



ANTIBIOTIC USAGE IN THE INTENSIVE CARE UNIT SETTING IN MALI

Anaesthesiology

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ABSTRACT

Antibiotics remains an issue in intensive care units (ICUs), because of its overuse and the emergence of bacterial resistance. The objective of the study was to evaluate the prescription of antibiotics in ICUs at university teaching and the regional hospitals in Mali.

PATIENTS AND METHODS: It was a cross sectorial retrospective and multicentric study over six months. The inclusion criteria were, all the patients hospitalized in ICUs at least for 48 hours with antibiotic treatment. We also included the cost of the daily consumption of antibiotics. The Microsoft excel was used for data entry and the data analysis was done with the software Epi info version 3.5.2.

RESULTS: Five hundred sixty-and-six (566) patient files responded to the inclusion criteria. The antibiotics prescription rate was 43.3%. The mean age of the patients was 36.8 ± 20.7 . The women were more represented (59.7%). The monotherapy (60.6%) was the most common concept use. The third-generation cephalosporin (3GC) was used in monotherapy (27.7%). The average volume of consumption of antibiotics in monotherapy was the highest. The analysis of the data showed that the volume consumption of antibiotics was different according to grade of the prescribers which was respectively 98972.3 for anaesthesia & intensive care residents and 74990.7 for anaesthetist-intensivist. The treatment was reviewed during the first 48 hours (99.8%) and was readapted in 106 of the patients (18.7%). We mainly increased the doses of antibiotics 77.4%. The average duration of the treatment was 5.2 ± 3.7 (days).

CONCLUSION: The use of antibiotics remains high and uncontrol in intensive care units in Mali, which could be explain by the limited blood culture testing and insufficient of qualified human resource in some of the regional hospitals.

KEYWORDS

Antibiotics, Intensive Care, Review, Increase, Decrease, Duration of Treatment.

INTRODUCTION

The rational use of antibiotics for the control of multi-resistant bacteria has become a significant public health issue. The proper use of antibiotics seems to be a must for the security of the planet. In Africa, antibiotic therapy in hospitals raises many socio-economic and behavioral problems. Thus, the good usage of antibiotic remains a big challenge for these countries.

The consumption of antibiotics remains high in ICUs because of the prevalence of severe infections and the severity of the clinical picture of patients. Treatment is initially empirical and often uses broad-spectrum antibiotics [1-2]. Consumption is estimated to be 70% of patients hospitalized in intensive care in France [3], making the ICU a place of increased antibiotics consumption. In the United States, the percentage of patients receiving antibiotic treatment increased from 32% to 53% between 1988 and 1994 (4). During the same period, the use of broad-spectrum antibiotics increased by 24 to 47 % (4). Such an increase in consumption is not without consequences because it contributes to the emergence of resistance and high cost. The treatment is broad-spectrum and is unsuitable in 30 to 50% [1-5], thereby,

highlighting the misuse of antibiotics in ICUs. There is ample literature on the link between prescription antibiotics, their volume and the emergence of resistance (4,5).

The proper use of antibiotics has been a going discussion amongst experts worldwide, and there has been experimentation of various strategies. One of the principles of control of bacterial resistance is to ensure the proper use of antibiotics to avoid the emergence and spread of MRBs (multi-resistant bacteria), to reduce the volume of consumption and the treatment duration. Thus, the proper use in antibiotic therapy starts with choosing the correct antibiotic, dosage for the suitable duration that is right patient. In order to fulfil these conditions, the choice must take into account three parameters: the site of infection, the bacteria and the underlying conditions [5]. The current attempts to reduce this trend are the usage of written protocols, re-evaluation of treatments within 24 to 72 hours after the initiation of treatment, and reducing prescription duration.

We began this work to evaluate antibiotic therapy in seven Intensive Care Units in Mali.

METHODOLOGY

This study took place in the ICUs of four university teaching hospitals and three regional hospitals in Mali. The data collection occurred between January 1 and June 30th, 2018; as a cross-sectorial, multicentric retrospective and analytical study. The study population involved patients hospitalized ICUs for at least 48 hours with a prescription of antibiotics. The criteria initially focused on the daily antibiotic consumption in terms of price (Price x daily quantities) [8]. The second was the reassessment, readaptation and duration of the treatment after 48 hours.

