International Orthopaedics (SICOT) (2011) 35:1257–1260
DOI 10.1007/s00264-010-1128-z

ORIGINAL PAPER

Occurrence of fever in the first postoperative week does not help to diagnose infection in clean orthopaedic surgery

Ilker Uçkay · Americo Agostinho · Richard Stern · Louis Bernard · Pierre Hoffmeyer · Blaise Wyssa

Received: 31 July 2010 / Revised: 9 September 2010 / Accepted: 9 September 2010 / Published online: 25 September 2010

Abstract Postoperative fever is often misinterpreted as a sign of infection, especially when occurring after the third postoperative day. We assessed the epidemiology of postoperative fever in adult orthopaedic patients and its association with infection. Among 1,073 patients participating in a prospective observational study, 198 (19%) had a postoperative fever (>38°C). Thirteen patients (1.2%) had a surgical site infection and 78 patients (7.3%) had remote bacterial infections during their hospital stay. Including asymptomatic bacteriuria, 174 patients were given antibiotic therapy for a median duration of six days. In multivariate analysis, no clinical parameter was associated with fever, including haematoma (odds ratio 0.9, 95%CI 0.6–1.3), infection (1.6, 0.7–3.7), or antibiotic use (1.6, 0.9–3.0). The maximum temperature on each of the first seven postoperative days did not differ between infected and uninfected patients (Wilcoxon rank-sum tests; $p>0.10$). We conclude that fever, even up to the seventh postoperative day, is not substantially helpful to distinguish infection from general inflammation in clean orthopaedic surgery.

All authors received no financial support, grants, or royalties and have no financial interests that could lead to a conflict of interest. All authors state that they have read and approved the manuscript. It has not been published elsewhere nor is it under consideration for publication elsewhere. Parts of the manuscript were presented at the 20th Conference of the European Wound Management Association, Geneva, on June 27, 2010 and at the annual meeting of the Swiss Society for Infectious Diseases, Lausanne, on September 3, 2010, Poster P128.

I. Uçkay (✉) · A. Agostinho · R. Stern · L. Bernard · P. Hoffmeyer · B. Wyssa
Orthopaedic Surgery Service,
Geneva University Hospitals & Medical School,
4, Rue Gabrielle Perret-Gentil,
1211 Geneva 14, Switzerland
e-mail: Ilker.Uckay@hcuge.ch

L. Bernard
Division of Infectious Diseases, Bretionneau Hospital,
University Hospitals of Tours,
Tours, France

Introduction

Fever occurring in recently operated patients is more frequent than surgical site infection (SSI). Although the association of fever and recent surgery is well known, fever persisting after the third postoperative day is often a concern to surgeons and nurses and leads to further investigation [1–4]. When an infection is suspected following orthopaedic implant surgery many patients presumably receive antibiotic therapy without clear reason [2, 5] or perioperative prophylaxis is prolonged beyond one day in exceptional situations [6], all with potential adverse effects of unnecessary therapy [7]. Often, an extensive work-up is performed in case of fever [2]. Additionally, postoperative patients may have remote infections such as pneumonia or urinary tract infection, further increasing postoperative temperatures [7–9]. In this study, we prospectively assessed the epidemiological profile of fever during the first postoperative week following clean orthopaedic surgery. We established risk factors and investigated their association with antibiotic use and prophylaxis.

Material and methods

The Orthopaedic Surgery Service of Geneva University Hospitals performs more than 5,000 operations annually [10]. An intravenous dose of 1.5 g of cefuroxime and

preoperative chlorhexidine bathing [11] is standard preoperative prophylaxis. All patients undergoing surgery routinely receive medication to alleviate pain during the first postoperative week, in most cases ibuprofen (with or without paracetamol). Antibiotics are usually prescribed when there is an established remote infection or in cases of malodorous urine or pathological urine sediment in patients with diabetes mellitus, and in patients with dementia and orthopaedic implants.

