Antibiotic Consumption in the Department of Infectious and Tropical Diseases, Point G University Hospital, Bamako, 2020

Consommation d'antibiotiques au service des maladies infectieuses et tropicales du Centre Hospitalier Universitaire Point G, Bamako, 2020

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Abstract

Introduction: Global consumption of antibiotics increased by 65% between 2000 and 2015. This use has been boosted by an explosion in the use of antibiotics in low- and middle-income countries. The aim of this study is to assess the antibiotic consumption of patients hospitalised in the infectious and tropical diseases department in Mali. **Methods**: This is a prospective six-month study from 15 July to 31 December 2020 of patients who received antibiotics while hospitalised in the infectious and tropical diseases department of the Point G University Hospital. All hospitalised patients who received either probabilistic or targeted antibiotic therapy were included in this study. Antibiotic consumption was calculated using the ATC DDJ method. The adequacy between the germs subsequently isolated and the probabilistic antibiotic therapy was evaluated. **Results**: We included 130 patients out of 184 hospitalised in the department, representing a frequency of antibiotic use of 70.6%. The population studied had a sex ratio of 1 and an average age of 40.7±13.1 years. The main indication for probabilistic antibiotic therapy was sepsis secondary to pulmonary infection (34.6%), and the main indication for targeted antibiotic therapy was E. coli gastroenteritis and Mycobacterium tuberculosis pulmonary infection, each with a frequency of 25.5%. The most frequent bacteria isolated in the various pathological products were Escherichia coli, Klebsiella pneumoniae and Mycobacterium tuberculosis. The most commonly used antibiotics were cotrimoxazole with 944.8 DDD (i.e., 263.3 DDD/1000DH), followed by β-lactams with 140.5 DDD (i.e., 39.5 DDD/1000DH), then 5-nitroimidazoles with 131.5 DDD (i.e., 36.6 DDD/1000DH). Overall antibiotic consumption was 1417.8 DDD and 365.1 DDD/1000DH. **Conclusion**: This study is a first and a review of the situation with a view to improving the monitoring of antibiotic consumption and the frequency of bacterial resistance in the coming years.

Keywords: Antibiotics, consumption, defined daily dose (DDD), bacteria, infections

Résumé

Introduction : La consommation mondiale d'antibiotiques a augmenté de 65 % entre 2000 et 2015. Cette augmentation a été renforcée par l'explosion de la consommation d'antibiotiques dans les pays à revenu faible et intermédiaire. L'objectif de cette étude est d'évaluer la consommation d'antibiotiques chez les patients hospitalisés au service des maladies infectieuses et tropicales au Mali. **Méthodes :** Il s'agit d'une étude prospective de six mois, du 15 juillet au 31 décembre 2020, portant sur les patients ayant reçu des antibiotiques lors de leur hospitalisation au service des maladies infectieuses et tropicales du Centre Hospitalier Universitaire Point G. Tous les patients hospitalisés ayant reçu un traitement antibiotique probabiliste ou ciblé ont été inclus dans l'étude. La consommation d'antibiotiques a été calculée selon la méthode ATC-DDJ. L'adéquation entre les germes isolés ultérieurement et le traitement antibiotique probabiliste a été évaluée. **Résultats :** Nous avons inclus 130 patients sur 184 hospitalisés dans le service, soit une fréquence d'utilisation d'antibiotiques de 70,6 %. La population étudiée avait un sex-ratio de 1 et un âge moyen de 40,7 ± 13,1 ans. La principale indication du traitement antibiotique probabiliste était le sepsis secondaire à une infection pulmonaire (34,6 %), et la principale indication du traitement antibiotique ciblé était la gastro-entérite à *Escherichia coli* (25,5 %) et l'infection pulmonaire à *Mycobacterium tuberculosis*, (25,5 %). Les bactéries les plus fréquemment isolées dans les différents produits pathologiques étaient *Escherichia coli*, *Klebsiella pneumoniae* et *Mycobacterium tuberculosis*. Les antibiotiques les plus utilisés étaient le cotrimoxazole avec 944,8 DDJ (soit 263,3 DDJ/1000 JH), suivi des β-lactamines avec 140,5 DDJ (soit 39,5 DDJ/1000 JH), puis des 5-nitroimidazoles avec 131,5 DDJ (soit 36,6 DDJ/1000 JH). La consommation globale d'antibiotiques était de 1417,8 DDJ et 365,1 DDJ/1000 JH. **Conclusion :** Cette étude constitue une première évaluation et un état des lieux, dans le but d'améliorer le suivi de la consommation d'antibiotiques et la fréquence de la résistance bactérienne dans les années à venir.

