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Clinical Efficacy of Prolonged First-Line Treatment against *Helicobacter pylori* in Ouagadougou

Nômawendé Inès Compaore[1], Couna Christiane Some[2], Nanelin Alice Guingane[3], Tegwinde Rebeca Compaore[4], Marie Nina Compaore[5], Roger Sombie[2], Alain Bougouma[2]

[1]Service of Medicine and Medical Specialties, Medical Center with Surgical Antenna El Fateh-Suka, Ouagadougou, Burkina Faso
[2]Service of Hepato-Gastroenterology of Yalgado Ouedraogo University Hospital Center, Ouagadougou, Burkina Faso
[3]Service of Hepato-Gastroenterology of the University Hospital Center of Bogodogo, Ouagadougou, Burkina Faso
[4]LABIOGENE, Laboratory of Molecular Biology and Genetic, University of Ouagadougou, Ouagadougou, Burkina Faso
[5]Epidemiology/Health Science Center of Houston, Houston, United States of America
Email: noomadoc@gmail.com

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Abstract

Background: *Helicobacter pylori* (*H. pylori*) infection is a public health concern. In fact, due to bacterial resistance, treatment strategy is a challenge. It is then more recommended to prolong first-line treatment. In order to be acceptable, the clinical efficacy of treatment must be higher than 90%. Aim: We aimed to assess the outcome of prolonged first-line treatment among adults. Patients and Methods: The study was cross-sectional among adults and patients were treated for *H. pylori* eradication for the first time during 10 to 14 days. Recruitment was made from March 2019 in six private polyclinics and two hospitals of the city of Ouagadougou. We used monoclonal antigen (Ag) test on the stool samples for diagnostic and for the patients follow up. Chi squared (X^2) tests and ANOVA for the comparison of percentages and means were determined using with STATA® software program in the bilateral 95% confidence interval for the statistical analysis. Results: In the different medical centers for 19 months, 365 patients were compiled. The sex-ratio was 0.64. The average age was 43.55 years. The treatment efficacy was 92.88%. Treatment efficacy was better with p-value $<10^{-3}$ depending on prescriber: gastroenterologist (94.07%), general practitioner (75%); compliance before treatment: excellent (95.88%) or bad (50%); number of consultations: ≥four (94.35%), three (96.32%), two (78.85%). Triple therapies efficacy was 90.81%; p = 0.19. Quadritherapy efficacy was 95%; p = 0.5. Conclusion: This research is a contribution to the advent of national or African recommendations.

Keywords

Helicobacter pylori, Treatment Efficacy, Triple Therapies, Quadritherapy

1. Introduction

Helicobacter pylori (*H. pylori*) infection is a public health concern. In Burkina Faso and other developing countries, the prevalence of this infection remains high (80%) [1] [2] [3] [4]. However, it's tending to fall (less than 50%) in many countries [5] [6] [7].

It's necessary to follow up after treatment in order to confirm its efficacy when the eradication rate is over (≥) 80% [5]. To be acceptable, clinical efficacy of treatment must be higher than 90% [8] [9]. *H. pylori* treatment follow up can be done with a urea breath test or monoclonal antigen test on stool sample [5] [8] [9].

H. pylori eradication leads to gastric cancer prevention, patients' clinical well-being and reduced health costs [4] [5]. However, bacterial resistance is growing, and treatment strategy is a challenge [5] [8] [10]. And it is more recommended to prolong first-line treatment [5].

In Burkina Faso there are several publications on *H. pylori* epidemiology [1] [2] [3]. We found neither national nor African recommendations on treatment [11]. Local antimicrobial resistance is the determinant of successful *H. pylori* treatment [12]. A prospective molecular study attested a low-level primary clarithromycin resistance of *H. pylori* on 2018 [3]. *H. pylori* eradication rate after seven days triple therapy was poor (22.3%) in a neighboring country [13]. Western countries currently use sequential quadruple therapy or bismuth-based [13]. This study was done to assess the outcome of prolonged first-line treatment (10 to 14 days) among adults. We compared different regimens implemented in current practice and the aim was to select the best first line treatment.