Microsoft Excel was the primary tool for data entry and, the data analysis was done with the software Epi info version 3.5.2. Quantitative variables have indicated a central tendency indicator (mean, proportion) framed by a 95% confidence interval for proportion and parametric comparison of continuous, and the Chi2 test for methodological testing. To compare the observed treatment with the outcome, we used the Wilcoxon test for matched series. The different averages of the volume consumptions were calculated as follows, the average daily dose of the different antibiotics then the average dose stay (average dose stay = average daily dose X the number of days of hospitalization) and the average of the Volume of consumption corresponded to the price of each molecule x the average dose stay [6]. Confidentiality of the data was ensured throughout the study.

Patient confidentiality is paramount and there is no conflict of interest.

RESULTS

There was a total of One thousand-three-hundred and eight patients' admission in the ICUs during the study period. Five hundred sixty-six patient's files had information on prescribed and received antibiotics treatment with a rate of 43.3%. The mean age of the patients was 36.8 ± 20.7 . The women were more represented 59.7%. Hundred and thirty patients (23.0%) received at least one antibiotic as a monotherapy before admission in ICUs which include the third Generation Cephalosporin (37.7%), Aminopenicillin, Oxapenam (14.6%), Fluoroquinolone (1.5%) and Carbapenem (0.8%). The arguments of prescribing antibiotics were based on the clinic (58.8%), national protocol (31.1%) and microbiological (0.7%). The characteristics of antibiotics prescribed are listed in Table I. One hundred and sixty-four patients received either antibiotherapy (71.0%) or prophylaxis (29.0%). Among the patients who received antibiotherapy 86 were changed into antibiotherapy based on the clinic. The average duration of prophylaxis was 4 ± 1.8 days. A total of 488 patients received antibiotic therapy. The sites of infection identify were gynaeo-obstetric (30.2%), digestive (18.4%), urinary (12.0%), pulmonary (8.1%), cutaneous-mucosal (4.2%), osteoarticular (2.3%) and cerebro-meningeal (1.2%). The prescription was made by of anesthesia & intensive care residents (53.5%) and anaesthetist & intensivist (35.3%). Three hundred and twenty-three patients received monotherapy (57%). The modalities of prescription are listed in Table II. The 3GC was the most commonly used in monotherapy (48.6%) then Amino penicillin (32.8%). The bitherapy was either the combination of 3GC + 5 Nitro imidazole (68.7%) or Amino penicillin + 5 Nitro imidazole (16.3) or 3GC + aminoglycoside (15%). The tritherapy was the combination of 3GC + 5 Nitro imidazole + Aminoglycoside (88.2%). The volumes consumption of antibiotic listed in Figure 1. The average volume of consumption was 239673.6 in monotherapy, 98811.4 in bitherapy and 36322.8 in tritherapy. According to prescribers, the volume consumption was 98972.3 for & anaesthetist intensivist, 74990.7 for the residents and 72240.7 for paramedics. The treatment was re-evaluated in 99.8% of the cases which was 97% within 48 hours and 2.8% after 48 hours. The treatment was re-adapted in 106 patients (18.7%). The re-adaptation criteria were clinical (89 patients) and microbiological (17 patients). The treatment was escalated (77.4%) and de-escalation (22.6%). The average duration of treatment was 5.2 ± 3.7 days with the range 2 to 41.

COMMENTS AND DISCUSSION

The ICUs remain a place for high consumption of antibiotics. This original study in Mali had evaluated the use of antibiotics in ICUs with a limited resource. The limitations of this study were, its retrospective character, lack of information on the targeted bacteria and the expected duration of treatment in the patients' files. This study carried out in 7 hospitals with an ICU shows a frequency of 43.3% of antibiotic use. This figure can be superimposed on the data in the literature. Lemanissier, Aubry and al who found 46.4% of patients hospitalized in

intensive care under antibiotics. In our series the prescription criteria were clinical in 58.8% followed by national consensus in 31.1%. This attitude is found in the majority of series where empirical treatment is based on clinical arguments [2-5]. Contrary to our data, lung disease is largely in the lead, followed by urinary tract infection in several series [10-13].