Mots-clés : Antibiotiques, consommation, dose définie journalière (DDJ), bactéries, infections

INTRODUCTION

Antibiotic consumption remains a major concern worldwide because of its impact on antimicrobial resistance. It increased by 65% between 2000 and 2015. This increase is partly due to explosive use in middle- and low-income countries. This situation poses a threat to global health [1]. Several tools have been used to assess antibiotic consumption. The most widely used is the Defined Daily Dose (DDD). Antibiotic consumption in the European Union, estimated as a defined daily dose per 1000 hospital days, was 21.9 DDD/1000 hospital days for the city sector (reference). In Africa, we have not found any data on continental antibiotic consumption in defined daily doses. However, fragmentary studies have been carried out in certain countries such as Morocco, where antibiotic consumption increased from 9.68DDD/1000Hab/day in 2003 to 13.85DDD/1000Hab/day in 2012 [2]. In a study conducted at the Gabriel Touré University Hospital Center (CHU) in Bamako, based on 12,861 prescriptions recorded between January 1 and June 30, 2004, 6,000 prescriptions included antibiotics, corresponding to a prevalence rate of 46.7% [3]. The aim of this study was to evaluate antibiotic consumption in the infectious and tropical diseases department at Point G.

PATIENTS AND METHODS

A prospective and evaluative study was conducted over a six-month period, from July 1 to December 31, 2020, in the Department of Infectious and Tropical Diseases at Point G University Hospital. Patients who had used antibiotics during the study period and who had given their consent to participate were included in the study. The sociodemographic, clinical, paraclinical and therapeutic data from the survey were recorded from the patients' files on a pre-established form. The data were entered and analysed using SPSS 22.0 software. Antibiotic consumption was calculated in Defined Daily Doses (DDD) according to WHO standards.

$$DDD = \frac{\text{Number of boxes distributed} \times \text{Number of tablets per box} \times \text{Amount of active ingredient per tablet (in grams)}}{\text{WHO DDD (in grams)}}$$

This is the total number of hospital admissions, including day and week admissions. The day of admission and the day of discharge generally count as a single day of hospitalization, so the number of day-patients or number of patient-days is equal to all the days on which the patient is present minus one day [4,5].

RESULTATS

During the study period, we enrolled 130 patients out of 184 hospitalised in the department, representing a frequency of antibiotic use of 70.6%. Among our patients, 5 benefited from targeted antibiotic therapy. In the remaining cases, treatment was empirical, with therapeutic adjustments made in 47 patients after the results of the antibiotic susceptibility test became available. Treatment was probabilistic in (78/130), i.e., a frequency of 60%.

From a sociodemographic point of view, the population studied had a sex ratio of 1 and a mean age of 40±13.1 years (Table I).

Table I: Socio-demographic characteristics of patients hospitalised in the Infectious and Tropical Diseases Department of the Point G University Hospital who received antibiotic therapy

Feature	Workforce	Frequency (%)
Gender		
Male	65	50.0
Female	65	50.0
Age (mean ± SD)	40±13.1 years	
]15-25]	18	13.8
]26-36]	30	23.1
]37-47]	**47**	**36.2**
]48-58]	20	15.4
]59-80]	15	11.5
Total	**130**	**100**

Clinically, the main indication for probabilistic antibiotic therapy was sepsis with a pulmonary portal of entry, followed by cerebral toxoplasmosis with 80.8% and 33.8% respectively (Table II). Gastroenteritis and tuberculosis were the main indications for targeted antibiotic therapy, with 10% and 10.8% of patients respectively (Table III). Overall antibiotic consumption was 1417.8 DDD and 365.1 DDD/1000DH. The most commonly used antibiotics were: cotrimoxazole with a DDD equal to 944.8 and a DDD/1000DH equal to 263.3; followed by β-lactams with 140.5 DDD and 39.5 DDD/1000DH and 5-nitroimidazoles with 131.5 DDD (or 36.6 DDD/1000DH).

