METRONIDAZOLE AND ACNE

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Abstract. The strong activity of metronidazole against obligate anaerobes suggested that the organism Propionobacterium acnes and the disease acne vulgaris might respond to treatment with this drug. Thirty-three clinical isolates of P. acnes were tested and found to be highly resistant to metronidazole. Prospects for its successful use in acne are remote.

Key words: Metronidazole; Acne

Metronidazole (Flagyl, Poulenc Ltd.) is best known for its anti-trichomonad activity but its effectiveness in the anaerobic infection Vincent's angina was noted by Shin (7) as long ago as 1962. Its potential usefulness against other obligate anaerobic bacteria was not fully realised at that time. Interest in metronidazole in this regard was reawakened by recent findings of its powerful activity against a wide variety of anaerobic organisms (4, 5, 9).

Propionobacterium acnes is fundamentally implicated in the pathogenesis of acne vulgaris (2, 3). This organism is an obligate anaerobe and might be expected to respond to metronidazole if it were sensitive. The sensitivity of 33 strains of P. acnes to metronidazole is reported.

MATERIALS AND METHODS

Strains

Twenty-four clinical isolates of P. acnes were derived from blood cultures in which they represented skin contaminants. A further seven strains (origin unspecified) were obtained from the Ontario Central Public Health Laboratory. The remaining two strains were isolated from skin swabs and an intravenous solution respectively. All strains were Gram-positive bacilli, obligate anaerobes, catalase-positive and indole-positive (P. acnes group I).

Sensitivity tests

The agar dilution method using the Steers (8) replicator was used. Susceptibility to metronidazole was determined on brain-heart infusion agar enriched with 5% horse blood. Duplicate serial dilutions of metronidazole solution were added. The solution was prepared by dissolving 0.1 g of metronidazole powder in 5 ml methanol, adding 5 ml 0.02 M phosphate-buffered saline to give a concentration of 10000 µg/ml, dispensing in 2.0 ml aliquots and storing at ~70°C. Working standards from 5.0 to 100 µg/ml were prepared by further dilution in 0.02 M phosphate-buffered saline. A 48-hour subculture of the P. acnes in cooked meat medium was adjusted to an optical density of 85 at 620 nm (corresponding to a count of 1.75x10^8 cfu/ml) on a Spectronic 20 spectrometer (Bausch & Lomb). Inocula of 7x10^6 cfu were delivered with a Steers replicator. Control plates without antibiotic and a control organism, Bacteroides fragilis of known sensitivity, were included in each test series. Plates were incubated at 37°C for 48 hours in anaerobic jars after air had been evacuated and replaced with a gas mixture containing approximately 95% N2 and 5% CO2. The MIC was determined as the lowest concentration of metronidazole permitting no visible growth.

RESULTS

All thirty-three strains of P. acnes were highly resistant to metronidazole (>100 µg/ml) at levels well beyond the therapeutic range of 10-20 µg/ml. The control strain of B. fragilis was sensitive to <5 µg/ml.

DISCUSSION

With the discovery that many obligate anaerobes are highly sensitive to metronidazole the potential activity of this drug against P. acnes, the possible aetiological anaerobe in acne, was greeted with welcome anticipation. Metronidazole possessed other attributes which suggested its usefulness in acne.
vulgaris. It is given by mouth. It is safe, non-toxic and virtually without side effects (10). Its serum half-life is around 8.7 hours and it is not protein-bound (6). Yet these pharmacologic qualities cannot be taken advantage of, for the work described here confirms the recent observation by Chow et al. (1) of metronidazole resistance in *P. acnes* and makes the prospects for the successful use of this drug in acne remote.

REFERENCES


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