A prospective single-centre, non-randomised, observational study included all adult patients admitted to hospital for clean orthopaedic surgery over a one-year period. The purpose was to show that pathogens colonising the site during surgery had no correlation with the infecting pathogens of a possible future SSI [12]. However, the database was large enough to perform this satellite study. The same study nurse (AA) followed up all patients on a two-day basis noting demographic variables, surgical parameters including haematoma, and postoperative care until hospital discharge. Antibiotic-related parameters were also assessed. Data concerning infections and antibiotic use were cross-checked by an Infectious Diseases physician (IU) [10, 13]. SSI was defined as the presence of pus inside a collection or discharge, or progressing erythema around the incision [8, 9]. The patient was considered febrile if there was an axillary temperature ≥38°C (100.4°F), independent of antipyretic medication. Antibiotic use was defined as administration of antimicrobial agents for prophylaxis, therapy for remote infection and asymptomatic bacteriuria altogether. We summated these different indications because often perioperative prophylaxis progressed directly to therapy of asymptomatic bacteriuria or treatment of postoperative aspiration pneumonia. In the clinical reality of the immediate postoperative period, it is often difficult to distinguish between prophylaxes and onset of antibiotic treatment for diagnosed or suspected infection.

The primary outcome parameter was the occurrence of postoperative fever. A multivariate logistic regression analysis adjusted for case mix. Variables with a p value ≤0.05 in univariate analysis were included in a stepwise forward selection process while antibiotic-related parameters were fixed covariates. For group comparisons, we used the Wilcoxon rank-sum test. P values ≤0.05 (all two-tailed) were significant. STATA™ software (9.0, STATA Corp, College Station, USA) was used.

Results

A total of 1,073 patients (639 males; median age 70 years) underwent surgery with a median duration of 120 minutes. Surgery was emergency for 538 patients and related to fractures in 540 cases. A total of 887 patients underwent implantation of an implant, including 418 joint arthroplasties. The overall median length of hospital stay was 13 days (interquartile range, 11–16 days). The patient populations developing postoperative fever vs. no fever were equal (Table 1).

Infections and antibiotic use

Forty-eight patients (4%) had no preoperative antibiotic prophylaxis, 722 (67%) received a single dose, 63 a one-day prophylaxis (6%), and 184 patients at least for 48 hours or beyond (17%). In addition, 78 patients (7.3%) had remote bacterial infections during their hospital stay [13], including 48 urinary tract infections, 26 pneumonia, two combined respiratory and urinary tract infections, one septic bursitis and one axillary abscess unrelated to the surgical site. Thirteen patients (13/1,073; 1.2%) had SSI mostly with *Staphylococcus* spp [16], of whom ten required incision and drainage in the operating room. In total, 91 patients were

Table 1 Characteristics of 1,073 patients with and without postoperative fever >38°C

Patient characteristics	Fever (n=198)	p-values	No fever (n=875)
Female gender (n, %)	115 (42%)	0.61	159 (58%)
Median age	72 y, range 16–98	0.90	71 y, range 17–101
Immune suppression[a]	11 (36%)	0.58	19 (43%)
Mean Charlson morbidity index [14]	0.65, range 0–6	0.59	0.73, range 0–4
Mean ASA score [15]	0.69, range 1–4	0.34	0.67, range 1–4
Trauma surgery	126 (46%)	0.11	148 (54%)
Fracture surgery	125 (46%)	0.10	146 (54%)
Luxation	5 (36%)	0.58	9 (64%)
Elective arthroplasty	91 (44%)	0.81	118 (56%)
Below knee surgery	24 (35%)	0.17	44 (65%)
Duration of surgery	130 min, range 50–690	0.15	120 min, range 30–440
Postoperative haematoma	76 (41%)	0.41	111 (59%)

χ^2-test or Wilcoxon rank-sum tests, as appropriate

[a] Immune suppression implies diabetes mellitus, steroid medication >15 mg prednisone equivalent, solid organ transplantation, or hemodialysis

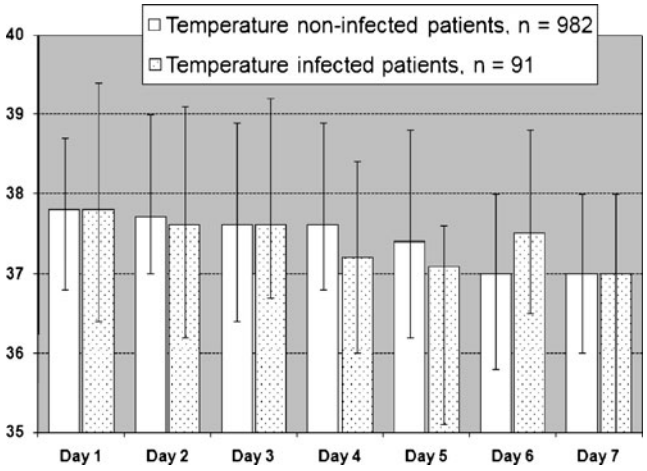

Fig. 1 Median temperatures over the first seven postoperative days. *Bars* 95% confidence intervals

infected. Including those treated for asymptomatic bacteriuria (10^5 CFU bacteria/ml urine), 174 patients (16%) were given antibiotics following surgery for a median duration of six days (interquartile range, 4–9 days). Superficial and/or deep haematoma was detected in 384 patients (36%), and eight of these patients had to undergo an unplanned re-operation for incision and drainage of the haematoma.