Table II: Distribution of patients hospitalised in the Infectious and Tropical Diseases Department of the Point G University Hospital, by indication for probabilistic antibiotic therapy

Indication for empirical antibiotic therapy	Yes (n, %)	No (n, %)
Pulmonary source sepsis*	105 (80.8)	25 (19.2)
Cerebral toxoplasmosis	44 (33.8)	86 (66.2)
Sepsis due to gastrointestinal source	44 (33.8)	86 (66.2)
Bacterial pneumonia	36 (27.7)	94 (72.3)
Tetanus	16 (12.3)	114 (87.7)
Sepsis with cutaneous source	12 (9.2)	118 (90.8)
Intestinal amoebiasis	9 (6.9)	121 (93.1)
Shigellosis	9 (6.9)	121 (93.1)
Digestive coccidiosis	7 (5.4)	123 (94.6)
Bacterial meningitis	6 (4.6)	124 (95.4)
Bacterial brain abscess	5 (3.8)	125 (96.2)
Eradication of *H. pylori*	5 (3.8)	125 (96.2)
Pneumocystis	5 (3.8)	125 (96.2)
Bacterial encephalitis	5 (3.8)	125 (96.2)
Bacterial vaginitis	5 (3.8)	125 (96.2)
Cellulitis	2 (1.5)	128 (98.5)
Orchi-epididymitis	2 (1.5)	128 (98.5)
Pyelonephritis	2 (1.5)	128 (98.5)

* non-tuberculous bacterial pneumonia

In the beta-lactam family, the most widely consumed molecules were 3rd generation cephalosporins, in particular ceftriaxone, followed by amoxicillin with respectively 52 DDD (i.e., 14.5 DDD/1000DH) and 36.5 DDD (i.e., 0.2 DDD/1000DH). For the 5-nitroimidazole family, metronidazole had a consumption of 131.5 DDD (i.e., 36.6 DDD/1000DH) (table IV).

Table III. Distribution of patients hospitalized in the Department of Infectious and Tropical Diseases at Point G University Hospital, by indication for targeted antibiotic therapy

Indication for targeted antibiotic therapy	Yes (n, %)	No (n, %)
Gastroenteritis	13 (10.0)	117 (90.0)
Tuberculosis	14 (10.8)	116 (89.2)
Bacterial pneumonia	8 (6.2)	122 (93.8)
Cystitis	7 (5.4)	123 (94.6)
Bacterial superinfection with pulmonary TB	4 (3.1)	126 (96.9)
Pyelonephritis	2 (1.5)	128 (98.5)
Vaginitis	2 (1.5)	128 (98.5)
Liver abscess	2 (1.5)	128 (98.5)

The bacterial isolates obtained from the cultured pathological specimens were predominantly *E. coli* (30%), followed by *K. pneumoniae* (15%), *M. tuberculosis* (14.2%), *S. aureus* (10.6%), and *Pseudomonas* spp. (6%). The *E. coli* isolated from our various pathological products were 100% sensitive to the following antibiotics: ertapenem, amikacin, tobramycin and furans. *K. pneumoniae* had 100% sensitivity to the following antibiotics: cefoxitin; ertapenem; imipenem; fosfomycin; norfloxacin; tobramycin; kanamycin; fusidic acid and erythromycin.