2. Methodology

The study was cross-sectional in cohort of Burkinabe patients from March 2019 to September 2020 in the city of Ouagadougou. Patients' recruitment was made in six (6) private polyclinics (El-Fateh Suka, Nina, Notre Dame de la Paix, SANDOF, Yati and Cercle d'or medical Center) and two hospitals (Yalgado Ouedraogo University Hospital Center and Saint Camille Hospital of Ouagadougou). Patients were at least 18 years old and treated for *H. pylori* eradication for the first time during 10 to 14 days.

The minimum size calculated using the OpenEpi® software was 356 based on the Fleiss® method with continuity correction. We set the power at 80%; the sparrow size ratio, unexposed/exposed to 1; the percentage of the unexposed with results at 80% and that of the exposed at 91%. Patients were grouped according to their level of education into several occupational groups: no high

school diploma, middle manager; senior manager and others (students and retirees). The terms middle and senior managers referred respectively to less than 3 years and over 3 years in college.

We used monoclonal antigen (Ag) test on patients stool samples for *H. pylori* infection's diagnostic. The test was also used for following up after treatment: follow up for at least four weeks and not more than 12 weeks after the end of treatment (beyond possible reinfection). To be valid, it had to have been done remotely from taking proton pump inhibitors (PPIs) more than 2 weeks and/or an antibiotic and/or bismuth more than 4 weeks.

The PPIs used were prescribed as a single daily or twice-daily dose: omeprazole 20 mg, lanzoprazole 30 mg, esomeprazole 20 and 40 mg or pantoprazole 20 and 40 mg. The different therapeutic regimens according to the associated antibiotic therapy applied were:

Triple therapies:

- three lines of standard: amoxicillin 1000 mg 2 times daily ± clarithromycin 500 mg 2 times daily or metronidazole 500 mg 2 times daily
- high doses: amoxicillin 750 mg 3 times daily + metronidazole 500 mg 3 times daily;
- sequential: amoxicillin for the first 5 to 7 days and the following days clarithromycin + metronidazole;

Quadritherapy:

- concomitant: amoxicillin + clarithromycin + metronidazole;
- bismuth: 3 capsules (bismuth potassium sub citrate 140 mg + tetracycline hydrochloride 125 mg + metronidazole 125 mg and potassium 32 mg) × 4 times daily;
- high doses + clarithromycin;
- with Cefixime (replaced of amoxicillin): Cefixime 200 mg 2 times daily + metronidazole + clarithromycin.

The parameters used to assess treatment were: compliance before treatment (excellent, good, acceptable, bad and very bad), treatment tolerance (excellent, good, acceptable, bad and very bad), duration of treatment (10 days, 11 to 13 days and 14 days), prescriber (gastroenterologist or general practitioner), delay before control (4 to 6 weeks, 7 to 8 weeks, 9 to 10 weeks, 11 weeks) and Number of consultations (2, 3, ≥4).

Clinical efficacy of the prolonged first-line treatment was attest by a negative Ag test control after treatment.

The data was collected in anonymous evaluation form for each patient and then compiled in STATA® (College Station, TX) software program.

Chi squared (X^2) tests and ANOVA for the comparison of percentages and means were carried out in the bilateral 95% confidence interval for the statistical analysis.

Our study includes all those who gave their informed consent, completed their treatment for the first time during 10 to 14 days and who have been seen at least

twice. Our objective was to collect anonymously the data's of at least 178 patients in each group. Triple therapies or quadritherapy were randomly assigned by prescribers.

3. Results

From June 09, 2019, to August 06, 2020, 365 patients were compiled for the study.

Extended first line therapy failed in 26 patients (7.12%). Treatment efficacy was 92.88%.

The results of the post-therapeutic control were summarized according to the socio-demographic risk factors in "Table 1", treatment risk factors in "Table 2" and other therapeutics risk factors in "Table 3".