Fever

Postoperative fever was noted in 198 patients (18%). The median maximal temperatures on the first through to the seventh postoperative day were 37.8°C, 37.6°C, 37.6°C, 37.6°C, 37.2°C, 37.0°C, and 37.0°C, respectively (Fig. 1). Among febrile patients, 53 (53/198, 27%) had fever only during the first or second postoperative day. The majority showed occasional febrile peaks up to one week after their intervention. The maximum temperature of each of the first seven days postoperative did not differ between infected and uninfected patients (Wilcoxon rank-sum tests, $p=0.10$). However, crude group comparisons revealed a significantly longer hospital stay for febrile patients (16 vs. 13 days; $p<0.02$). Further evaluation revealed that only patients with fever after the second postoperative day stayed longer ($p=0.01$). This was not the case when high temperatures were measured only during the first two days postoperatively ($p=0.10$).

Multivariate analysis

Multivariate analysis failed to show formal statistical association of fever with any clinical variable (Table 2), albeit there was a tendency. Remote infection was associated with fever in only univariate analysis, but not when adjusted for confounders in multivariate analysis. Limb surgery, foot & ankle surgery, and BMI showed significant interaction with sex and age and were exempt from multivariate analysis. Antibiotic use (prophylaxis, therapy for remote infection and asymptomatic bacteriuria) was not formally associated with remote infection when adjusted in multivariate analysis. The goodness-of-fit value of our final model was not significant ($p=0.51$).

Table 2 Logistic regression with outcome "fever over 38°C / 100.4°F"

Associations	Univariate analysis	Multivariate analysis
Patient characteristics		
Female sex	0.9, 0.6–1.3	0.8, 0.5–1.3
Age between 40 and 60 years[a]	**0.5, 0.3–1.0**	0.5, 0.3–1.1
Age >60 years[a]	0.7, 0.4–1.3	0.7, 0.4–1.3
ASA score ≥3 points[b] [15]	**1.5, 1.0–2.2**	1.0, 0.9–2.5
Charlson morbidity index	0.9, 0.7–1.2	na
Body mass index >35 kg/m^2	1.3, 0.9–1.9	na
Surgery		
Insertion of implant	0.9, 0.5–1.7	0.8, 0.4–1.5
Limb surgery	0.8, 0.3–2.0	na
Foot & ankle surgery	0.7, 0.4–1.3	na
Duration of surgery for ≥90 minutes	1.2, 0.7–1.9	1.4, 0.8–2.3
Haematoma	0.9, 0.6–1.2	0.9, 0.6–1.3
Antibiotics		
Single dose antibiotic prophylaxis	1.6, 0.7–3.7	2.1, 0.8–5.4
One day antibiotic prophylaxis	1.5, 0.5–4.5	2.1, 0.6–6.9
Prophylaxis for more than 48 hours	1.8, 0.7–4.7	2.5, 0.9–6.8
Presence of remote infection	**2.2, 1.2–4.1**	1.6, 0.7–3.7
Antibiotic use[c]	**1.9, 1.2–3.0**	1.6, 0.9–3.0

na analysis not performed due to interaction

Data are presented as odds ratio with 95% confidence intervals. Results in **bold** are statistically significant (two-tailed p value ≤0.05)

[a] Compared to <40 years

[b] Compared to ASA scores of 1 and 2 points

[c] Antibiotic use was considered prophylaxis and treatment of remote infection, and treatment of asymptomatic bacteriuria

Discussion

In conclusion, we evaluated 1,071 patients for postorthopaedic fever, infection, and antibiotic use in a heterogeneous population of orthopaedic patients. Fever as a general hallmark of inflammation was frequent with an incidence of 19%, despite the fact that all patients were under antipyretic medication [1]. This high frequency is supported by other reports [1–4, 17, 18]. Only a quarter of all febrile patients were febrile exclusively during the first two postoperative days. The majority had occasional temperature peaks for up to one week postintervention. Stratified daily temperature was similar between infected and uninfected patients, or between patients under prolonged antibiotic use or those who did not receive antibiotics, as reported previously by Than et al. from Hungary [5]. Thus, fever was no proof of SSI or of remote infection, but only an expression of general inflammation, and thus it does not help to diagnose clinical infection [2]. Moreover, occurrence of postoperative fever does not seem to be related to a worse outcome, which has also been reported in a prospective trial enrolling 2,311 immune suppressed patients with colorectal cancer [18].