Table IV: Antibiotic consumption among patients hospitalized in the Department of Infectious and Tropical Diseases at Point G University Hospital

Antibiotic family	Antibiotic	DDD	DDD/1,000 bed-days
β-Lactams	Amoxicillin	36.5	10.2
	Amoxicillin + clavulanic acid	24.5	6.8
	Ceftriaxone	52.0	14.5
	Cefixime	27.5	7.6
5-Nitroimidazoles	Metronidazole	131.5	36.6
Aminoglycosides	Amikacin	11.0	3.1
	Gentamicin	8.0	2.2
Quinolones	Ciprofloxacin	32.0	9.0
	Norfloxacin	5.0	1.4
	Ofloxacin	5.0	1.4
Macrolides/ Lincosamides	Clindamycin	68.5	19.1
	Azithromycin	40.5	11.3
	Erythromycin	17.0	4.7
	Clarithromycin	14.0	3.9
Sulfamethoxazole +Trimethoprim	Cotrimoxazole	944.8	263.3
Total		1417.8	395.1

DISCUSSION

During our study, we recruited 130 patients who had received antibiotic therapy out of a total of 184 hospitalised patients, i.e., a frequency of 70.6%. Of these, 125 patients had received initial probabilistic treatment, 86 of whom had received probabilistic antibiotic therapy only and 39 of whom had received first probabilistic and then targeted treatment. In addition, 5 patients had benefited from targeted antibiotic therapy from the outset.

In the Infectious Diseases Department of the Point-G University Hospital, we recruited as many women as men who had received antibiotic therapy, giving a sex ratio of 1. A similar study in Morocco carried out by Droussi S in an intensive care unit in 2018 found a sex ratio of 1.75 with a male predominance. [6]. Indeed, in the general population, men have more access to care than women, but the infectious diseases department of the CHU du Point-G is a reference department for the management of HIV, this predominantly female infection has a hospital prevalence of 74.6%

[7]. Thus, the high proportion of women in our department could have rebalanced the sex ratio found in favour of men in the intensive care unit in Morocco, giving a sex ratio of 1.

The 37 to 47 age group was the most represented, with a frequency of 36.2% and an average age of 40.7 ± 13.0 years. This average age is slightly lower than that found by Mokrani S and Hamdani S in an intensive care unit in Algeria, i.e., 49.0 ± 22.9 years [8]. This difference could be explained by the fact that in this intensive care unit bedridden patients, often elderly, are hospitalised, whereas in our unit the majority of hospitalizations concern PLWHA, a disease of young subjects of sexually active age.

Sepsis with a pulmonary source was the main indication for empirical antibiotic therapy (34.6%), followed by probable cerebral toxoplasmosis and sepsis with a gastrointestinal source. This result is similar to that of Droussi S, who also found in his study in the Meknes intensive care unit in Morocco in 2018 that respiratory infection was the main indication for antibiotic therapy with a frequency of 39% [6]. Respiratory infections are the leading cause of morbidity among infections worldwide [9]. Gastroenteritis and tuberculosis were the main indications for targeted antibiotic therapy with a percentage of 25.5% each in our study; on the other hand, in a similar study at the Mohamed VI University Hospital in Marrakech, Hortamlah K found urogenital infection to be the main indication for targeted antibiotic therapy at 37%, followed by pneumonia and bacteremia at 18.5% each [10]. It should be noted that, in our setting, blood cultures are rarely performed, unlike sputum samples for acid-fast bacilli (AFB) detection, which are provided free of charge, and stool cultures, which are easier to carry out.

The frequency of antibiotic use among patients hospitalized during our six-month study in the Department of Infectious and Tropical Diseases at Point G University Hospital was 70.6%. This rate is comparable to that reported by Saleem Z et al. in Pakistan in 2018, who found a prevalence of 77.6% [11]. In contrast, Hortamlah K in Morocco in 2017 and Daniau C et al. in France in 2017 reported lower rates of 41.8% and 15%, respectively [10,12]. The high frequency of antibiotic use observed in our study and in another resource-limited country such as Pakistan, compared with more developed settings such as Morocco and Europe, may be explained by the predominance of infectious diseases in our context and the widespread use of empirical therapy, which can sometimes result in viral infections being mistakenly treated as bacterial infections.

