RANTES 和 MIP-1α在牙周炎病人血清中之濃度變化

The Variation of Concentrations of RANTES and MIP-1α in the Serum of Patients with Periodontitis

中文摘要

牙周炎起因於牙菌斑微生物和宿主防衛機制的交互作用。被感染組織的白血球的積聚和活化是發炎的特徵。被 G(－) 細菌感染的特徵是炎性介質與趨化性介質的提高釋放。近來的研究，已有病患因牙周炎引起周邊血血清中炎性介質如介白質-1 及腫瘤壞死激素提高的報告。因此，最近的研究對可能因牙周炎導致血清中其它其它炎性介質提高，所造成對全身其他器官疾病的影響有極大的興趣。

在 2000 年，Gamonal 等學者的報告指出趨化性介質 RANTES (Regulated on Activation, Normal T cells Expressed and Secreted)可於牙周炎患者的牙齦溝液中檢測出,並且其濃度與健康患者的牙齦溝液中檢測出之濃度有統計學上之差異。RANTES 此一趨化性介質會選擇性地吸引並刺激 macrophages 和淋巴球等白血球。而白血球於宿主對牙齦溝下菌叢的反應中扮演很重要角色。

爲了進一步了解不同嚴重度牙周炎病人周邊血液中趨化性介質家族中 RANTES 和 macrophage inflammatory protein 1-α (MIP-1α)之差異及是否受罹患糖尿病影響，我們從國泰綜合醫院的牙周病科選出三十三位病人（19 位男性和 14 位女性），年齡從 19 歲到 68 歲，平均年齡爲 45.30 歲。病人選擇的標準是最少有 14 顆自然牙齒，排除第三顆大臼齒，至少包括 10 顆後牙，患者在前 6 個月內沒有接受抗生素或非類固醇抗發炎藥物治療。口腔健康評估後區分爲成人牙周炎和牙齦炎或健康的。牙齦炎或健康的病人，牙齦有微量或沒有發炎現象，且只顯示小量的附連喪失。在牙周炎病人，至少 5-6 顆牙齒牙周囊袋深度>6 公釐和附連喪失> 3 公釐，在 X 光片中有廣泛的齒槽骨喪失。依照牙周囊袋深度將病人區分爲 3 組，分別爲： 1) Group1 (n=9): 牙周囊袋深度< 4 公釐，2) Group2 (n=17): 4 公釐 ≤牙周囊袋深度≤ 6 公釐，和 3) Group3 (n=7): 牙周囊袋深度>6 公釐。Supragingival plaque accumulation (PI)用 O’ Leary Plaque Control Index 來測量，且所有病人的 PI 都在 20%以下。

測量並記錄牙周囊袋深度（PD）和附連喪失 （ALoss）。先用 Kruskal-Wallis Test 來分析，再用 Mann-Whitney U Test 來比較組和組之間的差異。然後用 General Linear Model 的 Univariate Analysis of Variance，來做年齡和性別 (covariates) 的調整。周邊血液樣本在患者進行牙周手術或 orthognathic 外科手術時，以 veni-puncture 取得 20ml (vacutainer，with heparin)。血清樣品以螢光免疫分析法 enzyme linked immunosorbent assay (ELISA) 檢測三組病人群中趨化性介質家族中 RANTES 和 MIP-1α的濃度。個體之 RANTES 和 MIP-1α的濃度以 subject mean ± standard deviation 表示。

我們的結果顯示，對慢性牙周炎患者而言，只要牙周囊袋深度≥4 公釐，血液中

RANTES 的濃度都比健康的個體要高，即使有更深的牙周囊袋深度和更多的附連喪失，都不會進一步對血液中 RANTE 濃度的改變有太大影響。也就是說，只要有慢性牙周炎，牙周囊袋深度及附連喪失和血液中 RANTES 的濃度沒有任何線性關係。

另外再依照糖尿病病史的有無(HbA1C 維持在 10%以下控制良好的糖尿病病人)，將慢性牙周炎病人再次分爲兩組(Group A:有慢性牙周炎無糖尿病，GroupB:有慢性牙周炎有糖尿病)，每組 11 人，分析顯示，有慢性牙周炎的個體有或無糖尿病，都不會進一步對血液中 RANTES 濃度的改變有太大影響。即使經過修正年齡和性別因素，只要有慢性牙周炎，糖尿病的有無與血液中 RANTES 濃度的變化沒有任何相互關係。

