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# Ciprofloxacin usage at a local hospital

SHORT REPORT

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**BACKGROUND**
The use of quinolones is subject to strict conditions, in part because of their known tendency to drive antimicrobial resistance. Use of quinolones in Norwegian hospitals increased dramatically from their launch in the 1980s to a peak in 2012. Since then, usage has decreased and had almost halved by 2019. However, little information is available on whether the use of quinolones in hospitals is in accordance with national guidelines.

**MATERIAL AND METHOD**
This study included inpatients over 12 years of age who were prescribed quinolones at a local hospital in the Central Norway Regional Health Authority in the period 1 September–31 December 2018. An expert group of infectious disease specialists evaluated the use of quinolones against the national guidelines for the use of antibiotics in hospitals.

**RESULTS**
The use of ciprofloxacin was considered to have been inconsistent with therapeutic recommendations in 45 out of 49 (92 %) inpatient stays in the medical, surgical and orthopaedic departments.

**INTERPRETATION**
In a local hospital, ciprofloxacin was used all too frequently for indications outside those recommended in the Norwegian guidelines.


## Main points

In 92 % of cases, the use of ciprofloxacin at a local hospital in Norway fell outside the therapeutic recommendations in the national guidelines for the use of antibiotics in hospitals.

Findings from diagnostic microbiology were not taken into account in 90 % of cases.

Fluoroquinolones have been available in Norway since the 1980s, with ciprofloxacin accounting for the greater part of usage. From 1999 to 2012, usage almost tripled. It then decreased thereafter and had almost halved by 2019 (1).

Fluoroquinolones are highly potent antibiotics which exert their bactericidal effect through inhibition of DNA gyrase and DNA topoisomerase IV (2). A range of pathogenic microbes are in principle sensitive to fluoroquinolones. However, the emergence of resistance has increased sharply and is running largely parallel to usage (3).

No other class of antibiotics has the same mechanism of action as the fluoroquinolones. The class is considered key to the treatment of certain specific and serious infections, and the use of fluoroquinolones is subject to strict conditions in hospitals and the primary healthcare service (4). Approved indications include certain intra-abdominal infections in cases of beta-lactam allergy, some urinary tract infections when preferred antibiotics have been shown to be ineffective, and other specific infections such as bone, joint and prosthetic joint infections, abscesses, and mycobacterial infections (as a supplement).

A Norwegian study from 2010 showed that in care homes, fluoroquinolones were often used for indications other than those listed in the national guidelines (5). The aim of the current study was to survey the use of fluoroquinolones at a local hospital in Norway and to evaluate the reasons given for their use contrary to national therapeutic recommendations.

## Material and method

The study was conducted at a local hospital with departments of internal medicine, general surgery and orthopaedics. The hospital had no antimicrobial stewardship measures in place prior to the study, and did not implement any such measures during the study.

In the period 1 September–31 December 2018, inpatients who received antimicrobial therapy with fluoroquinolones were identified upon arrival in the hospital departments and were prospectively evaluated for inclusion. The study was non-interventional: data collection did not influence the prescribing of antibiotics. Only the departmental managers for doctors and nurses were informed that general information was to be collected on antibiotic usage.

Patients' personal details, clinical status, and information on any relevant diagnostic tests and treatment were obtained by review of medical records. The antimicrobial therapy was then compared with the recommendations in the Norwegian national guidelines for the use of antibiotics in hospitals (4). Two independent specialists in infectious diseases at a university hospital then performed an equivalent analysis of the antimicrobial therapy, while blinded to the conclusions of the study group.

Simple descriptive statistics were used to describe the patients. The study was evaluated and approved by the Regional Committees for Medical and Health Research Ethics (reference no. 2018/1239), the research authorities, the Data Protection Officer and the local departmental management team in the health trust.

## Results

Fluoroquinolones were prescribed to 50 unique patients, of whom 49 met the study inclusion criteria. Of these, 51 % were men and the average age was 71 years (range 19–97 years). One patient was excluded owing to lack of information about treatment following transfer from another hospital.

The patients were distributed between the disciplines of internal medicine (74 %), surgery (22 %) and orthopaedics (4 %). Only ciprofloxacin was used during the study period.

The average duration of treatment with ciprofloxacin was 9 days (range 1–28 days), and the median was 8 days. Ciprofloxacin treatment was initiated prior to hospitalisation for 6 % of the patients, in acute admissions for 12 %, during the hospital stay for 71 %, and upon discharge for 10 %.

Antibiotic allergy was noted in the medical records of 10 of 49 patients (20 %).

Forty-four patients had an infection that required treatment with antibiotics, while 5 patients had either a probable viral infection or non-infectious inflammation (Table 1). The antibiotic guidelines advised use of ciprofloxacin for 2 patients (4 %), and antibiotics other than ciprofloxacin for 40 patients (82 %). In two patients, the guidelines did not provide a specific therapeutic recommendation for either the microbe or the condition, but treatment with ciprofloxacin nevertheless seemed appropriate. Overall, use of ciprofloxacin was unwarranted in 45 out of 49 patients (92 %).

