance is a global problem requiring re-evaluation of the practice of antibiotic use[1]. Judicious antibiotic stewardship requires clinicians to establish an evidence-based rationale for antibiotic use, by conducting rigorous appraisal of current evidence, and dissemination of research findings[1,2]. Policymakers are increasingly concerned with the problem: in the English National Health Service, infection prevention and control procedures became a statutory obligation on healthcare providers in 2015[3]. It is therefore timely to reassess the evidence for antibiotic use in common clinical scenarios.

In the context of hand injuries, evidence supports the use of postinjury antibiotic prophylaxis[4] in open fractures, crush injuries and human bites[5–7] . Evidence for the use of antibiotic prophylaxis for other hand trauma is limited. These injuries comprise between 1·6 and 30 per cent of all emergency attendances[8–10], and constitute the largest economic impact of all injury types[11]. Given the perceived cost to limb and livelihood of a severe hand infection, the lack of a standard rationale encourages antibiotic use[12].

This study sought to establish an evidence-based rationale for the prophylactic use of antibiotics in the management of open hand trauma. The available evidence from comparative studies was evaluated systematically to obtain

Table 1 Search terms

(((Injury[Title/Abstract] OR wound[Title/Abstract]) OR trauma[Title/Abstract]) OR laceration[Title/Abstract]) AND ((hand[Title/Abstract] OR finger[Title/Abstract]) OR digit[Title/Abstract]) AND ((antibiotic[Title/Abstract] OR antibacterial[Title/Abstract]) OR prophylaxis[Title/Abstract])

reasoned conclusions in order to disseminate clear guidance on how best to manage these injuries.

Methods

Search strategy

A search was performed of MEDLINE and Embase via OvidSP (all fields), PubMed (title/abstract), the Cochrane Database of Systematic Reviews and the Cochrane Central Register of Controlled Trials (searched 3 September 2015). The trial registries ClinicalTrials.gov and the World Health Organization International Clinical Trials Portal (http://apps.who.int/trialsearch/Default.aspx) were also searched, to identify unpublished trials (searched 3 September 2015). The search strategy (*Table 1*) was developed to retrieve all studies and reviews of antibiotic use for hand injuries in humans. Searches were not limited by date, language or publication status. Search results were screened independently for relevance by two authors. Full-text articles were retrieved via the Bodleian Library (Oxford, UK) and British Library (London, UK). Disagreements on study eligibility were resolved by consensus, with reference to the senior author if required. The study protocol was registered prospectively with the PROSPERO database (http://www.crd.york.ac.uk/PROSPERO/; trial identifier CRD42014014412).

All studies comparing the rate of wound infection in patients given an antibiotic *versus* either placebo or no antibiotic in the context of surgical treatment for a simple hand wound were included. Studies included surgery ranging from simple wound excision and suture in the emergency department to formal tendon and nerve repairs under general anaesthesia in the operating theatre (*Fig. 1*). Both adult and paediatric studies were included. Interventional and observational studies were included. Studies of bite wounds, fractures, crush injuries, areas other than the hand, experimental models and those with no control group were excluded. Where there were two or more clinically homogeneous studies, data were pooled in a meta-analysis. For studies included in the meta-analysis, the outcome measure was the rate of postoperative infection. Existing reviews were screened to ensure all relevant primary studies were included.

Fig. 1 Simple hand laceration (class III), typical of those included in this analysis, treated by wound excision and suture