The average age was 43.55 years.

The sex-ratio was 0.64 in favor of women (p-value not significant).

The residency was mix for four patients. Those residing in urban areas were 57.89%.

The higher the level of education, the longer the treatment was prolonged, and it was associated to better result of treatment.

Treatment efficacy was better (p-value < 10^{-3}) depending on compliance before treatment: excellent (95.88%) or bad (50%). Good tolerance was associated to better results but a ratio could not be established among our patients.

Treatment efficacy was better (p-value < 10^{-3}) depending on prescriber (gastroenterologist) and higher number of consultations.

Table 1. Treatment outcomes by socio-demographic risk factors.

Socio-demographic risk factors (%)	Ag *H. pylori* control test		p-value	X^2
	Ag − N (%)	Ag + N		
Age				
22 to 40 years old (46.30)	159	10	0.91	0.15
41 to 60 years old (40.55)	132	15		
61 to 90 years old (13.15)	47	1		
Gender				
Male (38.9)	135	7	0.19	0.14
Female (61.1)	204	19		
Residency				
urban (57.89)	196	13	0.70	0.43
Rural (42.11)	141	11		
Profession				
No High school diploma (42.46)	139 (89.68)	16	0.02	0.21
Middle manager (34.79)	120 (93.70)	7		
Senior Manager (13.5)	46 (95.83)	2		
Others (9.59)	34 (97.14)	1		

Table 2. Treatment outcomes by treatment risk factors.

Treatment risk factors (%)	Ag *H. pylori* control test		p-value	X^2
	Ag − N (%)	Ag + N		
Compliance before treatment				
Excellent	186 (95.88)	8	10^{-4}	10^{-4}
Good	118 (92.91)	9		
Acceptable	23 (82.14)	5		
Bad	4 (50)	4		
Very bad	8 (100)	0		
Treatment tolerance[a]				
Excellent	134 (97.10)	4	0.17	10^{-3}
Good	104 (90.43)	11		
Acceptable	61 (84.72)	11		
Bad	28 (100)	0		
Very bad	12 (100)	0		
Duration of treatment				
10 days	122 (89.71)	14	0.048	0.29
11 to 13 days	9 (100)	0		
14 days	208 (94.55)	12		

[a]The reported reasons for poor tolerance were: the high number of tablets to swallow (28 patients); insomnia (4 patients); constipation (4 patients); polyarthralgia (4 patients) and discomfort (4 patients). There was intolerance to metronidazole for 8 patients and to clarithromycin for 4 patients.

Table 3. Treatment outcomes by others therapeutics risk factors.

Others therapeutics treatment risk factors (%)	Ag *H. pylori* control test		p-value	X^2
	Ag − N (%)	Ag + N		
Prescriber				
Gastroenterologist	318 (94.07)	19	10^{-4}	$<10^{-4}$
General Practitioner	21 (75)	7		
Delay before control				
4 to 6 weeks	234	19	0.91	0.26
7 to 8 weeks	52	0		
9 to 10 weeks	45	7		
11 weeks	8	0		
Number of consultations				
2	41 (78.85)	11	10^{-3}	10^{-3}
3	131 (96.32)	5		
≥4	167 (94.35)	10		

The results of the post-therapeutic control have been summarized according to antibiotics regimens and or anti-secretory regimens in "Table 4".

Treatment efficacy was not related to antibiotics regimens, antisecretory type or dosage. A single dose of Omeprazole (20 mg) twice daily was 91.37% therapeutically efficient (p-value not significant).

Table 4. Treatment outcomes by antibiotics regimens.

