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Pharmacology applied to geriatric medicine

Pharmacoeconomic and clinical aspect of a sequential intravenous to oral therapy plan in an acute geriatric ward



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ARTICLE INFO

Article history:

Received 8 September 2015

Accepted 25 October 2015

Available online 21 November 2015

Keywords:

Antibiotics

Elderly

Fluoroquinolone

Sequential antibiotic therapy

ABSTRACT

Introduction: Sequential antibiotic therapy (SAT) is an important phase of treatment and an attempt to bring the change to oral treatment forward. We assessed the impact of SAT on the costs of antibiotic treatment on hospitalized elderly patients.

Methods: This was a prospective study in which 204 patients were assessed. Duration and costs of IV and oral treatment were recorded, as well as the day for switching from IV to oral treatment, mean stay and readmissions, and the results were confronted between the two phases of the study: observational and interventional. Mean antibiotic intake was defined as defined daily dose per every 100 stays (DDD/100S).

Results: Fifty-two were included in the observational phase and 59 in the interventional phase, mean age 80.0 ± 7.4 , 52.3% women. Changeover of treatment was brought forward an average of 1.7 and 1.3 days with ciprofloxacin and levofloxacin, respectively, during the intervention phase compared to the observational phase ($P < 0.001$). The mean cost per unit in the intervention phase was reduced by 28.64 € with levofloxacin and by 24.28 € with ciprofloxacin. Intravenous DDDs/100S were reduced from 0.069 ± 0.023 to 0.042 ± 0.006 ($P < 0.001$) for levofloxacin and from 0.068 ± 0.029 to 0.038 ± 0.012 ($P < 0.001$) for ciprofloxacin.

Conclusions: Pharmaceutical intervention based on a SAT achieved reduction of the length of treatment of antibiotic IV treatment and thus also achieved a reduction in treatment costs. The intervention was not associated to an increase in relapse and was therefore efficient and cost effective.

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1. Introduction

Efficient treatment of infections includes selection of the most appropriate medication and the adequate dose during enough time to eradicate the infection and minimize secondary effects and selection of resistant strains.

In addition, the channel for medication delivery is an important factor.

Sequential therapy is viewed as a method for more efficient use of antibiotics. Sequential therapy is defined as a changeover from the intravenous (IV) formulation to oral administration of the same medication, maintaining the same pharmacological strength [1,2].

IV administration of medication achieves immediate plasma levels and guarantees therapeutic compliance, which makes it useful in emergencies or in certain pathologies where, due to the type of microorganism, or location of the infection, it is necessary

to use this mode of delivery exclusively. Therefore in illnesses such as meningitis, endocarditis or sepsis the use of a sequential antibiotic therapy is counter-indicated (SAT) [3].

Keep in mind that swallowing problems and the size of the tablets can reduce the salary possibility to switch to oral administration, especially in geriatric populations.

However, in other circumstances (such as pneumonia, genitourinary infections, skin and soft tissue infections, gastrointestinal infections and febrile neutropenia) and depending on the evolution of the infection, SAT has been shown to be a cost-effective alternative [3,4].

The main inconveniences of IV are that it causes a considerable increase of both direct and indirect costs [4–9], reduces patient mobility, and increasing the risk of bed rest [10].

The principal advantages of oral administration are: that it is more comfortable and less aggressive for patients, it avoids the risk of phlebitis, it allows early mobilisation of hospitalized patients and, especially, that it is more economic in terms of direct costs of treatment (vials, solvents, galenic formulation) as well as indirect

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costs (vascular catheters, infusion systems, human resources, length of hospital stay) [11,12]. Furthermore, contrary to what might be thought, oral treatment is not less efficient than IV [13,14].

A complication of antibiotics in general, and fluoroquinolones in particular, is the increased risk of *Clostridium difficile* infections (CDIs) [15]. The bioavailability of fluoroquinolones not depends on the route of administration, and probably this is the reason why the risk of CDIs is the same between the oral or intravenous administration [16].

These facts mean that, as long as a patient's situation is appropriate and there is a therapeutic arsenal, which is efficient when orally administered, it is recommended that the administration route is changed as soon as possible [3,13].

The first step in order to carry out a correct SAT is training about the main aspects of this type of therapy [1,17]. After this, patients who are possible candidates for SAT must be properly selected and, finally, the treatment's effectiveness must be assessed.

Antimicrobial medication use optimization programmes are included as a quality and effectiveness criterion in therapeutic audits in order to optimize the use of antimicrobials and reduce the risk of selecting resistant strains through improper use [18].

