The Biocompatibility of Nitinol in Knee Joint Spaces and Femoral Tunnels: An Experimental Study in Rats

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Abstract: Currently the most common method of reconstructing a ruptured anterior cruciate ligament (ACL) is by using bone-patellar tendon-bone (BPTB) or semitendinosus, gracilis tendon autografts. Although good results are reported, donor morbidity continues to be a problem. To overcome these complications, synthetic grafts have been investigated. However, to date no prosthetic graft has been developed as an alternative to patellar or hamstring tendon autografts. The aim of the present study was to assess the biocompatibility of nitinol in rat knee joint spaces and distal femoral bones. Ten male, healthy Wistar albino rats, weighing between 300-350 g, were used. The right knee joint of each rat was reached by medial longitudinal parapatellar dissection. The femur distal was penetrated by a size 0.5 mm of Kirshner wires. Twenty nitinol wires were placed in the bone tunnel (0.125 mm in diameter and 5 mm long). In addition one nitinol wire was placed in the joint space. Following hemostasis, the layers were closed with interrupted sutures. The same procedure was repeated for the left side without placing any nitinol wire. The rats were allowed unrestricted weight bearing. Two animals died of unknown reasons during follow-up. The remaining rats were sacrificed 8 weeks after surgery. The knees were removed by careful dissection and the nitinol wires were removed. The sections taken from these specimens were stained with standard hematoxylin and eosin and with Mason trichrome and examined under the light microscope. The bone tunnels were filled with osteocytes and chondrocytes. In two specimens of the nitinol group, moderate synovitis was detected. The synovitis rate in the study group was found to be statistically insignificant. In conclusion, the short term biocompatibility of nitinol in the rat knee joint space and femoral tunnel was found to be within acceptable limits.

Key words: Anterior cruciate ligament; Biomaterials; Nitinol; Prosthetics; Synthetic grafts

Introduction

Anterior cruciate ligament (ACL) injuries are most commonly seen among young healthy individuals. Due to the surrounding synovial fluid and poor vessel supply ACL injuries cannot be treated neither conservatively nor by primer suturing⁶. The current concept is to reconstruct the ruptured ACL most commonly by using Bone-patellar tendon-bone (BPTB) or hamstring autografts. Although good results are reported , some morbidities of donor sides including anterior knee pain, patellar tendonitis, infrapatellar contracture related with BPTB harvest and hamstring weakness, saphenous nerve injury related with hamstring harvest are reported⁷. To overcome these complications, allografts and prosthetic grafts have been investigated. However, the use of allografts is not advantageous due to a limited donor tissue supply, delayed biological incorporation, risks of disease transmission and tissue rejection. Also, no synthetic graft could have been developed as an alternative to the patellar or hamstring tendon autografts.

Nitinol is a shape memory material which is constructed from nickel (Ni) and titanium (Ti). It was firstly developed at the Naval Ordinance Laboratories (NOL).The name originated with the merger of the abbreviations⁸. Nitinol (NiTi) has shape memory, superelasticity and high damping properties⁹. It has been used in cardiovascular surgery, otolaryngology, ophthalmology and general surgery⁸-⁹. In orthopaedic surgery; plates, intramedullary nails staples, special designed expanding implants, porous implants as bone graft substitute, cervical disc prosthesis, vertebral rods made out of nitinol are are currently used⁸. To date, it has not been used intraarticularly. We hypothesized that nitinol may be used in ACL reconstruction. The aim of this study was to investigate the biocompatibility of nitinol in rat knee joint space and distal femoral bone.

Materials and Methods
Ten male, healthy wistar albino rats, weighing between 300-350 g were used. The study protocol was performed in accordance with the Guide for the Care and Use of Laboratory Animals, and was reviewed and accepted by the institutional animal care and usage committee. The both limbs were shaved and cleaned by Betadine (povidone-iodine) solution. The right knee of each rat was exposed via an anterior skin incision under ketamine hydrochloride anesthesia. Following the skin incision the knee joint was reached by medial longitudinal parapatellar dissection (Fig. 1a). The femur distal was penetrated by a size 0.5 mm of Kirshner wire. Fifty nitinol wires, 0.125 mm in diameter and 5mm long (Fig. 2), were placed in the bone tunnel (Fig. 1b, c). In addition one wire was placed in the joint space. Following hemostasis, the layers were closed with interrupted sutures. The same procedure was repeated for the left side without placing any Nitinol wire.