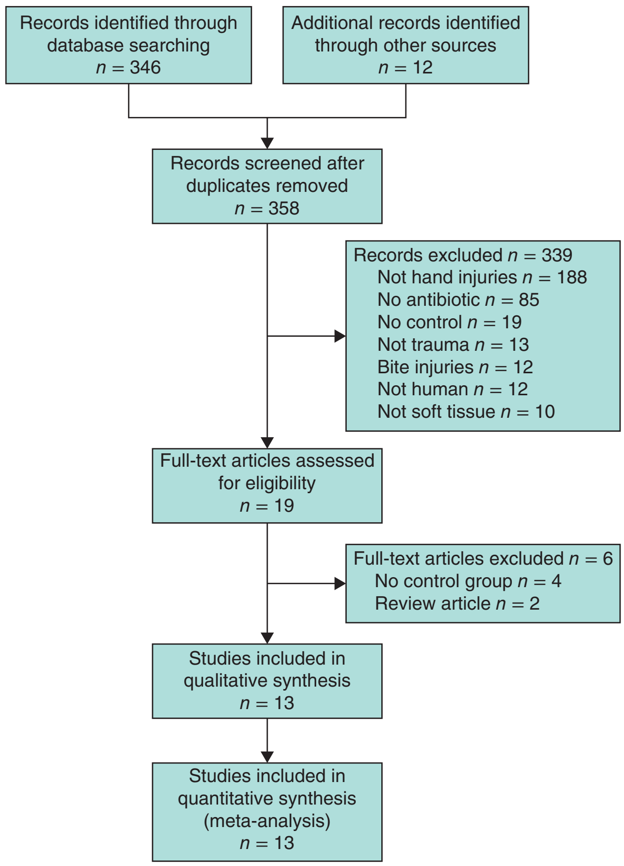

Fig. 2 PRISMA diagram showing selection of articles for review

Reference	Infection rate: Antibiotics	Infection rate: Control	Weight (%)	Risk ratio	A	B	C	D	E	F	G
Altergott *et al.*[14]	1 of 66	1 of 69	1·3	1·05 (0·07, 16·37)	+	–	–	–	+	+	
Aydın *et al.*[15]	5 of 194	8 of 190	8·3	0·61 (0·20, 1·84)	–	–	+	+	+		
Beesley *et al.*[16]	1 of 70	1 of 75	1·3	1·07 (0·07, 16·80)	–	–	+		+		
Berwald *et al.*[17]	0 of 49	1 of 24	1·0	0·17 (0·01, 3·95)	+	+	+	+	+	+	
Cassell and Ion[18]	5 of 100	4 of 126	6·0	1·57 (0·43, 5·71)	–	–	–	–	+		
Grossman *et al.*[19]	2 of 174	1 of 91	1·8	1·05 (0·10, 11·38)	–	–	–		+		
Haughey *et al.*[20]	17 of 160	18 of 234	25·1	1·38 (0·73, 2·60)	–	–	–		–		
Platt and Page[21]	8 of 97	5 of 27	9·4	0·45 (0·16, 1·25)							
Roberts and Teddy[22]	20 of 205	13 of 100	23·3	0·75 (0·39, 1·45)		–	–		+		
Roodsari *et al.*[23]	3 of 44	3 of 81	4·1	1·84 (0·39, 8·74)						+	
Stone and Davidson[24]	2 of 75	1 of 65	1·8	1·73 (0·16, 18·68)							
Whittaker *et al.*[25]	9 of 102	8 of 55	12·5	0·61 (0·25, 1·48)		+	+	+	+		
Worlock *et al.*[26]	5 of 71	2 of 34	4·0	1·20 (0·24, 5·86)					+		
Total	78 of 1407	66 of 1171	100·0	0·89 (0·65, 1·23)							

Heterogeneity: $\tau^2 = 0{\cdot}00$; $\chi^2 = 8{\cdot}16$, 12 d.f., $P = 0{\cdot}77$; $I^2 = 0\%$
Test for overall effect: $Z = 0{\cdot}69$, $P = 0{\cdot}49$

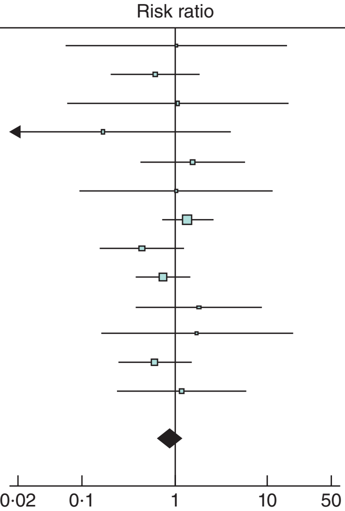

Fig. 3 Forest plot showing infection rate after surgery for simple hand injury in patients with *versus* without therapeutic antibiotics. A Mantel–Haenszel random-effects model was used for meta-analysis. Risk ratios are shown with 95 per cent c.i. The risk of bias in each study is also summarized: –, high risk of bias; +, low risk of bias; A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel (performance bias); D, blinding of outcome assessment (detection bias); E, incomplete outcome data (attrition bias); F, selective reporting (reporting bias); G, other bias

Data collection and analysis

Studies were assessed for risk of bias using the Cochrane Collaboration's tool[13]. Two authors extracted data independently on the number, age and allocation of trial participants, the nature of the injury sustained, the dose, timing and choice of antibiotic, the comparator and the postoperative infection rate.