至於 MIP-1 α，在研究個體的血清中，不論是否有慢性牙周炎或罹患糖尿病都沒有偵測到 MIP-1 α 的存在。

綜言之，基於本研究的結果，我們建議，罹患慢性牙周炎的病人血清中 RANTES 的濃度會上升，MIP-1 α 的濃度則無此情形; 而且 RANTES 濃度之上升與牙周炎病人的牙周囊袋深度及附連喪失和有無罹患糖尿病無關。

英文摘要

It is general accepted that periodontal disease results from the interaction of the host defense mechanisms with the infecting microorganisms. Infection with gram-negative bacteria is characterized by the accumulation and activation of leukocytes in the affected tissues with an enhanced release of inflammatory and chemotactic cytokines (chemokines). Recently, there has been great interest in the systemic effects of serum proinflammatory cytokine levels potentially elevated by periodontitis.

The first evidence on the presence of the chemokine RANTES (Regulated on Activation, Normal T cells Expressed and Secreted) in the gingival crevicular fluid (GCF) of patients with periodontitis. RANTES is a chemokine that selectively attracts and activates macrophages and lymphocytes which plays critical roles in the host response to the subgingival microflora. We hypothesized that the concentrations of chemokine, RANTES and macrophage inflammatory protein (MIP-1alpha), might express differently in adult periodontitis patients in response to the disease severity. The purposes of the present study are to investigate: 1) the association between chemokine (RANTES and MIP-1alpha) and severity of periodontitis, and 2) the changes of chemokines (RANTES and MIP-1alpha) concentrations in adult periodontitis patients with or without well-controlled type 2 diabetes mellitus.

To achieve the specific goals, thirty-three patients (19 males and 14 females) for this study were selected from the periodontal department of Cathay General Hospital and were divided into 3 groups, which were: 1) Group1 (n=9): probing depth (PD)< 4mm，2) Group2 (n=17): 4mm ≤probing depth (PD)≤ 6 mm，and 3) Group3 (n=7):

probing depth (PD)>6 mm.

In patients with periodontitis, at least 5-6 teeth had sites with probing depth>6mm and with attachment loss>3 mm and extensive radiographic bone loss. Attachment loss (ALoss) and probing pocket depth (PD) measurements were taken. Dichotomous measurement of supragingival plaque accumulation (PI) (O'Leary Plaque Control Index) was made and all patients were under 20%. 20 m1 (Vacutainer, with heparin) of peripheral blood samples were taken by veni- puncture from each subject at the time of periodontal surgery or orthognathic surgery. Serum samples were assayed by an enzyme linked immunosorbent assay (ELISA) to determine the levels of RANTES and MIP-1α. The concentrations of RANTES and MIP-1α at healthy and diseased individuals were calculated as subject mean ± standard deviation. We used Kruskal-Wallis test of SPSS version 10.0 to analyze first, then used Mann-Whitney U test to compare the differences between groups. Furthermore, Univariate Analysis of Variance of General Linear Model was used to adjust the covariates effects of age and sex.

Our data demonstrates that, for both periodontitis groups (4mm≤PD≤6mm and PD>6mm), concentrations of RANTES in the serum are significantly higher than that of the healthy group and there are no statistically significant differences between both periodontitis groups. For MIP-1α, there are no statistically significant differences between those three groups in present study.

According to the existence of well-controlled type 2 diabetes mellitus, we subdivided the periodontitis patients into two groups, which were adult periodontitis and periodontitis with well-controlled type 2 diabetes mellitus. The concentrations of RANTES in the serum between both periodontitis groups (periodontitis without diabetes and periodontitis with well-controlled diabetes) do not have statistically significant differences.

In conclusion, this present study demonstrates that the concentrations of RANTES but not MIP-1α will elevate in the serum of periodontitis patients. Furthermore, the probing depth, attachment loss, and existence of well-controlled diabetes mellitus do not influence the concentrations of RANTES and MIP-1α in the serum of periodontitis patients.