This condition alone justifies half of the antibiotic prescriptions in ICUs [4]. Our study was carried out in surgical ICU with a different population than medical ICUs where most of the data comes from. The high frequency of empirical treatment is explained by the absence of diagnostic procedures in some centers. This may explain the timid use of biology in our series. This situation explains the misuse of broad-spectrum antibiotics with combinations of two or even three antibiotics [7,8]. The volume of antibiotic consumption was high in our series. In our sub-region, ceftriaxone remains the most used antibiotic in probabilistic (98.2%) and its prescription is inappropriate in 29.5% and not guided by a protocol [9,10]. Our method of calculating consumption volumes could be discussed because in other series the method of calculation was the defined daily dose. Our choice is justified in order to understand the economic impact and also on the ecosystem. Other methods of calculation are described in the literature and adopted by countries with limited ICU [3,4,11]. The analysis of volumes reveals an increase in consumption which challenges prescribers on strategies and reflections for a decrease. Indeed, there is a correlation between the consumption of antibiotics agents and the emergence of multi-resistant bacteria. Thus, the reduction in consumption requires the provision of diagnostic tools to prescribers, as some studies show (3,12,13). Bacteriological examinations make it possible to reduce the consumption of anti-infectives by 20%. Also, the recommendations insist on bacteriological samples before any antibiotic therapy. Infectious emergencies requiring antibiotics before four hours are generally limited to septic shock, bacterial meningitis and febrile neutropenia [14-17]. In other cases, a wait-and-see attitude must be advocated. After a reassessment that was performed in the majority of cases in our series at 72 hours of treatment.

The recommendations envisage this systematic reassessment at 48-72 hours and consider de-escalation [3]. The attitude consisted of a therapeutic escalation in 77% on clinical criteria. The insufficient contribution of bacteriology could explain this situation, which is found in structures with limited resources [9]. De-escalation is the safe method in the proper use of antibiotics because it reduces the risk of selections of resistant mutants and contributes to a reduction in the volume of consumption. De-escalation consists in closely adapting the spectrum of curative antibiotic therapy to the data of the antibiogram. This strategy is guided by bacteriological results but also can be guided by local epidemiology (12,13). Short-term treatments are increasingly recommended in several series with a median of 6 days (18,19,20). In our series this trend was respected in the majority of cases. Microbiology plays an important role in this strategy with other potential benefits such as a reduction in antibiotic-related side effects and a reduction in costs and conversely too short treatment can be a source of relapses with a risk of increased mortality and morbidity (21,22,23). In the face of these alarming findings, it is urgent to develop a program for the proper use of antibiotics adapted to our local realities in order to reduce the emergence of bacterial resistance with a significant reduction in the consumption of antibiotics.

CONCLUSIONS

The consumption of antibiotics remains high in services in ICUs Mali with insufficient intake of microbiology. The proper use of anti-infectives is a combination of strategies leading to a reduction in consumption in order to prevent the emergence of resistant bacteria. Efforts must be made to raise the level of the technical platforms in order to increase the contribution of microbiology.

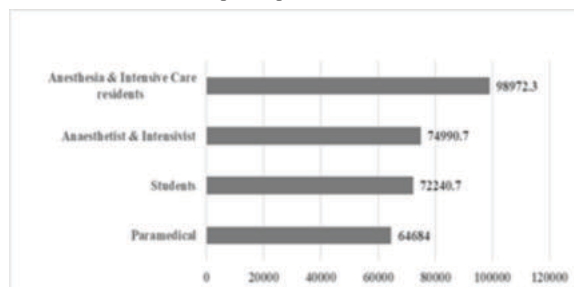
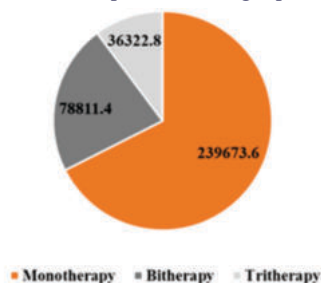
Table 1: Characteristics of the prescription

