Foreign-body reactions to polyglycolide screws.

Observations in 24/216 malleolar fracture cases

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Out of 216 patients with displaced malleolar fractures operated on using absorbable polyglycolide screws, 24 developed a transient local nonbacterial inflammatory reaction on an average 3 months after the operation. Upon histopathologic examination, these tissue responses were found to be nonspecific foreign-body reactions. Neither the age of the patient nor the number of screws used in the fixation affected the incidence of the reactions. The first-generation screws that were colored with an aromatic quinone dye showed a higher incidence, 19 reactions among 105 patients, than the new noncolored implants, 5 among 111 patients ($P < 0.01$). No deleterious effect of these tissue responses on the union of the fractures could be detected, but the possible long-term consequences of this complication are so far unknown.

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Soon after the clinical introduction of internal fracture fixation implants that were made of absorbable polyesters, it became obvious that these devices occasionally evoked a delayed abacterial inflammatory reaction (Böstman et al. 1987, Partio et al. 1990, Rokkanen 1990, Ruf et al. 1990, Steinmann et al. 1990). Upon histopathologic examination, these tissue responses showed the characteristics of a typical nonspecific foreign-body reaction (Böstman et al. 1990, Poigenfürst et al. 1990).

These inflammatory lesions have occurred with implants made of pure polyglycolide or polylactide, as well as with those made of glycolide-lactide copolymer (Böstman et al. 1989, Hirvensalo 1989, Böstman 1991). The reported incidence has varied from 3 percent in chevron osteotomies of the first metatarsal bone (Hirvensalo et al. 1991) to 22 percent in the distal radius (Hoffmann et al. 1989). However, biopsy specimens obtained from patients operated on using absorbable implants, but having no clinical symptoms or signs of an inflammatory reaction, have also demonstrated a similar histologic picture of a foreign-body reaction (Böstman et al. 1990). The reasons for the variation in the degree of clinical manifestation of these tissue responses are not known.

In this study, all the clinical inflammatory reactions emerging among 216 patients with malleolar fractures operated on using absorbable polyglycolide screws were prospectively examined. The aim was to determine the factors influencing the incidence of the complication in a large series of patients with a common, rather uniform type of fracture.

Patients and methods

Between May 1987 and October 1990, we treated 216 adult patients with displaced malleolar fractures with polyglycolide screws. The series was consecutive with the exception of those patients whose ability to cooperate was reduced by alcoholism or by a serious psychiatric disorder; hence, these patients were managed using other methods. The mean age of the patients was 37 years, and the male:female ratio was 0.9. There were 119 unimalleolar fractures, with unilateral use of the screw, and 97 bimalleolar or trimalleolar fractures, in which the fixation required insertion of the screws on both the medial and lateral sides of the ankle. There were no open fractures.

The screws measured 4.5 mm in major thread diameter and 30 to 70 mm in length. Until December 1988, all the screws contained a dark green aromatic quinone dye that originated from the Dexon suture raw material (Davis & Geck, Gosport, United Kingdom), of which the self-reinforced polyglycolide screws were manufactured (Bioscience, Tampere, Finland). From May 1987 till December 1988, 105 patients were treated with the colored, first-generation screws; and by October 1990, a sufficient number for statistical comparison, 111 patients, had been operated on using the new, noncolored "beige" screws.

No prophylactic antimicrobial agents were given to the patients. Protruding polyglycolide screw heads were cut off before the wounds were closed. Postoperatively, the ankle was immobilized in a plaster cast for 6 weeks. Partial weight bearing was started at

Table 1. Observations in 24 patients with inflammatory tissue response

A	B	C	D	E	F	G	H	I	K
1	F	43	2	4	1	7	2	2	14
2	F	18	2	3	1	11	1	1	
3	F	37	1	1	1	5	1	1	
4	F	49	2	2	1	16	1	1	
5	F	42	2	2	1	8	2	2	21
6	F	23	2	4	1	15	1	2	
7	M	42	1	1	1	26	1	1	
8	F	41	2	4	1	12	1	1	
9	F	41	2	4	1	5	2	1	7
10	F	46	1	1	1	10	2	1	18
11	F	53	2	2	1	8	2	2	10
12	M	28	2	3	1	8	2	1	3
13	M	55	1	2	1	11	2	1	7
14	M	25	1	1	1	12	1	1	
15	F	21	1	1	1	12	1	1	
16	F	47	2	2	1	9	2	2	26
17	F	31	1	1	1	12	1	1	
18	M	29	2	2	1	8	2	2	24
19	F	41	1	2	1	9	2	1	19
20	M	43	1	2	2	26	1	1	
21	M	39	2	2	2	10	2	2	28
22	M	42	1	2	2	12	1	1	
23	M	57	1	1	2	8	2	1	99
24	F	58	2	2	2	12	1	1	

