Evaluation of Fluoroquinolone Prophylaxis in Preventing Bacterial Infection in Neutropenic Afebrile Patients Without Leukemias or HSCT: A Systematic Review

THE DARTMOUTH INSTITUTE FOR HEALTH POLICY & CLINICAL PRACTICE

Mona T. Yazdi DO[1,2]; Divya Avula, MPH[2], Erica Gotow, MD,[1,2] Natalie B. Riblet, MD[1,2]

Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire[1]
The Dartmouth Institute for Health Policy and Clinical Practice[2]

Dartmouth Health

BACKGROUND

Per 2010 Infectious Diseases Society of America (IDSA) Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer, routine use of fluoroquinolone chemoprophylaxis in low-risk populations (defined as those with solid tumors or lymphoma undergoing chemotherapy) is not recommended to prevent fevers in neutropenic patients as it was not found to impact all-cause mortality. Our primary objective was to determine if there has been new substantial evidence on the utility of antibiotic prophylaxis for neutropenic patients admitted to the hospital who are afebrile without leukemia or hematopoietic stem cell transplants (HSCT).

OBJECTIVE

Our objective was to assess the effects of fluoroquinolones vs placebo in prevention of probable or confirmed bacterial infection in neutropenic patients with cancer who did not have leukemias or HSCT. Secondary outcomes of interest included febrile episodes, mortality, and adverse effects of antibiotic use.

METHODS

Search methods:
We searched Medline via PubMed, The Cochrane Central Register of Controlled Trials, and SCOPUS from inception through 2/17/2022 for published articles in English.

Selection criteria:
Randomized control trials comparing fluoroquinolones to placebo in preventing neutropenic fever and bacterial infections in patients over the age of 18 with cancer who did not have leukemias or HSCT.

Data collection and analysis:
Three reviewers individually reviewed articles and manually collected data. Each article was reviewed by at least two reviewers with any disputes resolved by a third reviewer. Quality assessment and assessment for risk of bias using Cochrane Risk of Bias 2.0 Tool was also conducted by at least two reviewers for each article. We used a random effects model to calculate summary odds ratios (OR) with 95% confidence intervals (CI), and p-values.

