SHORT COMMUNICATION

Neisseria Meningitidis Isolates with Moderate Susceptibility to Penicillin

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Summary

Neisseria meningitidis is one of the important cause of meningitis and has always been extremely susceptible to penicillin. Nevertheless, moderately penicillin resistant strains have been reported in some parts of the world. To our knowledge, there is no such report in Malaysia. We report two clinical isolates that were found to have MICs of decreased susceptibility to penicillin by the agar dilution method.

Key Words: Neisseria meningitidis, Penicillin, MIC

Introduction

Neisseria meningitidis strains were considered to be extremely susceptible to penicillin with most of the isolates showing minimum inhibition concentration (MIC) ≤ 0.06 mg/l. However, meningococcal isolates with low level of resistance to penicillin have been documented. Some of the definitions used are 'moderately penicillin resistant', 'decreased susceptibility', 'relative resistant' and 'moderately susceptible strains'. These strains have been described in Europe, North and South America, reporting different rates of strains with decreased susceptibility to penicillin with MICs of 0.12-1 mg/l[1]. As far as we are aware there is no documented case of moderately susceptible penicillin of *N. meningitidis* strains in the Malaysian literature. We report two clinical isolates of penicillin moderately susceptible *N. meningitidis* in Kuala Lumpur Hospital.

Two isolates of *Neisseria meningitidis* were recovered from blood of 2 patients that represented sporadic cases of meningococcal infection. The strains were grown in the laboratory on chocolate agars and gonococcal selective agars with incubation at 37°C in CO_2 atmosphere overnight. Standard microbiology tests (oxidase, carbohydrate utilization and nitrate) and Vitek® (bio Merieux Inc, Hazelwood, MO) identification system were used for organism identification. Serogroups were determined by slide agglutination with polyclonal antisera to serogroups A, B, C, Y, W135 and Z. The first isolate was found to be serogroup W135 and in the second isolate was untypeable. The isolates were tested negative for beta-lactamases by the nitrocefin disc test.

The susceptibility of *N. meningitidis* isolates to penicillin in invasive cases is routinely tested in our laboratory. Oxacillin disc was used to screen for susceptibility to penicillin by the Kirby-Bauer method and the NCCLS[2] zone interpretive criteria for *Streptococcus pnuemoniae* was used as a presumptive susceptible breakpoints. The two strains were found to be resistant to penicillin. Both the strains were subsequently submitted to the Institute for Medical Research for MIC determination where NCCLS reference agar dilution method was used. The MICs of *N. meningitidis* group W135 and the untypeable strain were 0.125 mg/l and 0.5 mg/l respectively. These

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values were considered to have decreased susceptibility to penicillin (MIC ≥0.12 mg/l) using *S. pneumoniae* breakpoint for meningitis.

Discussion

The current NCCLS guideline does not advocate testing of *N. meningitidis* isolates by the disc diffusion method and there is no interpretive criteria for *N. meningitidis* by this method. The susceptibility of *N. meningitidis* to penicillin is best detected by MIC determination with the agar dilution or broth microdilution methods and NCCLS breakpoints for *S. pneumoniae* is used as its presumptive susceptible breakpoints. The methods are rather laborious and hence clinical microbiology laboratories in Malaysia do not embark on such procedures. The use of E-test which is less laborious has been described in determination of MIC in *N. meningitidis*[3]. Apart from its cost, for some laboratories, the E test will be a practical method to determine the antimicrobial susceptibility of *N. meningitidis*. Other parts of the world have been observing the existence of *N. meningitidis* moderately susceptible to penicillin. In Canada, accumulated data between 1997-2000 showed a rising trend of these isolates as high as 34.6%[4]. Spain is another country where these moderately susceptible strains have become more frequent. The incidence of these strains increased from 0.4% to 43% in 5 years[5].

Relative resistance to penicillin is due to a reduced affinity of penicillin-binding protein 2. Although the clinical significance is uncertain, clinicians should be alerted to the possibility of their occurrence. Third generation cephalopsporins i.e. cefotaxime and ceftriaxone will be an effective alternative to high doses of penicillin in the treatment of *Neisseria meningitidis* with moderate susceptibility to penicillin. The increase in levels of MIC of meningococcal to penicillin certainly is a cause of concern. Although, meningococcal disease in Malaysia is of low endemicity but the infections that result from it remain a serious health problem. The finding of the two meningococcal isolates with reduced susceptibility to penicillin in our case, raised the possibility that such strains are already occurring in our environment. This definitely warrants a surveillance study not only looking at the incidence but the sero/subtypes distribution as well. It is timely that such a study is underway in the Institute for Medical Research and it is hoped that the outcome will shed some light to the incidence in Malaysia.

References

1. Vázquez JA. The resistance of *Neisseria meningitidis* to antimicrobial agents: an issue still in evolutuion. Reviews in Med Microbiol 2001; 12(1): 39-45.
2. National Committee for Clinical Laboratory Standard (NCCLS) MIC Testing: NCCLS (M7) 2003.
3. Pérez-Trallero E, Gomez N, Garc_a-Arenzana JM: E-test as susceptibility test for evaluation of *Neisseria meningitidis* isolates. J Clin Microbiol 1994; 32: 2341-342.
4. Brown S, Riley G, Jamieson F. *Neisseria meningitidis* with decreased susceptibility to Penicillin in Ontario, Canada 1997-2000. Canada Communicable Disease Report 2001; 27: 9.
5. Sáez-Nieto JA, Lujan R, Berrón S. Epidemiology and molecular basis of penicillin resistant *Neisseria meningitidis* in Spain: A five year history (1985-1989). Clin Infect Dis 1992; 14: 394-402