A Case
B Sex
C Age
D Fracture type
  1 unimalleolar
  2 bimalleolar or trimalleolar
E Number of screws used for fixation
F Implant type
  1 colored
  2 noncolored
G Time of clinical manifestation of inflammatory response (weeks after operation)
H Severity of inflammatory response
  1 fluctuant swelling cured by needle aspiration
  2 discharging sinus
I Laterality of lesion
  1 unilateral
  2 bilateral
K Duration of discharge from sinus (days)

3 weeks and full weight bearing at 4 weeks. The patients visited the outpatient department for clinical and radiographic check-ups at 3, 6, and 12 weeks, and at 6 and 12 months. In addition, the patients were encouraged to present immediately with any possible abnormal symptoms during their recovery. A prospective protocol was kept of the clinical course of all the patients. Each patient with an inflammatory reaction was followed by the authors beyond the regular 1-year schedule, with the ultimate follow-up time in these patients ranging from 16 to 47 months. Biopsy specimens were taken whenever an incision or a debridement procedure was necessary. When only needle aspiration was performed, the inflammatory exudate was collected for cytologic examination and pH determination.

The statistical evaluation was done using the Mann-Whitney test when numeric variables were concerned and Fisher's exact test for nominal variables.

Results

In 24 patients (11 percent) with an uneventful early postoperative course, a painful erythematous, fluctuant local swelling emerged in the ankle with a median interval of 11 (5–26) weeks after the operation (Table 1). Among the 24 patients, there were 13 with bimalleolar screw fixations, 6 of whom developed a reaction on one side of the ankle only and 7 on both sides. The bacterial cultures were negative. None of the patients were known to be suffering from any general medical disorder.

In 6 patients a spontaneous sinus yielding liquid remnants of the screw had already formed when the patient sought medical attention for the reaction, whereas needle aspiration of a subcutaneous fluid accumulation was the primary treatment procedure in 18 patients. Despite prompt aspiration, another 6 of these 18 patients developed a discharging sinus. The sinuses occasionally required an incision under local anesthesia for drainage. When an incision was made, the fluid accumulation usually unloaded itself with pressure. In the ultimately 12 patients with a sinus, the median duration of the discharge was 19 (3–99) days (Table 1). No recurrent sinuses were encountered.

No redisplacements of the fracture fragments occurred among the patients with inflammatory reactions. Among the 192 patients with no inflammatory tissue responses, there were five bacterial wound infections and two failures of fixation necessitating a reoperation. With the exception of these 2 patients undergoing reoperation, all the other patients, irrespective of the absence or presence of an inflammatory reaction, showed completed clinical and radiographic union of the fracture at the 12-week, check-up visit.

Upon histologic examination of the biopsies, consisting mainly of fibroconnective tissue from the implant channel, the polymeric material was seen being phagocytized by macrophages and multinuclear foreign-body giant cells (Figure 1). The relative number of polymorphonuclear leukocytes was, as a rule, considerably greater than that of extravasated erythrocytes, indicating the presence of an inflammatory component. The median value of the pH determinations was 7.52 (7.25–8.00).

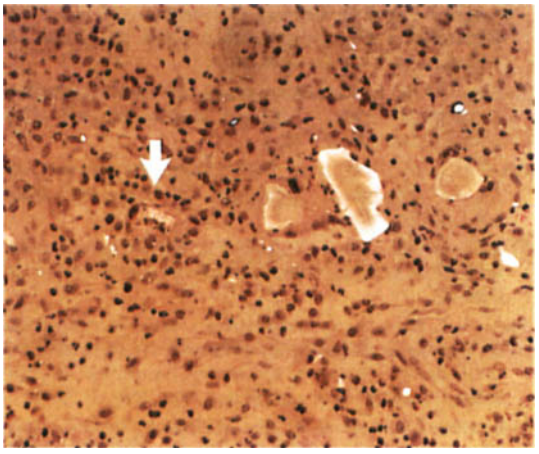

Figure 1. Histologic section under polarized light of a biopsy specimen from a patient with a clinically manifest noninfectious inflammatory sinus 12 weeks after fixation of an ankle fracture with polyglycolide screws. Whirls of polymorphonuclear leukocytes and a few foreign-body giant cells occur in the fibroconnective tissue obtained from the implant channel. Bright birefringent polymeric debris can be seen in the intercellular spaces and inside the multinuclear giant cells (arrow) as a result of active phagocytosis. HE, ×120.