FIGURES

Figure 1: Study Selection Diagram

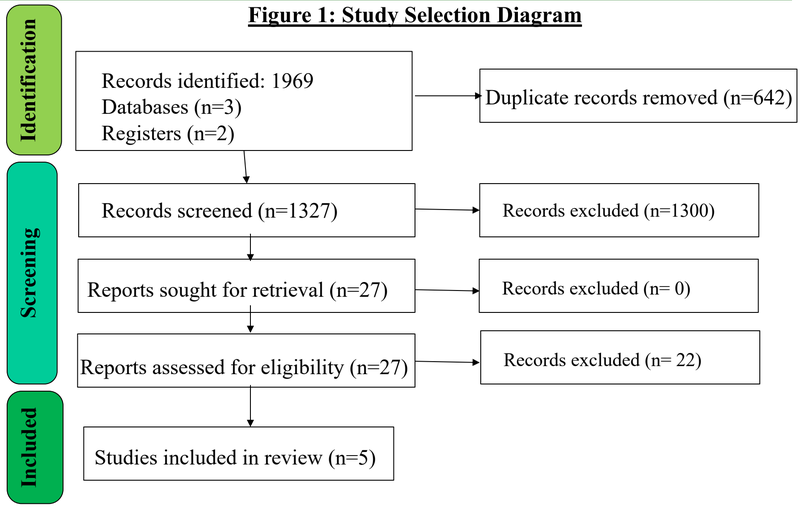


Figure 2: Forest Plot of Probable or Proven Infection in Included Studies

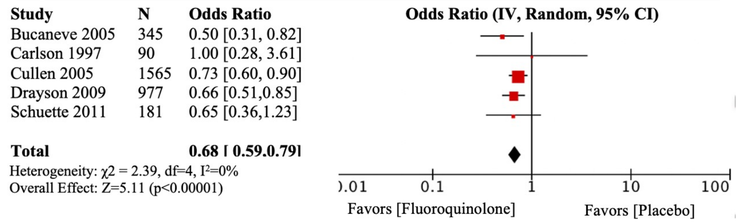


Figure 3: Forest Plot of Fevers in Included Studies

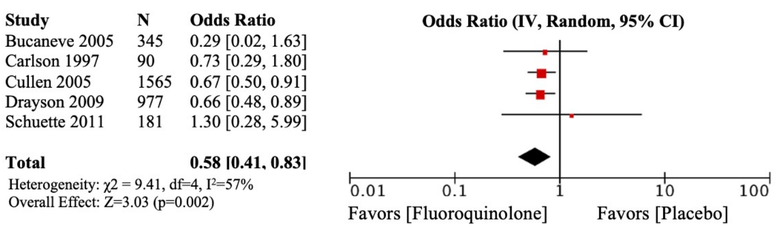
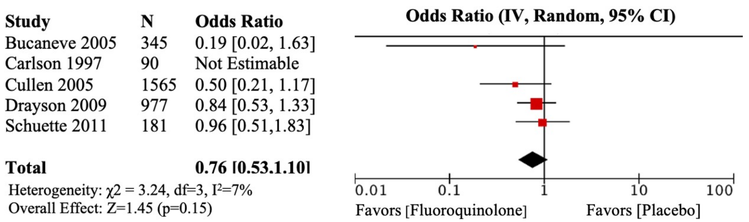


Figure 4: Forest Plot of Mortality in Included Studies



RESULTS

We analyzed 5 randomized control trials from 1991-2022 with a total of 3158 participants. Rates of probable or confirmed bacterial infection revealed 541/1562 (34.6%) infections in the fluoroquinolone group and 679/1560 (43.5%) in the placebo group (OR: 0.68, 95% CI: 0.59,0.79, $I^2 = 0\%$, $p<0.001$). Febrile episodes, 300/1566 (19.2%) were noted in the fluoroquinolone group and 407/1555 (26.2%) in the placebo group (OR: 0.58, 95% CI:0.41,0.83, $I^2 = 57\%$, $p=0.002$). Mortality of 113/1597 (7.1%) was noted in the fluoroquinolone group and 124/1508 (8.2%) in the placebo group, with odds ratio of 0.76 (95% CI:0.53,1.1, $I^2 = 7\%$, $p=0.15$). Most of the studies had a low risk of bias. Few were noted to have some concerns of bias due to trial registry information not being available for in-depth review. There were also some concerns for bias across studies about how "probable" infection and "febrile episodes" were defined. Antibiotic associated adverse events were more frequent in the fluoroquinolone groups and included neutropenia, leukopenia, diarrhea, dyspnea, vomiting, tendonitis, and more. Size of effect and certainty of evidence for outcomes was evaluated using GRADE methodology with each study found to have high quality methodology and summary statistics.

CONCLUSION

Our results were similar to previous findings and no significant additional evidence in the form of RCTs have changed these outcomes since the 2010 IDSA guidelines were published. Although evidence does not show that fluoroquinolone prophylaxis provides a statistically significant mortality benefit, it did show a statistically significant decrease in bacterial infections and febrile episodes. This may still provide clinical benefit to this population of patients, but must be weighed against the risks and consequences of long-term antibiotic use, which were not evaluated in these studies.

REFERENCES

Freifeld AG, Bow EJ, Sepkowitz KA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the infectious diseases society of america. Clin Infect Dis. 2011;52(4):e56-e93. doi:10.1093/cid/cir07

Schuette W, Nagel S, von Weikersthal LF, et al. Randomized phase III trial of docetaxel plus carboplatin with or without levofloxacin prophylaxis in elderly patients with advanced non-small cell lung cancer: the APRONTA trial. J Thorac Oncol. 2011;6(12):2090-2096. doi:10.1097/JTO.0b013e3182307e3c

Drayson MT, Bowcock S, Planche T, et al. Levofloxacin prophylaxis in patients with newly diagnosed myeloma (TEAMM): a multicentre, double-blind, placebo-controlled, randomised, phase 3 trial. The Lancet Oncology. 2019;20(12):1760-1772. doi:10.1016/S1470-2045(19)30506-6

Bucaneve G, Micozzi A, Menichetti F, et al. Levofloxacin to Prevent Bacterial Infection in Patients with Cancer and Neutropenia.. doi:10.1056/NEJMoa044097

Cullen M, Steven N, Billingham L, et al. Antibacterial prophylaxis after chemotherapy for solid tumors and lymphomas. N Engl J Med. 2005;353(10):988-998. doi:10.1056/NEJMoa050078

Carlson JW, Fowler JM, Mitchell SK, Carson LF, Mayer AR, Copeland LJ. Chemoprophylaxis with ciprofloxacin in ovarian cancer patients receiving paclitaxel: a randomized trial. Gynecol Oncol. 1997;65(2):325-329. doi:10.1006/gyno.1997.4630