

# Área: Medicina Baseada em Evidências

# EFFICACY OF AZITHROMYCIN ON THE TREATMENT OF SYPHILIS

## Introduction

Syphilis is a chronic disease caused by *Treponema pallidum* infection, sexually transmitted, that can commit all tissues. Despite the effectiveness of its treatment, it remains a public health problem mainly because of the increased prevalence of HIV seropositive patients.

The recommended treatment for early syphilis is an intramuscular injection of 2.4 million units of penicillin G benzathine. This therapy is associated with low cost and also the inexistence of problems with adherence to treatment. Although, the injection is painful and nearly 10% of the population has allergic reactions to penicillin.

Azithromycin, a broad-spectrum macrolide antimicrobial, has been used as a therapy for sexually transmitted diseases like chlamydia, non-gonococcal urethritis and gonorrhea. The drug was effective on experimental studies and also in a series of patients with syphilis.

The objective of this review is to elucidate the efficacy of azithromycin compared with benzathine penicillin on the treatment of patients with syphilis.

#### **M**ETHODS

We searched the Medline database using the following strategy through Clinical Queries (Therapy/Narrow) interface: (syphilis) AND (azithromycin) AND (penicillin). The search was completed on July 7, 2010.

Only randomized controlled trials, published in English, Spanish or Portuguese, comparing azithromycin with benzathine penicillin in patients with syphilis (primary, secondary or early latent) were included in this review.

Data analysis was based on the principle of intention-to-treat, where the patients with or without the intervention, which were followed up during the study period, were considered as outcome. Efficacy data were analyzed using the method of the absolute risk difference, adopting a confidence interval of 95%.

#### RESULTS

We selected three clinical trials  $^{1-3}$  comparing azithromycin with benzathine penicillin, totaling 499 patients in the study group and 471 patients in the control group.

One study<sup>3</sup> examined two dosages of azithromycin (2g and 4g) whereas the other two used the dosage of 2g. Penicillin G benzathine was administered at its conventional dose (2.4 million units) in all studies.

**Healing in three months:** Three studies have compared azithromycin with benzathine penicillin in the period of three months. One hundred and ninety-five patients in the study group and 190 patients in the control group didn't heal in this period. There was no statistically significant difference between groups (p=0.88,  $l^2$ =0%).

**Healing in six months:** Three studies have compared azithromycin with benzathine penicillin in a follow-up of six months. One hundred and fifty-six patients in the study group and 165 patients in the control group didn´t heal in this period. There was no statistically significant difference between groups (p=0.39,  $l^2=44\%$ ).

**Healing in nine months:** Two studies<sup>2,3</sup> have compared azithromycin with benzathine penicillin in a follow-up of nine months. Thirty two patients in the study group and 44 in the control group had no cure in this period. Azithromycin has increased the chance of cure in 8% (95%CI 0,01 to 0,15; p=0.02 and  $I^2$ =21%) when compared with benzathine penicillin, needing to treat 13 patients to obtain this benefit. (*Figure 1*)

Figure 1 - Meta-analysis comparing the absence of healing rates in a nine months follow-up between azithromycin and benzathine penicillin in patients with syphilis

Study	Azithromycin Pe			enicilin		Risk Difference	Risk Difference	
	Events	Total 1	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI	
Hook*	7	21	12	21	10.0%	-0.24 [-0.53, 0.05]		
Hook**	13	32	12	21	12.1%	-0.17 [-0.44, 0.11]		
Riedner	12	163	20	165	78.0%	-0.05 [-0.11, 0.02]	=	
Total (95% CI)		216		207	100.0%	-0.08 [-0.15, -0.01]	•	
Total events	32		44					
<b>Heterogeneity:</b> $Chi^2 = 2.52$ , $df = 2$ ( $P = 0.28$ ); $I^2 = 21\%$							05 025 0 025 05	
Test for overall ef	fect: Z = 2	.38 (P =	0.02)				-0.5 -0.25 0 0.25 0.5	

\*azithromicyn 2g \*\*azithromicyn 4g

### Conclusion

This review showed clearly that a single dose of azithromycin, orally, is as effective as the 2.4 million units of benzathine penicillin for treating syphilis. This fact as well as bacterial resistance to macrolides and to penicillin should be considered on the treatment of syphilis.

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