Treatment regimens (%)	Ag *H. pylori* control test		p-value	X^2
	Ag − N (%)	Ag + N		
Antibiotics regimens				
Triple therapies	**168 (90.81)**	17	0.6	0.9
Amoxicillin/clarithromycin	110 (93.22)	8		
Metronidazole/clarithromycin	1 (100)	0		
Amoxicillin/metronidazole	26 (81.25)	6		
High dose	27 (90)	3		
Sequential	4 (100)	0		
Quadritherapy	**171 (95)**	9	0.27	0.50
Bismuth	33 (91.67)	3		
Concomitant	112 (96.55)	4		
High dose	22 (91.66)	2		
With Cefixime	4 (100)	0		
Anti-secretory regimens				
Type of anti-secretory				
Omeprazole	233 (91.37)	22	0.13	0.12
Pantoprazole	34 (100)	0		
Lanzoprazole	44 (91.67)	4		
Oesomeprazole	28 (100)	0		
Anti-secretory Dosage				
Double unique (Pantoprazole et Oesomeprazole)	8 (100)	0	0.93	1
Simple twice daily (Omeprazole and others)	295 (92.48)	24		
Double twice daily (Pantoprazole/ Lanzoprazole and Oesomeprazole)	36 (94.74)	2		

4. Discussion

In that Burkina Faso, *H. pylori* prevalence is over 80% in various populations [1] [2] [3] [14] [15] [16], while in Europeans' and many developed countries it is less than 50% [5] [15]. It is accepted nowadays that geographic and socio-economics differences between populations is the main reason of these variations [4] [11]. Inadequate health-care system, lack of treatment guidelines, lack of standardized diagnosis and lack of data are several challenges encountered in Africa [11].

Middle-aged women, residing in urban areas were the most represented among our patients. In similar studies, no gender difference is established to this bacterium [4] [5] [13] [15]. In developing countries, *H. pylori* infection rate is more predominant in young adults [1] [2] [13]. Alcohol and tobacco seem to have no epidemiological effect [13].

The higher the level of education, the longer the treatment was prolonged, and it was associated to better result of treatment (p-value not significant) in this study.

The choice of the identification methods depends on the performance, the availability, the cost and other factors [17]. The pathological examination of gastric biopsies has high specificity and sensitivity [4] [5]. Breath test with urea la-

beled with carbon-13 or 14 is still the reference as a non-invasive test for checking the efficiency of *H. pylori* eradicating treatments [5] [13]. However its cost remains high and it is scarcely available in our country. Fecal antigen assays especially those based on ELISA have excellent sensitivity and specificity [5] [12]. Some serology tests have high sensitivity and specificity but need locally validated [5].

Prolonged first line treatment revealed an excellent clinical efficacy at 92.88% among our study population.

Concomitant quadritherapy (96.55%) was the best treatment regiment, followed by the triple therapy combining amoxicillin with clarithromycin (93.22%). Increasing doses of amoxicillin and metronidazole appeared to improve outcomes in triple therapy (from 81.25% to 90%) but not in quadritherapy (from 96.55% to 91.66%). Rates of 100% were observed but in very small numbers (<5 patients) with sequential triple therapy, which combined clarithromycin with metronidazole and quadritherapy with cefixime. The probable explanation is the low primary resistance of clarithromycin already mentioned in several studies [3] [5] [18] [19].

This study attests (p-value < 10^{-3}) that the treatment efficacy is better if the prescriber is a gastroenterologist, compliance before treatment is excellent and the number of consultations is over three (≥3). Tolerance was also associated with treatment efficacy, but the ratio could not be established among our patients. Among treatment failure risk factors there are antibiotics resistance to *H. pylori*, older age, low therapeutic compliance, the onset of treatment side effects [18] [20] [21] [22].

Treatment efficacy was not related to age, sex, residence, time before control, or antisecretory type. A single dose of Omeprazole (20 mg) twice daily, seems to have an excellent therapeutic efficacy (91.37%). Future studies are required.

Our study has selection bias due to its place in real life with expenses borne by patients. We have not assessed financial constraints. However, this may also be an advantage allowing us to describe the real challenges of managing *H. pylori* in a hospital setting in Ouagadougou.

5. Conclusion

International recommendations on *H. pylori*, particularly American, European and Asian are constantly updated. This research could contribute to the advent of national or African recommendations [5] [6] [8].

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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