**Table 1**

Clinical diagnosis, time of antibiotic initiation, justification, and duration of treatment with ciprofloxacin at a local hospital in the period 1 September–31 December 2018.

| Condition | Number of patients | Time of initiation | | | Reason for use documented | Treatment duration in days (min–max) |
|---|---|---|---|---|---|---|
| | | Prior to admission | During hospital stay | Upon discharge | | |
| Urinary or genital tract infection1 | 18 | 0 | 16 | 2 | 0 | 4–28 |
| Respiratory tract infection2 | 11 | 2 | 9 | 0 | 0 | 1–28 |
| Focus of infection unknown3 | 10 | 0 | 7 | 3 | 0 | 2–16 |
| Abdominal infection4 | 6 | 1 | 5 | 0 | 0 | 1–18 |
| Prophylaxis | 4 | 0 | 4 | 0 | 0 | 1–9 |

| Condition | Number of patients | Time of initiation | | | Reason for use documented | Treatment duration in days (min–max) |
|---|---|---|---|---|---|---|
| | | Prior to admission | During hospital stay | Upon discharge | | |
| Total | 49 | 3 | 41 | 5 | 0 | 1–28 |

[1]Urinary tract infection, urosepsis, epididymitis

[2]Pneumonia, bronchitis, pulmonary abscess, otitis

[3]Unknown focus of infection, 'pneumonia or urinary tract infection'

[4]Gastroenteritis, Helicobacter pylori infection, abscess, cholecystitis, colitis

A total of 442 days of ciprofloxacin treatment were recorded, of which 17 % were intravenous and 83 % were oral. Only 19 % were considered to be in accordance with indications in the guidelines, whereas 356 daily doses were unwarranted.

Diagnostic microbiology was performed in 41 patients (84 %) at the time of admission. Growth of a relevant pathogenic microbe was detected in 21 out of 41 specimens (51 %). For 90 % of these, the results of resistance determination favoured the use of antibiotics other than ciprofloxacin. Antibiotics were adjusted based on the microbiological findings in one patient.

## Discussion

Compliance with the national guidelines for the use of antibiotics in hospitals (4) is key to safe and rational antimicrobial therapy. Our study revealed that the use of ciprofloxacin was unwarranted in 92 % of patients.

Resistance to ciprofloxacin is widespread among microbes (6). According to the Norwegian Surveillance System for Antimicrobial Drug Resistance (NORM), 11.7 % of blood culture isolates and 9.3 % of urinary isolates of *Escherichia coli* were resistant to ciprofloxacin in 2018, with the corresponding figures for *Klebsiella* species being 8.1 % and 6.3 % (3). Epidemiological data on microbial resistance are the cornerstone of empirical therapy recommendations.

Careful consideration of the results of microbiological testing should form the basis for antimicrobial therapy. In our study, we found that the results of microbiological testing were not taken into account in 90 % of cases. In a prospective multicentre study in France, the absence of a clear diagnosis and lack of microbiological sampling were identified as independent risk factors for inappropriate antibiotic use (7).

Up to 10 % of patients are reported to have an antibiotic allergy (8), in common with 20 % of the patients in our study. This has been shown to lead to increased prescribing of broad-spectrum antibiotics, with adverse consequences (9). The large number of patients reported to have antibiotic allergies is likely to have contributed to the prescription of ciprofloxacin in our study, but this was documented in only half of cases. A realistic estimate for the prevalence of true

IgE-mediated antibiotic allergy is probably less than 1 %. Testing for antibiotic allergy is an appropriate strategy for increasing the cure rate with penicillin treatment, and is an effective antimicrobial stewardship intervention (8).

Fluoroquinolones have long been monitored with respect to side effects (10). In October 2018, health authorities specified that fluoroquinolones should be reserved only for certain specific and serious infections on the basis of new information about irreversible and disabling side effects in the nervous and musculoskeletal systems, as well as the rupture of aortic aneurysms (11).

Taken together, the mechanism of action, side effects, resistance profile and ecological shadow of fluoroquinolones suggest the need for restrictive therapeutic recommendations. The use of ciprofloxacin has halved in Norwegian hospitals in recent years (1), but our study nevertheless indicates that more than 90 % of usage still falls outside the therapeutic recommendations.

Data from the Norwegian hospital pharmacies' drug statistics database ('SLS') show that in 2018, Norwegian health trusts used an average of 2.28 defined daily doses (DDD) of fluoroquinolones per 100 bed days (95 % confidence interval 2.05–2.51) (12). This may indicate that our findings have good generalisability.

## Conclusion

This study has confirmed that ciprofloxacin is very often used in a manner inconsistent with therapeutic recommendations. We conclude that there is a need for hospital departments to exercise greater restraint in the use of this important class of antibiotics.

*This article has been peer-reviewed.*

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