臺灣地區鮑氏不動桿菌臨床分離株對Imipenem抗藥機制的研究 = Mechanisms of imipenem resistance in acinetobacter baumannii ..

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摘 要

鮑氏不動桿菌 (Acinetobacter baumannii) 為人體常在菌，也是目前院內感染最常被分離出菌種之一。本實驗為了研究這些A. baumannii分離菌株之相關抗藥機制，主要利用PCR技術、metallo-β-lactamases偵測技術、一維、二維蛋白電泳、南方墨點法及紙錠擴散法 (E-test) 來鑑定及分析。經由紙錠擴散法(E-test) 發現有16株對於imipenem抗生素呈現抗藥性，包含7株帶有blaIMP-1抗藥基因，MIC均大於32 μg/ml。另一方面用Kado-Liu方法抽取質體做南方墨點法也發現，blaIMP-1抗藥基因位於A. baumannii大質體上。因此，推測攜帶有blaIMP-1抗藥基因之菌株可能藉由質體來相互傳播。另外9株對imipenem呈現誘導性抗藥 (inducible resistance)，因其MIC介於8~32 μg/ml，而且其抑制圈內有散在性菌落。利用PCR實驗偵測結果發現這些菌株不帶有blaIMP-1、blaVIM、blaOXA-23或blaOXA-24抗藥基因，metallo-β-lactamase篩選也呈陰性反應。誘導性菌株以不同濃度imipenem培養 (0, 16, 32 μg/ml) 後，以一維蛋白電泳及MALDI-TOF MS 分析發現AmpC蛋白質表現量會因imipenem濃度愈多而增加，此AmpC蛋白質經比對後發現屬於blaADC-1類別抗藥基因產物。根據序列比對發現為新的ADC抗藥基因，將之命名為blaADC-29。同時也發現誘導性抗藥菌株高達85% 比例皆攜帶有blaADC-29與上游的ISAba1基因，推測ISAba1可能與造成AmpC蛋白質大量表現有相關性。以南方吸漬法證實blaADC-29位於染色體上，而blaIMP-1則位於質體上。當以即時定量聚合?連鎖反應偵測誘導性抗藥菌株blaADC-29、ompA及adeB之表現量時，發現blaADC-29及ompA表現量會隨著imipenem之濃度增加而增加，然而與efflux pump 相關的 adeB基因之表現量卻不受影響。本研究結果顯示鮑氏不動桿菌可能會因為攜帶抗藥基因blaADC-29與其上游的ISAba1，並藉由blaADC-29的高度表現而造成對imipenem具有誘導性抗藥，因此臨床上過度使用imipenem會促進該菌誘導性抗藥的表現。在病人臨床資料比對分析結果發現，使用imipenem抗生素在分別帶有carbapenem 敏感 (SS) 與非敏感 (包括SR 及 RR) 菌株之兩組病人的治療上，其用藥平均天數具統計差異性。

關鍵詞 : 多重抗藥性鮑氏不動桿菌 ; 乙內醯胺? ; 誘導性抗藥 ; 亞胺培南

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