Review: Oral and intravenous antibiotics do not differ for effectiveness in febrile neutropenic patients with cancer

Vidal L, Paul M, Ben-Dor I, et al. **Oral versus intravenous antibiotic treatment for febrile neutropenia in cancer patients.** Cochrane Database Syst Rev. 2004;(4):CD003992.

QUESTION

In febrile neutropenic patients with cancer, what is the comparative safety and effectiveness of oral and intravenous (IV) antibiotics?

METHODS

Data sources: Studies were identified by searching MEDLINE (1966 to 2002), EMBASE/Excerpta Medica (January 1980 to 2002), the Cochrane Cancer Network Register of trials (November 2002), the Cochrane Library (Issue 2, 2002), LILACS (1982 to 2002), several databases of ongoing trials, and conference proceedings; scanning bibliographies of relevant studies; and contacting experts and pharmaceutical companies.

Study selection and assessment: Randomized controlled trials (RCTs) that compared any oral antibiotic (given as a single drug or in combinations of oral antibiotics) with any IV antibiotic (given as monotherapy or combination therapy) in patients with cancer and chemotherapy-induced neutropenia or patients with cancer who had bone marrow transplantation and presented with fever. The oral antibiotics could be started after allocation ("initial oral") or after an initial course of IV antibiotics ("sequential IV to oral"). Assessment of study quality included allocation concealment, randomization method, blinding, and intention-to-treat analysis.

OUTCOMES

Mortality from any cause or mortality caused by the infectious episode at 30-day follow-up, treatment failure, and adverse events.

MAIN RESULTS

15 RCTs (n = 2511, age range 9 mo to 85 y) were included. IV antibiotics were compared with "initial oral" antibiotics in 10 RCTs and with "sequential IV to oral" antibiotics in 5 RCTs. In most trials, the antibiotics given orally (quinolones alone in 6 RCTs; quinolones combined with ampicillin-clavulanate, ampicillin-sulbactam, or penicillin V in 6 RCTS; and quinolone combined with clindamycin in 1 RCT) were different from those given intravenously.

Oral and IV antibiotics did not differ for mortality from any cause or mortality caused by the infectious episode, or for treatment failure or adverse events (Table).

CONCLUSION

In febrile neutropenic patients with cancer, oral and intravenous antibiotics do not differ for mortality, treatment failure, or adverse events.

Source of funding: No external funding.

For correspondence: Dr. L. Vidal, Rabin Medical Center, Petah Tikva, Israel. E-mail vidall@clalit.org.il.

Oral vs intravenous (IV) antibiotics in febrile neutropenic patients with cancer at 30 days*

Outcomes	Number of studies (n)	Weighted event rates		RRR (95% CI)	NNT
		Oral	IV		
Mortality from any cause or mortality caused by the infectious episode†	7 (1223)	3.6%	3.6%	9% (–62 to 49)	Not significant
Treatment failure†	15 (2511)	28%	30%	6% (–5 to 16)	Not significant
				RRI (CI)	NNH
Adverse events‡	11 (1536)	2.9%	1.9%	79% (–49 to 529)	Not significant

*Abbreviations defined in Glossary; weighted event rates, RRR, RRI, NNT, NNH, and CI calculated from data in article.

†A fixed-effects model was used.

‡A random-effects model was used.

COMMENTARY

Patients with neutropenic fever represent a heterogeneous group. The meta-analysis by Vidal and colleagues confirms that oral antibiotics are safe and effective compared with IV antibiotics in low-risk patients.

A limitation of this meta-analysis is the lack of consistent inclusion and exclusion criteria among the trials. There was marked heterogeneity in age groups, type of cancer, and presence or absence of soft tissue infections. It is therefore important to define "low risk." An international collaboration recently published a risk index score with a predictive value of 91% for identifying low-risk patients (1). This will be useful for improving management of these patients.

Based on the results of this meta-analysis, adult patients who develop neutropenic fever should be evaluated for symptoms and blood cultures should be taken. In otherwise-healthy patients considered to be low risk (1, 2), initial oral management with a fluoroquinolone combined with an amoxicillin-clavulinic acid formulation is reasonable. This review did not directly evaluate home therapy; further evidence is needed to assess the safety and efficacy of outpatient therapy specifically for low-risk patients with febrile neutropenia.

Jeanna Welborn, MD
University of California at Davis
Sacramento, California, USA

References

1. **Klastersky J, Paesmans M, Rubenstein EB, et al.** The Multinational Association for Supportive Care in Cancer risk index: A multinational scoring system for identifying low-risk febrile neutropenic cancer patients. J Clin Oncol. 2000;18:3038-51.
2. **Talcott JA, Siegel RD, Finberg R, Goldman L.** Risk assessment in cancer patients with fever and neutropenia: a prospective, two-center validation of a prediction rule. J Clin Oncol. 1992;10:316-22.