聚乳酸系骨釘骨板之短期活體內組織反應與降解變化

Tissue response and biodegradation of PLA bone screw and plate

中文摘要

本研究目的在觀察自製射出成型聚乳酸系骨釘骨板在骨組織內的組織反應與降解變化，做為製程改善與未來臨床使用之參考。所用材料成分含 5% 右型及 95% 左型的聚乳酸共聚物（5D/95L）polylactide，將所製 8ｍｍ 長 x 2ｍｍ 直徑之骨釘 18 支及 2 x 6 x 2.5ｍｍ^{3}之長型片 24 片（ =140000）做為實驗組，另取 6 支市售骨釘及 6 片市售骨板 (MacroPore=166000)做為比較用。所使用實驗動物為 24 隻 3-4 個月大，體重 3-4 公斤的紐西蘭兔，並將所使用材料及動物分為 A、B、C 三組進行。A 組中於實驗兔之右脛骨植入兩支骨釘，一支為自製骨釘,一支為 MacroPore 市售骨釘，並鑽一孔但不植入骨釘做為控制組;另於實驗兔之左脛骨植入兩支自製骨釘, 另標示一區不鑽孔不植入骨釘做為控制組。B 組採用 onlay1 模式於實驗兔之左右脛骨各植入一自製長型片。C 組也採用 onlay 模式於實驗兔之左脛骨植入一自製骨板，於右脛骨植入一市售骨板，各於不同時間點(1,4 及 12 週)將 A 及 C 組，而於(1，4，8 及 12 週)將 B 組內的植入物取出進行各種測試，包括 A 組的組織切片觀察及 B 組的三點彎曲變化、質量損失(weight loss)、分子量變化、結晶度變化及掃描式電子顯微鏡觀察斷面型態改變及 C 組的三點彎曲變化、質量損失(weight loss)、分子量變化。由 A 組的組織切片中觀察到 1 週時實驗組及對照組均出現急性炎症反應，4 週時則都轉為慢性炎症反應,12 週時炎症反應幾乎全消失，未見巨噬細胞。另外，B 組 12 週內的質量損失並不明顯，而初始彎曲強度為 147-157 MPa，第 4 週開始呈現變化，強度為 123-135 MPa，第 8 週時變為 100 —110 MPa，第 12 週時變為 71-93 MPa。重量平均分子量也由起始的 102 kDa 下降至 12 週時的 67 kDa。由長型測試片降解實驗 1-12 週的結果可知,可吸收性高分子聚乳酸在動物體內的降解過程中分子量會先下降，當分子量下降時，整體彎曲強度也會下降，但此時之重量並不會明顯減輕。由 C 組的結果得知市售骨板因較厚起始強度較強（50 MPa）而自製骨板只有 35 MPa，但 4 週時自製骨板仍然維持 100% ，市售骨板已降至 78% ，第 12 週時自製骨板仍有 74% 而市售骨板已降至 58% ，充分說明了自製骨板分子量又低又較薄且強度又維持較久。結論：射出成型自製的聚乳酸性骨釘骨板比類似分子量之商品強度高，於 12 週內對骨組織具有良好反應，且於體內降解過程中，機械強度呈漸減，似乎可將應力傳導到癒合中骨頭，符合理想的骨接合材料所需，是一種具潛力之口腔顏面骨折內固定成品，值得繼續研發。

英文摘要
The purpose of this inverstigation is to study the tissue response and degradation of PLLA in bone tissue. The materials used in this study included PLLA bone screws and bars which were composed of 5% D-form and 95% L-form polylactide. 18 PLLA bone screws with 8 mm in length, 2mm in diameter,24 PLLA bars (2×6×2.5 mm3)and 6 PLA plate were studied and 6 commercial plate and screws were control, (manufactured by Macropore) were control. 24 New Zealand white rabbits (3-4 months old, 3-4 kg weight) were the test animals, and they were divided into three groups (A and B、C) proceeding in this study. In group A：One PLLA screw and one commercial screw were implanted in the right tibia. Two PLLA screws were implanted in the left. Furthermore, one PLLA bar was implanted in both right and left tibia respectively with onlay model in group B. Also,one PLLA plate was implanted in the left tibia and one commercial plate in the right respectively with onlay model in group C . Many tests were done on each sample in 1, 4, 8 and 12 weeks which included the observation of tissue response in group A, and the change of three-points bending, weight loss, molecular weight, crystallinity and morphology of fracture surface by scanning electronic microscopy（SEM）in group B, and the change of three-points bending, weight loss and molecular weight in group C. It was clear that the tissue response in group A revealed good biocompatibility.Otherwise, it was showed that there was no difference in weight loss until 12 weeks, and the initial bending strength was 147-157 MPa. The molecular weight also decreased from 102 kDa to 67 kDa. It is clear that the bending strength decreased while the molecular weight decreased during the degradation process, but there was no weight loss at the same time in group B. In group C：The initial bending strength of commercial plate is stronger than controle（50 MPa：35 MPa）which is due to its thickness.Though, that strength decreased to 78% in 4 weeks and 58% in 12 weeks compared with controle group∶100% in 4 weeks and 74% in 12 weeks. It is evident that the self-manufactured plate by injection method has lower molecular weight but maintain strength long enough than commercial one. Conclusion∶ These results suggest that the BTO screws and plates are good biocompatable. They are potential products in the field of oral — maxillofacial devices in the future.