In vitro effect of deferoxamine on the efficiency of metronidazole against Capnocytophaga spp.

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Introduction

For successful proliferation in multicellular organisms, microbial pathogens must possess ability to acquire growth-essential iron from their hosts. Deferoxamine (DFO), a FDA-approved iron chelator, has been extensively used for parenteral chelation therapy in iron-overloaded states, especially during thalassemia. Capnocytophaga spp. are normal anaerobic inhabitants of the oropharyngeal flora, but may be involved in periodontal and systemic diseases.¹²

Metronidazole, a 5-nitroimidazole, has been regarded as an important therapeutic agent in the treatment of anaerobic and capnophilic infections. Recent data show an emergence of resistance in oral bacteria against antimicrobial agents, including metronidazole.³

The aim of this study was to investigate whether the exposure to the iron chelator DFO may increase susceptibility of Capnocytophaga spp. to metronidazole.

Materials and Methods

Three metronidazole resistant Capnocytophaga isolates (C. sputigena, C. gingivalis and C. leadbetteri) with MICs > 128mg L⁻¹ were selected. Capnocytophaga spp. isolates (OD₆₀₀=0.1) were primary incubated in presence of serial dilutions of DFO (0–0.24 mM) in brain heart infusion broth enriched with yeast extract (0.5%), hemin (5 μg mL⁻¹) and vitamin K₁ (1 μg mL⁻¹) (BH16).

Cells viability was determined by OD₆₀₀nm measurement in anaerobic conditions at 37°C after 24h. Threefold serial dilutions of metronidazole (128, 256, 512 mg L⁻¹) were prepared in BH16, with or without 0.24mM DFO.

Capnocytophaga isolates inoculated (10⁷ cells mL⁻¹) into the media were enumerated after 24h in anaerobic condition at 37°C.

Three metronidazole resistant Capnocytophaga strains (C. sputigena, C. gingivalis and C. leadbetteri) with MICs > 128mg L⁻¹ were studied. Experiments were performed in triplicate.

Results

The three metronidazole resistant clinical isolates of Capnocytophaga were all able to grow in BH16 supplemented with 0.24 mM DFO.

The effects of 0.24mM DFO on the metronidazole efficiency was evaluated on these strains. Antibacterial properties of three concentrations of metronidazole tested (128, 256, 512 mg L⁻¹) against Capnocytophaga increased in the presence of DFO, as shown by survival curves in absence and presence of DFO.

Cell number of Capnocytophaga spp. exposed to metronidazole (128, 256 and 512 mgL⁻¹) for 24h, in the presence or absence of DFO (0.24mM).

Conclusions

Our data showed that the iron chelator DFO increased the susceptibility of metronidazole resistant Capnocytophaga strains to metronidazole. This suggests that therapeutics decreasing iron concentration in oral fluids could be used as adjuvant treatment during periodontal disease.

Further investigations are required to better understand the mechanisms of action of DFO and other iron chelators on microbiota.

References


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