If confirmed in other trials, the demand for excessive work-up in patients with early postoperative fever, unless there are additional clinical symptoms and particular comorbidities such as neutropenia, remains questionable [2, 4].

Acknowledgments We thank Dr. Sadowski for his invaluable help in conducting the study.

References

1. Garibaldi RA, Brodine S, Matsumiya S, Coleman M (1985) Evidence for the non-infectious etiology of early postoperative fever. Infect Control 6:273–277
2. Saavedra F, Myburg C, Lanfranconi MB, Urtasun M, De Oca LM, Silberman A, Lambierto A, Gnocchi CA (2008) Postoperative fever in orthopedic and urologic surgery. Medicina (B Aires) 68:6–12
3. Pile JC (2006) Evaluating postoperative fever: a focused approach. Cleve Clin J Med 73:62–66
4. Burke L (2010) Postoperative fever: a normal inflammatory response or cause for concern. J Am Acad Nurse Pract 22:192–197
5. Than P, Málovics I (2000) Significance of postoperative fever after hip prosthesis implantation. Z Orthop Ihre Grenzgeb 38:430–435
6. Zywiel MG, Johnson AJ, Stroh DA, Martin J, Marker DR, Mont MA (2010) Prophylactic oral antibiotics reduce reinfection rates following two-stage revision total knee arthroplasty. Int Orthop. Mar 7 [Epub ahead of print]
7. Boehler M, Rustler T, Wolf D, Knahr K (1996) Antibiotic-associated colitis in orthopaedic patients. Int Orthop 20:204–206
8. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR (1999) Guideline for prevention of surgical site infection. Hospital infection control practices advisory committee. Infect Control Hosp Epidemiol 20:250–278
9. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM (1988) CDC definitions for nosocomial infections. Am J Infect Control 16:128–140
10. Uçkay I, Vernaz-Hegi N, Harbarth S, Stern R, Legout L, Vauthey L, Ferry T, Lübbeke A, Assal M, Lew D, Hoffmeyer P, Bernard L (2009) Activity and impact on antibiotic use and costs of a dedicated infectious diseases consultant on a septic orthopaedic unit. J Infect 58:205–212
11. Zywiel MG, Daley JA, Delanois RE, Naziri Q, Johnson AJ, Mont MA (2010) Advance pre-operative chlorhexidine reduces the incidence of surgical site infections in knee arthroplasty. Int Orthop. Jun 20 [Epub ahead of print]
12. Bernard L, Sadowski C, Monin D, Stern R, Wyssa B, Rohner P, Lew D, Hoffmeyer P (2004) The value of bacterial culture during clean orthopedic surgery: a prospective study of 1,036 patients. Infect Control Hosp Epidemiol 25:512–514
13. Uçkay I, Lübbeke A, Emonet S, Tovmirzaeva L, Stern R, Ferry T, Assal M, Bernard L, Lew D, Hoffmeyer P (2009) Low incidence of haematogenous seeding to total hip and knee prostheses in patients with remote infections. J Infect 59:337–345
14. Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 40:373–383
15. Owens WD, Felts JA, Spitznagel EL Jr (1978) ASA physical status classifications: a study of consistency of ratings. Anesthesiology 49:239–243
16. Nickinson RS, Board TN, Gambhir AK, Porter ML, Kay PR (2010) The microbiology of the infected knee arthroplasty. Int Orthop 34:505–510
17. Ishikawa S, Ohtaki A, Takahashi T, Sato Y, Koyano T, Hasegawa Y, Yamagishi T, Ogino T, Ohki S, Kamiyoshihara M, Morishita Y (1998) Management of postoperative fever in cardiovascular surgery. J Cardiovasc Surg (Torino) 39:95–97
18. Chen JS, Changchien CR, Tang R (2008) Postoperative fever and survival in patients after open resection for colorectal cancer: a long-term follow-up study of 2,311 prospectively enrolled patients. Dis Colon Rectum 51:1649–1655