

# Review: Twice-daily dosing of penicillin V is as effective as more frequent dosing for streptococcal tonsillopharyngitis

Lan AJ, Colford JM Jr. The impact of dosing frequency on the efficacy of 10-day penicillin or amoxicillin therapy for streptococcal tonsillopharyngitis: a meta-analysis. *Pediatrics*. 2000 Feb;105:E19.

## QUESTION

In patients with acute group A  $\beta$ -hemolytic streptococcal (GABHS) tonsillopharyngitis, is once- or twice-daily dosing of penicillin or amoxicillin less effective than dosing 3 (TID) or 4 (QID) times daily?

## DATA SOURCES

Studies were identified by searching MEDLINE and Dissertation Abstracts (to August 1998), abstracts of the annual Interscience Conference on Antimicrobial Agents and Chemotherapy (1983 to 1997), and bibliographies of relevant articles.

## STUDY SELECTION

Studies were selected if they were randomized controlled trials (RCTs) that compared different dosing frequencies of 10-day oral penicillin or amoxicillin while keeping the same total daily dose, based the diagnosis of acute GABHS tonsillopharyngitis on symptoms and positive throat culture results or positive antigen detection test results, and began antibiotic treatment at the time of diagnosis.

## DATA EXTRACTION

Reviewers assessed the quality of study methods (maximum weighted score 12) and extracted data on patient age, antibiotic regimens, number of patients in

each group, number of patients cured, and the cure rates (negative cultures).

## MAIN RESULTS

6 RCTs were included in the meta-analysis. Patients' ages ranged from 1 to 56 years in 5 RCTs. Quality scores ranged from 1 to 9 (mean score 4.8). 5 RCTs compared different dosing frequencies of penicillin V; 1 RCT compared penicillin V, TID or QID, with once-daily amoxicillin. Cure rates did not differ according to dosing frequency (Table). Heterogeneity existed among trials that compared more frequent dosing with once-daily dosing ( $P = 0.014$ ). When the study involving amoxicillin was excluded, heterogeneity was no longer statistically sig-

nificant, and once-daily doses led to a lower cure rate than did doses given 3 or 4 times daily ( $P = 0.006$ )\* (Table).

## CONCLUSION

In patients with acute group A  $\beta$ -hemolytic streptococcal tonsillopharyngitis, penicillin given twice daily leads to cure rates similar to those with doses given 3 or 4 times daily.

*Source of funding:* No external funding.

*For correspondence:* Dr. J.M. Colford, Jr., University of California, Berkeley, Department of Public Health Biology and Epidemiology, 113 Haviland Hall 7360, Berkeley, CA 94720-7360, USA. FAX 510-643-5163. ■

\* $P$  value calculated from data in article.

## Different dosing frequencies of 10-day penicillin or amoxicillin for acute group A $\beta$ -hemolytic streptococcal tonsillopharyngitis†

Comparisons	Number of RCTs	Weighted cure rates	RBR (95% CI)	NNH
Twice/d vs 3 or 4 times/d	4	84% vs 85%	2% (-5 to 8)	Not significant
Once/d vs 3 or 4 times/d	3‡	85% vs 92%	8% (-7 to 20)	Not significant
Once/d vs 3 or 4 times/d (excluding the amoxicillin study)	2§	79% vs 91%	14% (4 to 23)	9 (5 to 31)

†RBR = relative benefit reduction; RCTs = randomized controlled trials. Other abbreviations defined in Glossary; RBR, NNH, and CI calculated from data in article.

‡Heterogeneity is statistically significant.

§Study involving amoxicillin was excluded.

## COMMENTARY

The relevance of the meta-analysis by Lan and colleagues is strongly predicated on how and where one practices medicine. If you have ready access to adequate facilities for culture of throat swabs or antigen detection tests, or both, and are dealing with patients at risk for complications of streptococcal infection that warrant treatment with antibiotics, you will want to know whether less frequent dosing with penicillin will still effect a "cure." The answer to this question is important because of the evidence that suggests that adherence to once- or twice-daily dosing schedules is substantially better than more frequent schedules (1). On the basis of this meta-analysis of few methodologically adequate studies that addressed the relevant question, it seems that the answer is "no" for once-daily regimens and probably "yes" for twice-daily regimens. The use of amoxicillin in 1 trial is a red herring because the study does not contribute much to the overall conclusion. Penicillin remains the

drug of choice for streptococcal throat infection. However, the value of testing for and treating streptococcal throat infections is seriously questioned, particularly in the United Kingdom (2). Some U.K. clinicians argue that the available tests, including throat swabs, are expensive, impractical, and inadequate for improving diagnostic accuracy and that the benefits of antibiotics in low-risk patients do not outweigh the costs and risks.

Colin Bradley, MD  
University College Cork, Distillery House  
North Mall, Cork, Ireland

## References

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