The rats were allowed unrestricted weight bearing after recovery from the anesthesia. These animals were kept in individual cages and allowed free access to tap water and a standard pellet diet. The cages were housed in a temperature of 24 °C, humid air (55 %) and 12 hours of day/night light controlled room. Two animals died of unknown reasons during follow-up. No surgical wound infection was detected. The remaining rats were sacrificed 8 weeks after surgery. The knees were removed by careful dissection. Sixteen knees (8 from control group, 8 from Nitinol group) were prepared for histological examination. The specimens were fixed in 10 % neutral buffered formaldehyde for 2 days. The specimens were decalcified with 1.5 % aqueous hydrochloric acid for 3 days. After the Nitinol wires were removed the specimens were embedded in paraffin that allows obtaining 5-micron sections from each block and stained with hematoxyline eosin and Mason trichrome. The specimens were cut sagitally. Both groups were evaluated blindly by two senior pathologists under light microscopy.

**Statistical analysis**

Statistical Package for Social Sciences (SPSS) for Windows version 18.0 was used for statistical analysis. Two groups were
compared by Fisher’s exact test. p<0.05 was considered as significant for all statistical data.

Results

Nitinol wires could be removed with difficulty. The bone tunnels were filled with reactive osteocytes and chondrocytes (Fig. 3). In two specimens of the Nitinol group moderate to severe synovitis were detected (Fig. 4). Two groups were statistically similar in terms of the rate of synovitis (p=0.467)

Discussion

In this study we found that the short-term biocompatibility of Nitinol both in distal femoral tunnel and in the joint space were in acceptable limits.

Although the investigations on ACL prosthesis has been continuing for a long time, no material could have been developed as an alternative for either hamstring or BPTB grafts. Up to date, some of the reported ACL prosthesis are; carbon fiber prosthetics, gore-tex permanent prosthesis, dacron, leeds-keio artificial ligament, kennedy ligament augmentation device (LAD), ligament advanced reinforcement system (LARS) artificial ligament, tissue-engineered scaffolds. In the use of Carbon fiber prosthetics, migration of carbon wear particles into the joint space and regional lymph nodes are reported. To overcome this problem Alexander et al. Coated the carbon fiber prosthetics with a co-polymer of polyactic acid (PLA) and polycapralactone. However the long term results are unacceptable due to the high rate of rupture and poor functional outcomes. It is reported that the ACL reconstructions with Gore-Tex were three times more strength than normal ACL, but unacceptable loosening were reported in the long term follow up. Inspired by the use of Dacron grafts with success as a vascular surgery implant, various forms of Dacron grafts have been developed as a scaffold for ACL replacements. Although the short term results were satisfactory the long term functional results were poor. Likewise high rates of ligament ruptures in the long time follow up were reported with Leeds-Keio Artificial Ligament. Kennedy Ligament Augmentation Device was developed for the protection of the autograft from excessive stresses during the initial phase in order to obtain earlier resumption of pre-operative activity levels. However its use was abandoned due to intraarticular inflammation and synovitis. The Ligament Advanced Reinforcement System (LARS) consists of fibers made of polyethylene terephthalate (PET). Residue laxity is reported after ACL reconstruction with this material. Ventura et al reported 19 year follow up results of ACL reconstruction with PET and concluded that high rates of osteoarthritis and total ruptures were seen. Some in vitro studies investigating fibroblast-seeded synthetic scaffolds and collagen-based prosthetics are also conducted.

In the light of the data given above we can say that the main two problems of synthetic ACL grafts are functional insufficiency in long term and intraarticular inflammatory response.

Nitinol (NiTi) is a bio-implant material which key features are shape memory effect, super elasticity and high shock absorbing properties. Also it has the most closest elastic modulus to that of bone.

Singh et al reported the long term results of 133 NiTi clips used in 119 patients after cervical disoidectomy and concluded that these clips are accepted well by human tissue and do not interfere with MRI. Kapanen et al investigated the biocompatibility of nitinol in osteoblast-like ROS-17 cell cultures and reported good results. They also reported an animal study in which the effect of nitinol, stainless steel and titanium aluminium (6 %) vanadium (4 %) alloy (Ti-6Al-4V) on bone formation were compared and concluded that between implant groups the new bone area was largest in NiTi and had good biocompatibility. In an animal study porous Nitinol alloy with porosity of 66.1 % showed 51 % bone contact. Our study is the first one which investigates the intraarticular biocompatibility of Nitinol. The filling of the femoral tunnel with bone tissue, the difficulty of removing the wires, supported good bone biocompatibility and bone in-growth properties of Nitinol. This is also important for the stability of ACL reconstruction. We also think that the elasticity of Nitinol may be an advantage for good long term functional outcomes. Further biomechanical and clinical studies are needed to prove it.

The limitations of our study are the relatively small sample size due to ethical problems and the lack of biomechanical testings.

In conclusion the short term biocompatibility of Nitinol in the rat knee joint space and femoral tunnel was found to be in acceptable limits.

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