

Full Length Research Paper

Tolerance and observance of methotrexate in the treatment of rheumatoid arthritis at the university Hospital Bogodogo, Burkina Faso

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This study is aimed at assessing tolerance and observance of the patients with RA (rheumatoid arthritis) treated by methotrexate at University Hospital Bogodogo, in Burkina Faso. A cross-sectional study was conducted from July to September 2015 in outpatients with rheumatoid arthritis monitored in rheumatology service. Data were obtained from interview, by reviewing medical cards of the patients and consultation report forms. In total, 205 patients with RA were included. Among them, 135 were treated with methotrexate (65.9%). All patients treated with methotrexate took folic acid tablet weekly. The duration of RA evolution varied from 1 to 360 months with a mean of 48 month. The mean duration of treatment with methotrexate was 30.2 months. Among the patients treated with methotrexate, 28.8% observed adverse reactions, 53.3% declare taking their medication without break during the last month. Discomfort (8.9%) and nausea (5.9%) were the most frequent adverse effects. Stock out of methotrexate in community pharmacy (10.4%) and adverse effect (5.9%) were the main reasons of patient's inobservance. Methotrexate is always the cornerstone of RA treatment. This study confirms the good tolerance of methotrexate and difficulty of observance with this treatment.

Key words: Rheumatoid arthritis, observance, methotrexate, tolerance, Burkina Faso.

INTRODUCTION

Rheumatoid arthritis (RA) is an inflammatory, chronic and autoimmune pathology. Its prevalence in the world varies from 0.4 to 1% according to the gender, race or ethnicity,

period and regions (Gabriel, 2001; Igor et al., 2015). However, data about prevalence of RA are limited for the Sub-Saharan African region (Igor et al., 2015). Its

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Table 1. Distribution of patients with rheumatoid arthritis according to the anti-rheumatism drug used (n=205).

Anti-rheumatism drug	Number of patients (%)
Methotrexate only	132 (64.4)
Methotrexate + Hydroxy chloroquine	2 (0.9)
Methotrexate + Hydroxy chloroquine + Sulfasalazine	1 (0.5)
Hydroxy chloroquine	67 (32.7)
Sulfasalazine	3 (1.5)

hospital prevalence was estimated in African countries such as Togo (0.45%) (Houzou et al., 2013) and Burkina Faso (2.18%) (Ouedraogo et al., 2014). Because of the high cost of medical and pharmaceutical care with the use of most recent medicines, RA is a health public issue. Moreover, patients with RA cannot be very active in economic system. Immunosuppressive drugs are the base of the RA treatment and aims to improve symptoms prevent complications and improve quality of life. Considering the literature, methotrexate is the immunosuppressive drug most frequently prescribed (Sany et al., 2004; Weinblatt et al., 2013; Shinde et al., 2014). Patients using methotrexate are highly exposed to its adverse effects of two main factors: cytotoxic effect and prolonged duration of treatment. Inobservance to treatment is associated with relapse or persistence of RA. The previous studies about observance with methotrexate showed that the majority of patients have not a good adherence (Contreras Yanez et al., 2010; Bluett et al., 2015). About 40% patients are non-adherent to methotrexate (Bluett et al., 2019). Several studies were performed about RA in Burkina Faso (Ouedraogo et al., 2017; 2016; Yameogo, 2016). However, up until now, there was no research concerning adverse effects and observance with methotrexate in Burkina Faso. This work aimed to assess tolerance and observance of the patients with RA treated by methotrexate at university hospital Bogodogo.

METHODOLOGY

Population

A cross-sectional study was performed in patients that visited rheumatology service of the hospital Bogodogo from February to May 2017. The patients were included according to the following criteria: having RA agreeing with the American College of Rheumatology (ACR) and European League against Rheumatism Collaborative initiative (EULAR) classification for rheumatoid arthritis, diagnosis carried on by a physician, patient treated with methotrexate. Patient not having medical report form was not selected.

Variables

The survey form included the following variables:

- (1) Demographic characteristics: age, sex, residence.
- (2) Clinical data: antecedents, duration of RA.
- (3) Therapeutic data: immunosuppressive drugs including methotrexate and concomitant drugs.
- (4) Tolerance: adverse reaction notified in the medical report.
- (5) Adherence with methotrexate: discontinuity or temporary break of treatment with methotrexate, reasons of these breaks.

Data collection

Data were collected from June to July 2017. A resident pharmacy student has reviewed the medical dossiers of the patients and interviewed the patients to complete information during their medical visits.

Adherence includes two components: observance and persistence to treatment (Dossa et al., 2015). Only observance with methotrexate was measured on base of the patient's statement. The question to assess observance of the patient was: "During the last month, did you already miss a dose of your treatment with methotrexate?"

To assess adverse reaction of methotrexate, French method of causality assessment applied to individual cases of pharmacovigilance was used (Arimone et al., 2011). The score of intrinsic imputation ranged from I_0 (the lowest score) to I_6 (the highest score) according to the causality level.

Data analysis

Data were registered with Epi-Info 7. Patient was considered "observant" when he responded "No" at the question to assess observance. Statistical analyses were performed by calculated prevalence of patient's characteristics, methotrexate adverse effects and observance.

Ethical considerations

The head of the rheumatology service and the director of Hospital Bogodogo agreed the protocol before the starting data collection. Patients gave their consent for the interview.

