INFLUENCE OF TYPE OF MEDULLARY NAIL ON THE DEVELOPMENT OF LOCAL INFECTION

AN EXPERIMENTAL STUDY OF SOLID AND SLOTTED NAILS IN RABBITS

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Any operation involving the implantation of a foreign body increases the risk of infection. The implant material and its surface, the dead space, and any necrosis or vascular changes play a significant role in susceptibility to infection. We investigated the effect of the dead space in an intramedullary nail on the rate of local infection.

We inoculated the intramedullary cavities of rabbit tibiae with various concentrations of a human pathogen, of *Staphylococcus aureus* strain, and then inserted either a solid or a hollow slotted stainless-steel nail. We found a significantly higher rate of infection after use of the slotted nail (59%) than after the solid nail (27%) ($p < 0.05$).

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The treatment of open fractures has always been challenging, and one of the most severe complications is infection. Infection implies the presence of an adequate number of virulent micro-organisms which overwhelm the local defence mechanisms of the host. Additional factors, such as necrosis, compromised blood supply and hypoxia may then lead to formation of abscesses with spread by way of the Haversian and Volkmann canals. Soft tissue and/or bony necrosis are the effects of the

primary injury and of the operative procedure and have a positive effect on an imminent infection in the presence of a foreign body in the form of an implant.

Susceptibility to infection may be affected by a number of factors relating to the implant including its size and shape, the nature of its surface, the material of which it is made, the stability which it provides, and the method of insertion. Direct toxicity, corrosion and a foreign-body reaction are possible and, in addition, the physicochemical properties of the implant and the texture of its surface can affect the behaviour and therefore the virulence of the bacteria as well as the reaction of the host tissues. The probability of bacterial adhesion increases with the size of the implant and may interfere with surface and tissue integration (Gristina and Costerton 1985; Gristina 1987). Johansson et al (personal communication, 1992) showed in animal experiments on plate fixation that a compromise of the local blood supply was directly related to an increased susceptibility to local infection. Moreover, the shape of the implant may create dead space. In such poorly vascularised or avascular areas, the defence mechanisms of the body have limited access, and detritus and necrotic tissue provide favourable conditions for bacterial growth.

Numerous implants are available for the treatment of open fractures: the use of external fixators has become well-established with a relatively low postoperative rate of infection (3% to 14%) even after severe open tibial fractures (Bach and Hansen 1989; Holbrook, Swiontkowski and Sanders 1989; Krettek, Haas and Tschernse 1989). By contrast, plating or conventional reamed nailing of open tibial fractures is associated with postoperative infection rates of 10% to 35% (Schweiberer and Lindemann 1973; Smith 1974; Ruedi, Webb and Allgöwer 1976; Maatz 1983; Bach and Hansen 1989; Brumback et al 1989) and it is widely felt that these methods should be avoided. Recent experience has shown, however, that unreamed interlocking nails of smaller diameter give a lower infection rate (0% to 8%) while providing adequate mechanical stability (Krettek et al 1991; Santoro et al 1991; Oedekoven, Claudi and Frigg 1992; Whittle et al 1992; Melcher et al 1993).

In contrast to conventional nails, which are hollow and/or slotted, some commercially available unreamed

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nails are solid. This is because the original mechanical reasons for using a hollow slotted nail, to make it jam in the medullary cavity, have been made unnecessary by current locking techniques and by the result of the investigations made by Schandelmaier, Krettek and Haas (1991). An important question is whether a solid implant has any advantages over a hollow one in terms of susceptibility to infection.

The aetiology of infection is very complex, and its study in the clinical situation is therefore very difficult. Therefore, there is need for reproducible animal models in which some of the pathophysiological factors can be kept constant. The aim of this study was to establish an animal model to allow investigation of the role played by the hollow nail design in the pathogenesis of intramedullary infection.

MATERIALS AND METHODS

We used a modified version of the tibial osteomyelitis model of Norden (1970) in which the medullary cavity of 46 rabbits was inoculated with various concentrations of bacteria. The average weight of the rabbits was 3830 g ($\pm$ 240 g). For logistic reasons, we had to use 12 Burgundy rabbits and then 34 Chinchilla bastard rabbits.

Bacterial inoculum. A human-pathogenic, beta-haemolyzing *Staphylococcus aureus* strain (V 8189-94) was isolated from an infected hip prosthesis at the Department of Medical Microbiology, Kantonsspital, Lucerne, and used in the experiments.