As infection is a dichotomous outcome, risk ratios (RRs) and 95 per cent c.i. were calculated for each trial. Two authors assessed the participants, interventions and outcomes for clinical heterogeneity. Statistical heterogeneity of the included trials was assessed by both the χ^2 test and the I^2 statistic. A χ^2 test with $P < 0{\cdot}100$ or an I^2 value exceeding 50 per cent was taken to represent significant statistical heterogeneity. Owing to the variety of trial methodologies and antibiotic regimens used, trial data were pooled using the random-effects model. The prespecified sensitivity analysis was conducted according to the risk-of-bias judgement for allocation concealment (high *versus* unclear *versus* low), and for fixed-effect *versus* random-effects models for data synthesis. A prespecified subgroup analysis of only double-blind randomized clinical trials (RCTs) was performed. A funnel plot was used to investigate reporting bias. Statistical analysis was performed using RevMan 5.3 (Nordic Cochrane Centre, Copenhagen, Denmark).

Results

Some 358 records were screened and 19 full texts were assessed for eligibility (*Fig. 2*). A total of 13 studies[14–26] involving 2578 patients met the inclusion criteria and were suitable for meta-analysis. Within these studies, a more homogeneous group of five prospective RCTs with lower risk of bias, involving 864 patients, were also subjected to a separate prespecified meta-analysis.

Of the 13 studies included, five[15–17,25,26] were double-blind RCTs, five[14,18–20,22] were prospective trials and three[21,23,24] were observational cohort studies. Among the RCTs, the risk of bias was low in two relatively recent trials[17,25], high in two trials[15,16], and one older trial[26] did not describe its study design in sufficient detail to assess some forms of bias. All five prospective trials were at high risk of bias in at least one area, mostly owing to lack of blinding. The three cohort studies (2 prospective, 1 retrospective) were at inherently greater risk of bias because of their observational design, and did not map well to the domains assessed by the Cochrane risk-of-bias tool.

The results are summarized in *Fig. 3*. All 13 studies assessed the use of antibiotics following surgery for hand injuries, either as the whole study or as a separately tabulated subgroup. Five studies[17,19,22,25,26] had three arms, comparing different antibiotic regimens with a control group (*Table S1*, supporting information). Six

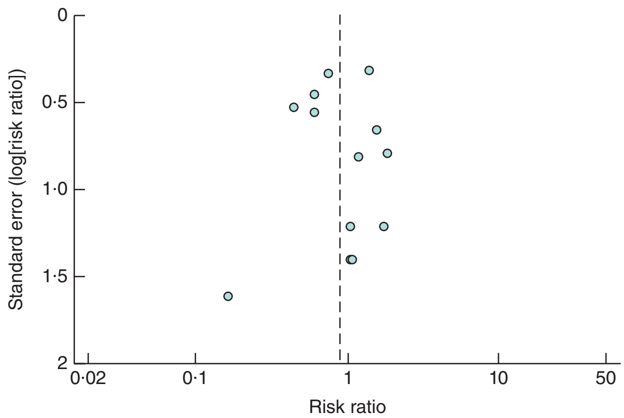

Fig. 4 Funnel plot of included studies

Fig. 5 Infected wound (class IV), typical of those excluded from this analysis. This appearance is suggestive of tenosynovitis, usually treated with urgent surgical washout, antibiotics and elevation

studies[14,15,17,19,20,26] gave a cephalosporin, four[16,18,22,25] penicillin (flucloxacillin or co-amoxiclav) and three[21,23,24] included any antibiotic prescribed. The trials were statistically homogeneous ($P = 0{\cdot}77$, χ^2 test, $I^2 = 0$ per cent), but a random-effects model was used owing to the heterogeneity of regimens.

Antibiotics had no significant effect on the infection rate compared with that in patients given placebo or no antibiotics (RR 0·89, 95 per cent c.i. 0·65 to 1·23; $P = 0{\cdot}49$). This absence of effect persisted throughout the prespecified sensitivity analysis. Restricting the meta-analysis to the five double-blind RCTs still showed no beneficial effect for antibiotics (RR 0·66, 0·36 to 1·21; $P = 0{\cdot}18$) (*Fig. 1*, supporting information).

