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ORIGINAL ARTICLE

Changes in peritoneal membrane with different peritoneal dialysis solutions: Is there a difference?

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ultrafiltration;
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Abstract *Background/Purpose:* The peritoneal membrane of long-term peritoneal dialysis (PD) patients is characterized by morphological and microvascular changes. It is said that lactate-based peritoneal dialysate is implicated in the development of these changes. The aim of this study is to compare the effects of long-term exposure to glucose-based, lactate-buffered (Dianeal), and biocompatible bicarbonate/lactate-buffered, low glucose degradation product (Physioneal) peritoneal solutions on the peritoneal membrane.
Methods: Thirty-nine incident PD patients were randomized into two groups: 19 patients with Dianeal dialysate (Group A) and 20 with biocompatible Physioneal dialysate (Group B). All patients used automated PD for a median of 31 months in Group A and 32 months in Group B. Three biopsies at one occasion only were taken from the peritoneal membrane at the end of the study. All samples were collected and fixed in accordance with a standardized protocol, and a histopathologist blinded to the clinical status and PD solutions allocated to the patients carried out the analysis.
Results: The commonest change observed was peritoneal fibrosis, seen in 35 out of 39 cases (89.7%); it was moderate to severe in 28 cases (71.8%) and mild in 11 (28.2%) cases. This was followed by loss of mesothelial cells (22 cases, 56.4%), elastosis (20 cases, 51.3%),

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increased blood vessels (15 cases, 38.5%), thick-walled blood vessels (10 cases, 25.6%), and finally chronic inflammation and mesothelial cell hyperplasia (7 cases, 17.9%, and 6 cases, 15.4%, respectively). Of the patients with blood vessel abnormalities, 22 (88.0%) exhibited significant fibrosis and only three (12.0%) did not. Of those without blood vessel changes, only six (42.9%) patients exhibited similar degree of fibrosis ($p < 0.01$). The prevalence of vascular changes, moderate to severe fibrosis, as well as mesothelial cell abnormalities increased as the duration of PD increased. The prevalence of fibrosis, mesothelial cell loss, and vascular abnormalities increased significantly with diabetes mellitus ($p < 0.001$).

Conclusion: There was no difference in the effects of long-term exposure to glucose-based, lactate-buffered, and biocompatible bicarbonate/lactate-buffered, low glucose degradation product peritoneal solutions on the peritoneal membrane. Risk factors other than PD dialysate composition need to be considered when assessing peritoneal membrane adequacy. The factors that were proved to be significant in our study are duration of end-stage renal disease, diabetes mellitus, and time on PD.

背景 / 目的: 在接受長期腹膜透析 (PD) 的病人間，腹膜會出現若干的形態學與微血管變化，這些變化被認為與採用乳酸鹽腹膜透析液有關。本研究旨在比較兩種透析液的長期暴露—乳酸鹽緩衝之 Dianeal®、與生物相容之 Physioneal® 對病人腹膜的影響。

方法: 共 39 位剛開始接受 PD 的病人被分為兩組：19 人接受 Dianeal 透析液 (A 組)、20 人接受生物相容之 Physioneal 透析液 (B 組)，所有病人接受的均為自動化 PD (APD)。研究結束時，我們對病人腹膜進行了活組織檢驗。

結果: 在 A 組及 B 組之間，間皮細胞消失分別發生於 52.6% 及 60.0% 的病人，間皮細胞增生則分別發生於 21.1% 及 15.0% 的病人 ($p > 0.05$)；嚴重間質纖維化分別發生於 42.1% 及 45.0% 的病人，中度間質纖維化則分別發生於 31.6% 及 25.0% 的病人 ($p > 0.05$)。在 A 組及 B 組的病人之間，彈性組織變性 (elastosis) 達到 "3+" 的比率分別為 15.8% 及 20.0%，達到 "2+" 的比率分別為 15.8% 及 15.0% ($p > 0.05$)；異常微血管增加則分別出現於 42.1% 及 35.0% 的病人 ($p > 0.05$)。在糖尿病患者之間、及接受 PD 較久的病人之間，腹膜病理性變化的比率均有所增加 ($p < 0.001$)。

結論: 長期採用以上兩種腹膜透析液於 PD 病人中，並未導致不同的腹膜變化。然而，以下因素則可能導致不同的腹膜變化：末期腎病、糖尿病、及 PD 的持續時間。

Introduction

Long-term peritoneal dialysis (PD) is blamed for the progressive structural and functional alterations of the peritoneal membrane.[1] The prominent findings in peritoneal biopsies in PD patients are mesothelial cell abnormalities, interstitial fibrosis, elastosis, and peritoneal membrane vasculopathy.[2] Functionally, the peritoneal membrane in long-term PD is characterized by loss of ultrafiltration (UF) capacity, which can generally be attributed to an increased effective vascular surface area. Evidence is mounting that high concentrations of glucose or lactate, glucose degradation products (GDPs), and low pH of dialysate solutions are central to the loss of peritoneal integrity. Some studies focused on the role of GDPs in the genesis of UF failure,[3–5] and others correlated the degree of peritoneal interstitial fibrosis with interstitial and vascular GDPs.[4] An inverse relationship was found between these peritoneal histologic changes and UF volume.[5] Mateijsen et al[6] described neovascularization of the peritoneum of long-term PD patients, and Aiello et al[7] reported similarity between peritoneum neovascularization in those patients and vasculopathy of diabetic retinopathy. In an attempt to link UF failure to different PD dialysate solutions, Seo et al[8] provided evidence that high glucose dialysis solutions increased the synthesis of vascular endothelial growth factor by peritoneal vascular endothelial cells, and pointed at the relationship between vascular endothelial growth factor, GDPs, and neovascularization of the peritoneum. Since then, other reports followed supporting this idea and stressing on the alleged relationship between GDPs and lactate concentrations in PD solutions and peritoneal membrane pathologic changes.[9–12] Recently, neutral solutions with low GDPs have been developed to prevent PD-related peritoneal damage and potentially to decrease the incidence of UF failure; these solutions replaced glucose with amino acids as osmolar effectors, and included neutral pH solutions buffered with either bicarbonate/lactate (Physioneal) or solely bicarbonate (Bicavera).[13] These so-called biocompatible solutions were expected to reduce morphological and functional deterioration of the peritoneum in PD patients. However, their effect on peritoneal histology has not been fully proved so far. Moreover, blood capillary density has been shown to increase with the use of such solutions.[14] These studies, surprisingly, did not consider other factors that may be responsible for the structural and functional deterioration of the peritoneal membrane. Age, duration of end-stage renal disease (ESRD), time on PD, as well as the effect of diabetes mellitus, all can play a significant role in inducing peritoneal membrane abnormalities. Time on PD has been shown, in longitudinal and cross-sectional studies, to negatively influence UF rates that decreased with treatment duration.[15–17] In keeping with these findings, the mean