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## ORIGINAL ARTICLE

# Papulopustular Rosacea: Response to Treatment with Oral Azithromycin<sup>☆</sup>

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### KEYWORDS

Papulopustular  
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### Abstract

**Introduction:** Oral tetracyclines and topical antibiotics have been used to treat papulopustular rosacea (PPR) for years, but it is not uncommon to find patients who do not respond to this standard treatment. In such refractory cases, oral azithromycin has proven to be an effective option.

**Material and method:** We conducted a prospective pilot study of 16 patients with PPR who were treated with oral azithromycin after a lack of response to oral doxycycline and metronidazole gel. At the first visit, the patients were assessed for baseline severity of PPR on a 4-point clinical scale and started on oral azithromycin. At the second visit, response to treatment in terms of improvement from baseline was evaluated on a 3-point scale. Patients were then scheduled for follow-up visits every 12 weeks to assess long-term effectiveness.

**Results:** All 16 patients experienced an improvement in their PPR following treatment with oral azithromycin. Eight weeks after completion of treatment, 14 patients (87.5%) showed complete or almost complete recovery (slight or no residual redness and complete clearance of papules and pustules). Only 2 patients experienced a new episode of inflammatory PPR lesions during follow-up.

**Conclusions:** The findings of this pilot study suggest that oral azithromycin could be a very effective short-term and long-term treatment for PPR resistant to conventional treatment.

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**PALABRAS CLAVE**

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papulopustulosa;  
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Tratamiento

**Rosácea papulopustulosa: respuesta al tratamiento con azitromicina oral****Resumen**

**Introducción:** El tratamiento de la rosácea papulopustulosa (RPP) ha consistido durante años en el uso de tetraciclinas orales y antibióticos tópicos. Pero no es infrecuente encontrar casos de RPP resistentes al tratamiento convencional. Azitromicina oral ha demostrado ser una opción eficaz para estos pacientes no respondedores.

**Material y método:** Se realizó un estudio piloto prospectivo con 16 pacientes con RPP no respondedores al tratamiento convencional (doxiciclina oral y metronidazol gel) que recibieron tratamiento con azitromicina oral. En la visita inicial (visita 1) se realizó una valoración basal del estadio clínico de la RPP, según 4 niveles de gravedad progresiva, y se inició tratamiento con azitromicina oral. A las 8 semanas de finalizar el tratamiento (visita 2) se evaluó la respuesta clínica según 3 niveles de mejoría respecto al estadio clínico basal. Posteriormente, para evaluar la eficacia de azitromicina oral a largo plazo, se realizaron visitas periódicas cada 12 semanas. **Resultados:** Todos los pacientes que recibieron tratamiento con azitromicina oral mejoraron de su RPP. A las 8 semanas de finalizar el tratamiento se objetivó un eritema facial residual débil o nulo, con desaparición completa de las pápulas y/o pústulas en el 87,5% de los pacientes. En cuanto al mantenimiento de la eficacia a largo plazo, únicamente 2 pacientes presentaron una recidiva de lesiones inflamatorias de RPP.

**Conclusiones:** Los resultados de nuestro estudio evidencian que azitromicina oral podría ser un fármaco de gran eficacia a corto y largo plazo para el manejo de aquellos casos de RPP resistentes al tratamiento convencional.

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**Introduction**

Papulopustular rosacea (PPR) is a chronic inflammatory disease characterized by facial erythema with papules and/or pustules located preferentially on the face.

Traditionally, it has been treated with oral tetracyclines (mainly doxycycline) and topical antibiotics, such as metronidazole.<sup>1</sup> An increasing number of treatments have become available in recent years, including oral isotretinoin<sup>2</sup> and anti-parasite drugs such as ivermectin, which can be administered topically<sup>3</sup> or orally.<sup>4</sup> In clinical practice, however, there are an appreciable number of challenging cases that do not respond to these conventional treatments. Azithromycin, a macrolide antibiotic, has been shown to a safe, effective treatment for PPR.<sup>5</sup> We designed a study to evaluate the use of azithromycin to treat PPR that failed to respond to conventional treatment at our hospital.<sup>6</sup>

**Material and Methods****Design**

We conducted a prospective pilot study of 16 patients with PPR between March 2016 and September 2017.

**Inclusion and Exclusion Criteria**

We included patients with PPR who had received conventional treatment with doxycycline 100 mg tablets every 24 hours and metronidazole 0.75% topical gel every 24 hours for 84 days and who had 1) experienced clinical deterioration (an increase in the number of inflammatory lesions) as a result of this treatment or 2) experienced early

recurrence (return of lesions within 8 weeks of treatment completion) despite a reduction in lesion number during treatment.

Patients with a known history of heart disease were excluded.

All the patients were informed in detail about oral azithromycin and alternative treatments and about the conditions of the study. Written consent was obtained in all cases. PPR was graded according to 4 levels of progressive clinical severity<sup>7</sup> (Table 1).

The patients were administered azithromycin 500 mg tablets for 12 weeks following the treatment regimen proposed by Bakar et al.<sup>8</sup>: 500 mg/d for 3 consecutive days a week for a month, followed by 250 mg/d (half a 500-mg tablet) for 3 consecutive days a week for another month, followed by 500 mg once a week for another month (total treatment duration: 12 weeks).

**Table 1** Clinical Stages of Papulopustular Rosacea<sup>a</sup>

Clinical Stage	Clinical Signs
I	Facial erythema with absence of papules and pustules
II	Facial erythema with 1–12 papules and/or pustules
III	Facial erythema with > 20 papules and/or pustules
IV	Facial erythema with papules and/or pustules and persistent solid edema (Morbihan disease)

<sup>a</sup> Adapted from Fernandez-Obregon.<sup>7</sup>

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