A funnel plot of the studies revealed no obvious publication bias (*Fig. 4*), although the interpretation of this is subjective and must be guarded given the relatively small number of studies.

Discussion

The main finding of this systematic review and meta-analysis of 2578 patients with simple hand injuries requiring surgery is that the use of a prophylactic course of antibiotics did not significantly reduce the subsequent infection rate compared with a placebo or no antibiotics. This persisted throughout the prespecified sensitivity analysis, and also when the analysis was restricted to RCTs alone. The findings related only to simple hand injuries and specifically excluded open hand fractures, crush injuries, bite wounds and grossly contaminated injuries. Assuming an infection rate of 5·6 per cent (the mean of the included studies), a power of 0·8 and α of 0·5 (2-tailed), 1752 patients would be needed to show a 50 per cent reduction in infection (effect size), fewer than the 2578 in this meta-analysis but greater than the 864 in the RCT-only subgroup.

This study should be interpreted in the context of its limitations. Only five of the 13 included trials were RCTs. Many of the trials were relatively small and did not meet current reporting standards, making an accurate risk-of-bias judgement impossible. This was further complicated by the limitations of the Cochrane tool when applied to non-randomized studies. Subgroup analyses were not feasible, but may have established whether antibiotics were of benefit in some potentially high-risk patients, for example smokers or diabetics. Furthermore, it is unclear whether the lack of apparent effect could be accounted for by failure of the antibiotic prescribed to provide adequate microbiological cover for the organism(s) responsible for subsequent infection. Given the choice of antibiotics to cover staphylococci and streptococci, this is unlikely. Finally, there is potential for significant variability in the surgical management of hand wounds, with factors including choice of skin preparation[27], the timing and extent of surgical debridement[18], choice of dressing and follow-up care, all of which may alter infection rates.

Wound contamination is also a subjective judgement; most studies in this meta-analysis used a variant of the classification adopted by the US Centers for Disease Control[28]. This places simple trauma under 'class III/contaminated', defined as open, fresh, accidental wounds (*Fig. 1*). Wounds with extensive devitalized tissue (such as crush injuries) and those with established preoperative infection or high-bioburden contamination (such as marine, sewage or agricultural contamination) would fall under 'class IV/dirty' (*Fig. 5*) and were excluded.

The findings of this meta-analysis differed from those of studies of perioperative antibiotic prophylaxis in elective surgery[29] and from existing guidelines[30] for lower limb trauma. This heterogeneity underlines the role of antibiotics as an adjunct to, rather than a substitute for, meticulous surgical wound management. They also differed from the recent evidence-based guidelines for plastic surgery from the American Association of Plastic Surgeons[31], although this is probably due to the different populations analysed (class III simple hand lacerations *versus* any contaminated hand surgery).

Hand injuries are extremely common and their global impact significant. Adopting an evidence-based protocol could prevent hundreds of thousands of unnecessary antibiotic exposures, reducing adverse events and costs. The focus should shift to delivering timely surgical intervention for hand injuries. Although a tipping point has yet to be defined, it is reasonable to assume that there exists a time beyond which the persistence of an untreated open hand wound makes subsequent infection more likely.

The UK National Institute for Health and Care Excellence (NICE)[32] published guidance on antibiotic stewardship in August 2015, recommending that 'Commissioners [of healthcare services] should ensure that antimicrobial stewardship operates across all care settings'. With a further report expected on antibiotic resistance in March 2016, it is likely that antibiotic prophylaxis will come under increased scrutiny. This meta-analysis of the use of antibiotic prophylaxis in simple open hand trauma found that antibiotics did not significantly decrease the infection rate. For simple open hand wounds that require surgery, there is no basis to support the use of antibiotic prophylaxis.

Disclosure

The authors declare no conflict of interest.

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Supporting information

Additional supporting information may be found in the online version of this article:

Table S1 Characteristics of included studies (Word document)

Fig. S1 Forest plot showing infection rate after surgery for simple hand injury in patients with *versus* without therapeutic antibiotics: randomized clinical trials only (Word document)