Overall antibiotic consumption evaluated over a 6-month period in 130 patients hospitalised in the infectious and tropical diseases department of the CHU Point-G was 1417.8 DDD and 365.1 DDD/1000JH. These figures are lower than those obtained by Droussi and Monkrani. Droussi in his study in the intensive care unit in Meknés, Morocco, found an overall consumption of antibiotics of 1691.9 DDD/1000DH in 2017 and 1604.7 DDD/1000DH in 2018[6]. Monkrani S and Hamdani S at Tizou Ouzou University Hospital in Algeria in 2017 found 1992.9 DDD and 1957.6 DDD/1000DH [8]. This difference in antibiotic consumption in our context could be explained, on the one hand, by pathologies leading to a longer duration of hospitalization in our study (19.5 ± 14.3 days) and, on the other hand, by serious pathologies in intensive care units requiring the administration of high doses of antibiotics.

Antibiotics from the sulphonamides and trimethoprim families were the most widely used, with 944.8 DDD and 263.3 DDD/1000DH respectively, followed by β-lactam antibiotics (140.5 DDD and 39.5 DDD/1000DH) and 5-nitroimidazole antibiotics (131.5 DDD and 36.6 DDD/1000DH) .

These figures are lower than those obtained by Monkrani S and Hamdani S at the CHU of Tizou Ouzou in Algeria in 2017, where Betalactamins were the main weapon in the anti-infective arsenal of antibiotics consumed with 948,8 DDD/1000DH, followed by Fluoroquinolones in 2nd position with a consumption of 383.98 DDD/1000DH, and in 3rd position Metronidazole with an antibiotic consumption of 383.87 DDD/1000DH [8].

The most commonly consumed drugs were the combination of sulphonamide + trimethoprim (cotrimoxazole), i.e., 944.8 DDD and 263.3 DDD/100JH, and the most commonly consumed drugs in the beta-lactam family were 3rd generation cephalosporins, in particular ceftriaxone, followed by amoxicillin, i.e., 52 DDD and 14.5 DDD/1000JH and 36.5 DDD and 10.2 DDD/1000JH respectively. The third most widely consumed drug is metronidazole 131.5DDJ 36.6DDJ/1000JH from the 5-

Nitroimidazole family . This finding differs from that of Monkrani S and Hamdani S, who found metronidazole and ciprofloxacin to be the most consumed antibiotics, with a DDD of 390.17 and 372.9 and 383 DDD/1000DH and 366.6 DDD/1000DH respectively [8]. This difference in the consumption of antibiotic molecules could be explained by the place where antibiotic consumption is assessed in a department providing care for PLHIV, as well as the treatment of cerebral toxoplasmosis with cotrimoxazole and the duration of treatment. The pathological specimens examined in our study predominantly yielded *E. coli*, *K. pneumoniae*, *M. tuberculosis*, and *S. aureus*. These results are in line with those reported in the Mali Antimicrobial Resistance Surveillance Newsletter for October 2019–November 2020 [14]. The antibiotic susceptibility of the isolates in our study was similar to that reported by Diakité, who found *E. coli* to be sensitive to gentamicin, amikacin, and colistin, with rates of 83.3%, 86.7%, and 100%, respectively [14].
Antibiotic susceptibility tests carried out on *K. pneumoniae* showed 100% sensitivity to the following antibiotics: cefoxitin, ertapenem, imipenem, fosfomycin, norfloxacin, tobramycin, kanamycin, fusidic acid and erythromycin. This result is similar to that of Daffe M in his study at the Rodolphe Mérieux laboratory in BAMAKO, which showed that imipenem and cefoxitin, amikacin and fosfomycin had good activity against Klebsiella pneumoniae strains, with sensitivity rates of 98.53%, 88.24%, 87.04% and 93.75% [15]. In the Mali antimicrobial resistance surveillance bulletin from October 2019 to September 2020, Klebsiella pneumoniae remained 92.2% sensitive to imipenem and 93% sensitive to amikacin [13].

CONCLUSION

Evaluating antibiotic use is a quality improvement initiative aimed at reducing bacterial resistance. In our study, antibiotic consumption was high, with the majority of treatments being empirical. Systematic recording of microbiological test results could represent an important step toward optimizing antibiotic therapy.

Conflicts of interest: The authors declare no conflicts of interest.

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