RESULTS

Characteristics of the patients

In total, 205 patients with RA were followed in the rheumatology service and 135 (65.9%) patients were treated with methotrexate. All patients treated with methotrexate took folic acid tablet weekly. The distribution of patients with RA according to the anti rheumatism drug is showed in the Table 1.

Table 2. Distribution of patients with rheumatoid arthritis treated with methotrexate according to socio-demographic characteristics and medical antecedent (n=135).

Socio-demographic characteristics		
Characteristics		Frequency (%)
Sex	Female	73.3
	Male	26.7
Age group	10-20	3.8
	20-30	16.1
	30-40	22.5
	40-50	21.2
	50-60	19.9
	60-70	10.6
	70-80	5.9
Residence	Urban area	92.8
	Rural area	7.2
	Gastrointestinal ulcer	10.4
	Hypertension	9.6
	Diabetes	3.7
	Sinus inflammation	2.2
Medical antecedent	Abortion	2.2
	Sore throat	1.5
	Asthma	1.5
	Smoking	1.5
	HIV	0,7
	Sickle cells disease	0.7
	Alcoholism	0.7

The Table 2 shows the distribution of patients according to the socio-demographic, clinical and therapeutic characteristics. The duration of RA evolution varied from 1 to 360 months with a mean of 48 month. The mean duration of treatment with methotrexate was 30.2 months.

Tolerance of the methotrexate

Among the patients treated with methotrexate, 59 adverse reactions were observed in 28.8% of them. The Table 3 indicates the distribution of adverse reactions cases according to the score of causality assessment. All

DISCUSSION

This study has some limits. Firstly, it has been conducted in patients visiting hospital and results cannot be applied to the global population of Burkina Faso. Secondly, the

the adverse reactions were previously described in the drug reference monograph Martindale (Sweetman, 2011).

Adherence to treatment with methotrexate

Among the 135 patients treated with methotrexate, 53.3% declare taking their medication without break during the last month, 24.4% did temporary one or several breaks of their treatment during the last month. The reasons of inobservance that patients declared are listed in the Table 4. However, some patients missed their medical visit (22.2%). Their observance could not be measured. observance of patients that didn't come at medical visits is not measured. In last, as any cross-sectional study using previous reported data, data about patients are missing in some medical reports.

Methotrexate was used in the majority of patients of our study (65.9%). Andia et al. (2016), found 60% in a study at Niamey National Hospital. In despite of the marketing

Table 3. Distribution of adverse reaction in patients treated with methotrexate according to the score of causality assessment (n=135).

Adverse reaction	Number of cases (%)	Score of causality assessment
Discomfort	12 (8.9)	I ₄
Nausea	8 (5.9)	I ₄
Vomiting	6 (4.4)	I ₄
Allergy	5 (3.7)	I ₄
Cough	5 (3.7)	I ₄
Stomach pain	4 (2.9)	I ₄
Vertigo	4 (2.9)	I ₄
Diarrhea	2 (1.5)	I ₄
Edema	2 (1.5)	I ₄
Anemia	3 (2.2)	I ₄
Transaminases augmented	3 (2.2)	I ₄
Interstitial lung disease	3 (2.2)	I ₄
	1 (0.7)	I ₆

Table 4. Reasons declared by patients to justify their inobservance with methotrexate treatment (n=135).

Reason	Frequency (%)
Stock out in community pharmacy	10.4
Adverse effect	5.9
Financial incapacity	3.7
Patient doesn't understand importance of treatment	2.9
Patient desires pregnancy	2.2
Patient travelling	1.5
Surgery of the eye	0.7

of biotherapies, methotrexate is again the main and first intention drug for RA treatment. Its good tolerance, efficacy and affordable cost make it a gold standard for RA medication.

Moreover, the ratio of sex was 0.36 for males. Women are the most affected by RA. The literature confirms high frequency of RA among women (Silman et al., 2002; Slimani et al., 2014; Andia et al., 2016). Patients had a mean age of 44.4 with age minimum and maximum of 10 and 77, respectively. Previous study found mean age of 45.9 in Niamey (Andia et al., 2016), 50.1 in Algeria (Slimani et al., 2014). Regarding the age range affected, RA can occur any age with a tendency in the 25 to 50 years (Le Loët et al., 2006; Slimani et al., 2014, Andia et al., 2016).

The majority of patients lived in urban area (92.8%). Lekpa et al. (2018) found 79.4% living in Dakar. RA was more frequent in urban population than rural individuals. Many environmental factors such as lifestyle would be associated (Hayem, 2002).

The score of imputation is higher than 4 for all adverse reactions. However, adverse effects were observed in

one-third of the patient (28.8%). Serious adverse effects were uncommon. These results confirm the good tolerance of methotrexate described in literature. The low frequency of anemia could be related to folic acid used concomitantly with methotrexate.

Finally, the results show that more of the half of patients was inobservant. Patients more frequently cited stock out in community pharmacy and adverse effects of methotrexate to justify their inobservance. There are also uncommon reasons in patients treated with methotrexate: desire of pregnancy and travelling. According to the literature, the main reason of treatment break was adverse effects (WHO, 2003).

Conclusion

This is the first study assessing the patient's tolerance and observance with methotrexate in Burkina Faso. The results corroborate data in literature suggesting in the one hand, that methotrexate has a good tolerance and in the other hand, that observance with methotrexate is

inadequate for most patients. Therapeutic education and strengthening methotrexate supply chain should be undertaken to improve the care of patients with RA in Burkina Faso.

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CONFLICT OF INTERESTS

The authors have not declared any conflict of interest.

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