The most appropriate antibiotics for sequential therapy should have a similar antimicrobial spectrum, be readily available in oral format and have a pharmacokinetics that allows administration every 12 or 24 hours, to make their administration easier and, especially, should have good tolerance (gastro-intestinal tolerance above all), a low potential for resistance selection and be relatively inexpensive [11,13]. One of the families of antibiotics that best fits these criteria is the fluoroquinolone group [13].

The main aim of this study is to assess the impact of pharmaceutical intervention on the costs of treatment via the implementation of sequential therapy with ciprofloxacin and levofloxacin in a geriatrics department.

2. Methods

Prospective study carried out at the Geriatrics Unit of the San Juan de Dios Hospital in León, Spain, which has 252 beds.

The study was carried out in two sequential phases of five months duration each. The first, observational, phase (Ph 1) took place between August and December 2010, during which time no intervention was carried out and contact was not established with the doctor and to select the control group. Later, there was a second, pharmaceutical intervention, phase (Ph 2) (January–May 2011) during which a sequential antimicrobial therapy programme using fluoroquinolones was implemented on all candidate patients, whilst informing the doctors in charge of these patients.

The study was approved by the Steering Committee and the Pharmacy Commission in agreement with the hospital Geriatrics Service and approved by the hospital Ethics Committee.

2.1. Patient selection

We prospectively included in the study all patients aged 65 or above in the Geriatrics Unit and who had been prescribed IV ciprofloxacin or levofloxacin, who had good oral tolerance, were haemodynamically stable and in whom a decrease in body temperature was observed.

Patients were selected from the unitary dose medication dispensation, with an assisted electronic prescription programme.

Patients receiving treatment with almagate, sucralfate, calcium or iron (due to a potential reduced absorption of fluoroquinolones), patients with nausea, vomiting, serious diarrhoea, a naso-gastric tube or intestinal motility alterations as well as patients with

sepsis, endocarditis, meningitis or with endovascular prosthesis infections were all excluded.

2.2. Pharmaceutical intervention programme

During phase 2, on the third day of IV treatment, the pharmacist (JdP), sent a note to the doctor with the electronic prescription system, advising him of the possibility of changing the administration route and stating the bioavailability of oral administration and the benefits of such a changeover. In the cases when the doctor continued to prescribe IV, the researchers spoke directly to him in order to inform him of the SAT programme.

2.3. Effectiveness variables used

The researchers used the following variables: number of days with IV and oral treatment, total duration of antibiotic treatment and of hospital stay, day of changeover from IV to oral, readmissions due to re-infection during the 30 days following discharge, diagnosis upon discharge in order to assess whether early readmission (within 30 days) could be considered a relapse due to infection. We also calculated the mean cost of antimicrobial treatment by group and by laboratory sale price (LSP) and mean antibiotic intake defined as Defined Daily Dose per 100 stays (DDD/100S). DDD/100S, is the assumed average maintenance dose per day for a drug used for its main indication in adults, established by the World Health Organization [19]. It is calculated with the following formula: $DDD/100S = (\text{annual intake in grams} \times DDD \text{ in grams}) / (100 \times \text{stays in a year})$. The defined daily dose (DDD) is the most widespread measurement for antibiotic intake in a hospital setting and allows comparisons to be drawn between hospitals in different countries.

2.4. Statistical analysis

A descriptive analysis of the studied variables was carried out by calculating averages and proportions. Values are expressed as numbers and percentages for the categorical values and as mean $\pm$ standard deviation for continuous variables with a normal distribution.

Variables that do not fulfil the normality assumption (Kolmogorov-Smirnov test) were non-parametrically analysed, so the averages were compared using the Mann-Whitney U test and proportions were compared using the chi-square test (χ^2).

Bilateral $P < 0.05$ values were considered significant. Statistical analysis was carried out using the Statistical Package for the Social Sciences (SPSS), version 15.0 (SPSS Inc., Chicago, IL).

3. Results

A total of 204 patients were assessed, of which 111 were recruited, 57 were treated with levofloxacin (27 in the observational phase and 30 in the intervention phase) and 54 with ciprofloxacin (25 in the observational phase and 29 in the intervention phase).

Of the 86 patients excluded during the observational phase, 56.9% were women, mean age 87.8, 42.1% were men aged 81.6 on average. The reasons for excluding these patients were: on adherence to treatment ($n = 31$), palliative care patients ($n = 10$), oral intolerance ($n = 25$), or because they presented haemodynamic instability ($n = 20$).

During the pharmaceutical intervention phase, 66 patients were considered to be candidates for SAT, 36 for ciprofloxacin and 30 for levofloxacin, of which a total of 59 interventions were accepted (89.4%): 30 for levofloxacin (100%) and 29 for ciprofloxacin (80.5%).

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