Characteristics of the prescription	Effective (N)	Frequency (%)
Treatment assessment frequency	Within 48 hours	549 97
	After 48 hours	16 2.8
	Not done	1 0.2
Type of therapeutic re-adaptation	Escalation	82 77.4
	De-escalation	24 22.6
Re-adaptation criteria	Clinical	89 84
	Antibiogram	17 26
Treatment duration (day)	2 to 7	474 83.7
	8 to 14	75 13.3
	15 to 21	13 2.3

Table 2: Antibiotics protocols used

Antibiotics protocols used	Effective (N)	Frequency (%)	
Monotherapy	3GC	137	27.7
	Aminopenicillin	106	18.7
	Aminopenicillin + Octapenam	60	10.6
Bithérapie	3GC + 5-Nitro amidazoles	101	17.8
	Aminopenicillin + 5-Nitroimidazole	24	4.2
	3GC + aminosides	22	3.9
Trithérapie	3GC + 5-Nitroimidazole + aminosides	15	2.7
	Fluoroquinolone + 5-Nitroimidazole + aminosides	2	0.4
Tetrathérapie	3GC + 5-Nitroimidazole + aminosides + Fluoroquinolone	1	0.2

3GC: Third Generation Cephalosporin.

**Figure 1: Volume of Consumption according to prescribers****Figure 2: Volume of Consumption according to the terms of prescription****REFERENCES:**

- J.J. Zambrowski. Pharmacoeconomie du traitement des infections sévères en réanimation. Ann Fr Anesth réanimation 2000; 19: 430-5.
- Marie-Emilie Clerc, Brigitte Haury et Sophie Stamenkovic. Les consommations d'antibiotiques dans les CHU en 2005. Solidarité-santé 2008, N°7.
- Cédric Bretonnière, Marc Leone, Christophe Milési, Benoît Misset : Stratégie de réduction de l'utilisation des antibiotiques à visée curative en réanimation (adulte et pédiatrique). Ann Fr Anesth réanimation: 2015; 1: 373–396
- D.Gruson, G. Hilbert, F. Vargas, R. Valentino, J.P. Cardinaud, G. Gbikpi-Benissan. Impact des nouvelles stratégies d'utilisation des antibiotiques en réanimation. Réanimation 2002; 11: 200-8.
- Marie Thuong, Jean-Ralph Zahar.al. Grille de surveillance de la prescription des antibiotiques en réanimation. Presse Med 2004; 33: 130-6.
- P. Pavese A, A. Bonadona B, J.P. Vittoz C. al : Apport d'une consultation systématique d'infectiologie à la maîtrise de l'antibiothérapie en réanimation. Réanimation 14 -2005 - 281-287
- Stéphane Gennai, Patricia Pavese.al : Evaluation de la qualité des prescriptions antibiotiques dans le service d'accueil des urgences d'un centre hospitalier général : analyse prospective de 211 prescriptions. Presse méd. 2008; 37: 6- 13
- Roger PM, Hyvernat H, Verleine-Pugliese S, Bourroul C, Giodano J. Consultation systématique d'infectiologie en réanimation médicale. Presse Méd 2000; 29: 1640-4.
- Youl E.N.H, Gnoula C, Ouédraogo M, Kabre B, Guissou LP. Antibiothérapie au centre universitaire Yalgado Ouédraogo : analyse de pratique de prescription de la ceftriaxone. J Sci Pharm Biol 2015; 16,2: 12-22.
- N. Koffi, A. Ngom, B. Kouassi, K. Horo, L. Mansaré, E. Ako-Danguy. Evaluation de l'antibiothérapie probabiliste dans les pneumopathies aiguës d'allure bactérienne hospitalisée en Afrique. Bull Soc Pathol Exo 2001; 94, 5, 397-400.
- Kuster SP, Ruef C, Ledergerber B et al. Quantitative antibiotic use in hospitals; comparison of measurements, literature review and recommendations for a standard of reporting. Infection 2008; 36: 549-59
- Garnacho-Montero J, Guisnet-Pizzarraya A, Escobedo-Ortega A, et al. De-escalation of empirical therapy is associated with lower mortality in patients with severe sepsis and septic shock. Intensive Care Med 2014; 40: 32-40.
- MOKART D, Slehofer G, Lambert J et al. De-escalation of antimicrobial treatment in neutropenic patients with severe sepsis: results from an observational study. Care Med 2014; 40: 41-9.
- Kumar A, Roberts D, Wood KE et al. Duration hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med 2006; 34: 1589-96.
- Siber SH, Garrett C, Singh R et al. Early administration of antibiotics does not shorten time to clinical stability in patients with moderate to severe community-acquired pneumonia. Chest 2003; 124: 1798-804.