Two or three colonies of this strain were inoculated in 80 ml of tryptone soya broth (TSB) and incubated overnight at 37°C in a water-bath shaker. At 120 minutes before operation 500 μ l of this solution were inoculated in 5 ml of TSB and reincubated for 110 minutes in the water-bath shaker to ensure that the suspension was in a logarithmic growth phase. Densitometric determination of the bacterial suspension was then carried out on a McFarland nephelometer (McFarland 1907) to a standard which corresponded to 4×10^6 staphylococci per ml. This result was confirmed in 80 preliminary tests in vitro. After centrifugation, the sediment was resuspended to obtain the desired number of bacteria in each 100 μ l of inoculum. The concentrations varied from 2×10^3 to 4×10^7 CFU (colony-forming units) per 100 μ l.

Implants. We used 90 mm medullary nails of 3 mm diameter, made of stainless steel. The hollow nails had a 0.5 mm longitudinal slit analogous to that in the AO universal nail. Because of the narrow medullary isthmus of the rabbit tibia and to compensate for the lack of elasticity of the solid as compared with the hollow nail, the diameter of the solid experimental nail was reduced to 2.7 mm in its distal third (Fig. 1).

Operation. Under endotracheal anaesthesia by a halothane and oxygen mixture, the patellar ligament of the left leg was divided and the medullary cavity of the tibia opened using a 3.5 mm hand drill. The latter was evacuated

with a 3 mm metal sucker and its distal half inoculated with 100 μ l of the specially prepared bacterial suspension. The nails, 23 solid and 23 hollow, were then advanced into the medullary cavity of the intact tibia with no additional reaming (Fig. 2). The contents of the medullary cavity were evacuated to avoid any proximal overflow of the bacterial suspension during nail insertion. The insertion site was sealed by sterile bone wax.

Two of the rabbits died at the time of operation. The remaining 44 animals were observed for a period of four weeks during which they were kept in separate hutches and fed normally. Their weight was checked three times each week and the wounds were kept under clinical supervision.

Evaluation. After 28 days the animals were killed by the intravenous injection of pentobarbital. The tibiae with the medullary nails were excised under aseptic conditions. The withdrawn medullary nails were rolled across tryptone soya agar (TSA) and then agitated in a vortex mixer in 10 ml thioglycollate. The cultures were incubated for 24 hours. The distal half of each tibia was crushed in a sterile bone mill, and the fragments suspended in 100 ml of TSA and incubated for 24 hours. We recorded a positive result only when there was bacterial growth in both investigations, interpreting growth on the surface of the nail with no concomitant bone infection as a negative result. All bacterial growths were lysotyped.

Experimental procedure. To use as few animals as possible, we employed a grouped sequential procedure. In phase I, we used six animals in each of phases Ia and Ib (12 Burgundy rabbits). In phase II we used 16 animals in each of phases IIa and IIb (32 Chinchilla bastard rabbits). The inoculum used for each investigative phase was determined by the results from the preceding phases, using an 'up and down' dosage technique (Ziegler,

Fig. 1

The specially designed implants used in the experiments, showing a solid and a hollow slotted nail.

Fig. 2a

Fig. 2b

Postoperative radiographs after implantation of a hollow slotted nail.

personal communication, 1993). In each phase, we used an equal number of hollow and solid nails. Our aim was to determine the level of concentration of bacteria at which different rates of infection would be observed in the two groups. Statistical evaluation to assess the differences was based on the chi-squared test, using $p < 0.05$ as significant.

RESULTS

There were no technical difficulties related to the implants or the operation.

Observation time. Two of the animals (one solid, one hollow nail) in phase Ia had to be killed after two weeks because of extreme weight loss and severe local infection after the inoculation of 4×10^7 CFU. Microbiological investigation confirmed the presence of severe bone infection. The other 42 animals survived without compli-

cations for the four-week observation period, initial weight loss being compensated in the ensuing weeks.

Microbiology. In every specimen with positive bacterial growth in the bone, there was also obvious growth from the surface of the nail. In four specimens (two solid and two hollow nails) there were signs of bacterial growth from the surface of the nail but not in the bone, and these results were assessed as negative. In every case, lysotyping showed that only the inoculated bacterial strain was present.

Evaluation. The infection rate for the entire test population ($n = 44$) was 43%. The rate for hollow nails (group 1), was 59% and for solid nails (group 2) 27%. This difference is statistically significant.

Fig. 3

Rates of infection for each of the experimental phases: H, hollow slotted nail; S, solid nail.