There was no difference between the patients with and without a clinically manifest reaction as regards mean age, male:female ratio, or number of screws used for the fixation; however, the noncolored implants showed a significantly lower incidence of clinically manifest reactions than the colored implants: viz., 4.5 versus 18 percent (Table 2).

Table 2. Patients without an inflammatory response versus patients with a clinically manifest inflammatory reaction. Mean *SD*

	192 patients without reaction	24 patients with reaction	*P*
Age	37 *13*	40 *11*	0.2
Men/women	92/100	9/15	0.5
Fracture type[a]	108/84	11/13	0.5
Number of screws	1.8 *0.9*	2.1 *1.1*	0.1
Patients with colored/ noncolored screws	86/106	19/5	< 0.01

[a]Unimalleolar/bimalleolar or trimalleolar fracture.

Discussion

The use of absorbable implants cannot yet be regarded as an established method of internal fixation, and consequently a comparison with conventional methods is mandatory. Even if metallic devices are associated with disadvantages, such as corrosion, stress-protection osteopenia, and rarely sensitization dermatitis (Rostoker et al. 1987, Black 1988, O'Sullivan et al. 1989), no soft-tissue complications comparable to the reactions presented in our study have been reported with the use of metallic implants in the fixation of ankle fractures. Thus, the abacterial, inflammatory tissue response is a complication unique to the absorbable polyester implants, whereas the incidences of bacterial wound infections and failures of fixation seemed to be of the same magnitude as those recorded with metallic devices (Lindsjö 1985, Mak et al. 1985).

The frequency of the clinically manifest inflammatory reactions in this study, 11 percent, was higher than has previously been reported with absorbable implants in ankle fractures (Rokkanen et al. 1985, Hirvensalo 1989, Böstman et al. 1990, Poigenfürst et al. 1990). However, in the present study also reactions that could be cured exclusively by a needle aspiration were included. It appears possible that some of these fluid accumulations would have subsided spontaneously, whereas the previous studies only reported patients with sinuses requiring surgical drainage.

The most important finding was the lower incidence of the reactions when using the noncolored screws. Nevertheless, manifest reactions occurred with these screws, too, and they were both clinically and histologically identical with those seen with the old, colored implants. Thus, because the quinone dye was not the cause of the reaction, it seems likely that the foreign-body reaction is an inevitable tissue response to the alpha-hydroxy polyesters themselves, whereas the interindividual variation in the clinical intensity of the reaction may be due to factors that influence the debris-clearing capacity of the bone.

In accord with a previous in vitro study in which the immune response to polyglycolide was investigated (Santavirta et al. 1990), no evidence of an immunologically mediated response emerged. The nonallergic nature of the reactions is also supported by the fact that unilateral reactions occurred in patients with bimalleolar use of the polyglycolide screws. In the light of present knowledge, it seems very unlikely that a concomitant low-grade bacterial infection, which is not detectable by standard laboratory techniques, is contributing to the reactions.

At incision, the subcutaneous tissue fluid accumulations, blended with polymeric debris, were often found to be expelled from the built-up pressure. The hydrophilic nature of polyglycolide has been verified also in other clinical applications of the polymer. Local fluid

accumulations could be seen on computed tomographic scans when Dexon mesh had been used in splenorrhaphy (Lange et al. 1988). Further, in a recent experimental study on dogs with a splenic wrap made of polyglycolide, an inflammatory foreign-body reaction was seen in biopsies obtained 40 days after the implantation procedure (Rogers et al. 1991). Previously, Dexon (polyglycolide) and Vicryl (glycolide-lactide copolymer) sutures have been reported to result in noninfectious granuloma or sinus formation in 5 percent of the patients that have had their abdominal wounds closed with these absorbable sutures (Gammelgaard and Jensen 1983).

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