- SPILF. 17th Consensus conference on bacterial meningitis. Short text. Med Mal Infect 2009; 39: 175-86.
- Davies JM, Lewis MP, Wimperis J, et al. Review of guidelines for the prevention and treatment of infection in patients with an absent or dysfunctional spleen: prepared on behalf of the british committee for standards in hematology by a working party of the hématology-Oncology task force. Br J Haematol 2011; 155: 308-17.
- Mohammed, S Duperret, J. m Vedrinne.al. Du bon usage des antibiotiques en réanimation : résultats d'un programme de rationalisation de la prescription. Ann Fr Anesth réanimation 1998; 17: 21-3.
- I. Deconick, A. Meybeck, D. Thellier.al : Impact d'une bi-antibiothérapie probabiliste et d'une désescalade précoce dans le traitement des pneumopathies acquises sous ventilation mécanique. Ann Fr Anesth réanimation 2014 - 24 : 60-63
- B. Georges, P. Cougot, J.F. Decun, M. Mazerolles : Durée du traitement antibiotique en réanimation : données actuelles. Ann Fr Anesth réanimation 2000; 19: 367-74
- M. Wolff, J. Chastre : Durée de l'antibiothérapie des infections sévères en réanimation. Ann Fr Anesth réanimation Réanimation 2006, 15: 168-175.
- Bouadma L, Luyt CE, Tubach F, et al. Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial) a multicenter randomized controlled trial. Lancet 2010; 375: 463-74.
- Noble V, Harbarth S, Graf JD, et al. Use of procalcitonin to shorten antibiotic treatment duration in septic patients: a randomized trial. Am J Respir Crit Care Med 2008; 177: 498-505.
- G. Potel, J. Caillon, C. Jacqueline.al. Dosage des antibiotiques en réanimation : quand et comment demander et interpréter les tests ? Réanimation 15 -2006- 187-192.
- I.
- Yapo Thomas-Aba-Eric Adehoss.al. E pily trop 2016 maladies infectieuses. Tropicales 25ème Edition 2016-978-64-5.
- V. Lemanissier, H. Aubry-Damon, A. Lepoutre.al : Etude des traitements antibiotiques. Enquête de prévalence nationale 2001.
- Y. Zarrouki, MA. Samkaoui : Consommation des antibiotiques en réanimation. Thèse méd. Faculté de médecine et de pharmacie - Marrakech 2009 N°98
- Kouanda Seni : antibiothérapie pratique au CHNYO : Etude de la relation prescription de suspicion et examens bactériologiques. Thèse méd. : Burkina Faso université de Ouagadougou faculté des sciences de la santé (F.S.S.) : 1996-1997, N° 36
- M. Clève, M.O. Baumea, C. Pommier : Audit des pratiques de prescription des anti-infectieux dans un service de réanimation polyvalente. Le pharmacien hospitalier et clinicien 2011; 46: 103-109
- M. Boubacar Ouattara : la place des antibiotiques dans l'arsenal thérapeutique en réanimation adulte du CHU Gabriel Touré. Thèse méd. FMOS 2014, N°40
- B. Armel ; K. Berechid ; S. Himmich ; M. Faroudy : Evaluation prospective des prescriptions antibiotiques dans le service des urgences d'un centre hospitalier universitaire marocain. Archives de Pédiatrie 2014; 21 : 938-943
- M. Jean-Claude Kiouba : L'usage des antibiotiques en milieu hospitalier. Thèse Phar. FMPOS 2001-2002, N°: 11
- E. audry-degardina, f. dubosa, b. s. Leteurtre.al : Evaluation de la prescription antibiotique dans un service de réanimation pédiatrique. Archives de pédiatrie 14 - 2007 - 157- 163
- P. SENGAL, V.M.F. BETHO, J.C. LOUKAKA, A. MOUKO. Prescription et consommation des antibiotiques dans un service de pédiatrie. Médecine d'Afrique Noire : 1993, 40 (3).