Figure 3 shows that the higher rate of infection associated with hollow nails was apparent in all four experimental phases, and also shows the 'up and down' changes in the doses of inocula. Those used in phase Ia were generally too high (4×10^7 , 4×10^5 and 4×10^3 CFU) whereas those selected for phase Ib were clearly too low (2×10^3 , 4×10^3 and 4×10^4 CFU). The inoculum dose was gradually increased in phase IIa (4×10^3 and 4×10^4 CFU) and phase IIb (2×10^5 and 4×10^5 CFU) to increase the rate of infection without causing infection in every animal. From the empirical results, the significance values for the differences between group 1 and group 2 were $p = 0.02$ for phase I and $p = 0.04$ for phase II).

Figure 4 relates the infection rate to the number of bacteria inoculated, and shows only the positive results. This clearly demonstrates that for an inoculum of 4×10^5 CFU or more the nail design has no effect on susceptibility to infection: the total infection rate for this level of inoculation is too high. An inoculum of less than 4×10^5 CFU caused only one infection in 16 solid nailings, but 8

Fig. 4

Rate of infection in relation to the size of the inoculum in colony-forming units. Only positive results are shown as the percentage for each type of nail.

infections in the 16 slotted nailings. The greatest difference between the two nail designs was apparent with an inoculum of 2×10^5 CFU.

DISCUSSION

We have already discussed the difficulty of animal experiments in research related to complex pathophysiological processes. There is not yet an ideal model for infection, but the rabbit osteomyelitis technique of Norden (1970) can be regarded as a standard for the investigation of numerous clinical phenomena. To ensure infection of the rabbit tibia, Norden supplemented the inoculation of the medullary cavity with the sclerosing agent, sodium morrhuate. Andriole, Nagel and Southwick (1973) modified the model by replacing the sclerosing agent with a stainless-steel intramedullary nail. Our experiment already implied the use of a medullary nail, and we therefore chose the modified model.

Most osteomyelitis models described in the literature aim to achieve a 100% infection rate, but Southwood et al (1985, 1987) and Johansson et al (1992) tried to obtain different rates of infection in various groups by administering graded inocula of bacteria. We did not choose the haematogenous infection model which was used by Johansson et al (1992) to assess tissue susceptibility to infection after plate fixation because it assumes an intact local blood supply, and this would not have been suitable for our possible future investigations, comparing reamed and unreamed nailing. The osteomyelitis model of Southwood et al (1985, 1987) was used to assess susceptibility to infection after the insertion of a hip prosthesis in rabbits and seemed most appropriate for our investigation. Because of the large number of animals required we would have preferred to have used a rat model, but this would have given considerable technical difficulties. Our use of intact tibiae would seem to be less clinically relevant but fracturing the bone would inevitably

have made the groups less homogeneous. One of our major objectives was to obtain the maximum amount of information using a minimum number of animals. The grouped sequential procedure took longer but the results seem to confirm that the additional effort was worthwhile.

The number of bacteria required to induce infection in the model which we used cannot be interpreted as an absolute value; extrapolation to a clinical situation is not reliable. It is interesting, however, that an inoculum of only 2×10^3 or 4×10^3 CFU led to bone infection in some cases. This number of micro-organisms would be regarded as very small in clinical terms. In four animals we obtained bacterial growth only from the surface of two solid and two hollow nails, with no concomitant bony infection. It would have been interesting to know how these cases would have developed over time. Either defence mechanisms would have dealt with the local accumulation of bacteria so that the infection never became symptomatic or cryptic, low-grade infection might have developed.

Our investigations have shown that in our model the utilisation of hollow slotted nails is associated with a statistically significant increase in local infection rate over that associated with solid nails. The implant material, its surface texture and the technical procedure for unreamed insertion of the nail in an intact tibia were identical for both nails. It therefore seems that the greater implant surface (nearly $\times 2$) of the hollow nail and the additional dead space do play essential roles in increasing the rate of infection.

While the influence of medullary nail dead space is one of the factors in the complex phenomenon of bone infection the manifestation of an infection is primarily influenced by the defence mechanisms of the host, an aspect which varies greatly and is not measurable. We had to use Burgundy rabbits ($n = 12$) in phase I and Chinchilla bastard rabbits ($n = 32$) in phase II, but found higher infection rates for the slotted nail in both phases. We do not believe that the conclusions were influenced by the change in experimental animals.

Conclusions. The animal model which we describe is useful for the *in vivo* study of infection with different intramedullary devices, and showed a higher risk for infection of slotted nails, as compared to solid nails. These results suggest that the use of a solid intramedullary nail could reduce the local infection rate, especially in the treatment of open fractures.

Further investigation is required on the effect of different types of nail and different implant materials with both reamed and unreamed insertion.

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