Research article

Barriers to the use of methotrexate in Ethiopia for rheumatic diseases: Insights from pharmacy providers

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Abstract

Objectives: African countries with a Low Human Development Index (LHDI) face competing social, economic, and health priorities that distract from the treatment of chronic conditions like Rheumatoid Arthritis (RA). Methotrexate (MTX) is standard of care for RA. We sought to determine MTX availability and dispensing practices of Pharmacy Providers (PP) in Ethiopia, an LHDI country.

Methods: Pharmacy Providers (PP) from across Ethiopia completed a survey regarding their experience with dispensing MTX for the treatment of rheumatic conditions. In addition, a semi-structured interview was conducted with two pharmacists serving the country's sole public rheumatology clinic. We report descriptive statistics from the survey and thematic analysis of the interview.

Results: Twenty-three PP working in hospital and community pharmacies completed the survey. Oral MTX was available in 13% of pharmacies and dispensed by two PP for rheumatic conditions. Only three PP felt comfortable educating patients taking MTX. Interviewed pharmacists identified barriers to MTX use including inconsistent availability for rheumatic diseases, and sub-optimal patient acceptance due to low health literacy combined with social and cultural determinants of non-adherence. Identified needs included specialty-specific tools and recommendations for prescribing, monitoring, and counselling patients regarding MTX that are appropriate to the local health and social environment.

Conclusion: We identified key factors limiting the use of MTX among Ethiopian patients with rheumatic conditions including drug availability, confidence of pharmacists counselling on MTX, and patient confidence in the drug. Enhancing access to MTX and promoting training of health care professionals in patient counselling could optimize the treatment of rheumatic patients in LHDI.

Key words: Methotrexate, Pharmacists, Low Human Development Index, Africa, ILAR, Rheumatoid arthritis

Introduction

African countries with a Low Human Development Index (LHDI) based on life expectancy, education and income per capita, face competing social, economic, health and poverty related issues that distract from the treatment of chronic conditions such as Rheumatoid Arthritis (RA)[1-4]. Methotrexate (MTX) is standard of care for RA and used for many other rheumatic diseases[5].When used and monitored appropriately, it is well-tolerated and effective in reducing morbidity and mortality associated with rheumatic conditions[6,7]. Safe and effective use of MTX requires input from multiple health care providers including dispensing pharmacists. Pharmacists are medication experts with a key role in collaborative care models of chronic disease management[8] and are well positioned to assist with medication use and general management of RA (i.e. reminding and encouraging patients about regular blood-work monitoring)[9].

Ethiopia, with over 102 million inhabitants (45% below the poverty line), is the most populated landlocked country in the world and the second-most populated nation on the African continent[10]. Ethiopia's health status is poor, even when related to other low-income countries including those in sub-Saharan Africa. Ethiopia's main health priorities are communicable diseases which are linked to poverty, poor sanitation facilities, lack of access to safe drinking water, malnutrition, and high migration rates[4]. Health care resources in Ethiopia are limited, and gross inequalities exist in access to health services amongst different regions of the country[1]. The limited number of health institutions, the poor distribution of medical supplies among regions and the disparity between urban and rural areas contribute to the inaccessibility of health care services to the population.

Rheumatology care in Ethiopia is challenging as there is no full time practicing rheumatologist in the country. The single public rheumatology clinic at Tikur Anbessa Specialized Hospital (TASH) in Addis Ababa is attended by rotating non-rheumatologists with limited expertise in prescribing or optimizing doses of methotrexate. In that clinic, the opportunity for patient counselling is limited due to the large number of patients requiring care, and the limited number of care providers (staff physicians and residents)[11]. In this setting, dispensing pharmacists could play a fundamental role to reinforce the safe use of MTX. Using a mixed methods qualitative study design, we sought to determine MTX availability and MTX dispensing practices of Pharmacy Providers (PP) in Ethiopia. This work will inform the development of culturally appropriate strategies to facilitate safe and effective use of MTX to treat rheumatic diseases.

Materials and Methods

Pharmacy providers survey: The Ethiopian Catholic Church– Social and Development Commission (ECC-SDCO) Health Department, a member of The Ecumenical Pharmaceutical Network (EPN), is the second largest health institution in Ethiopia after the public health system. The ECC-SDCO oversees 83 health institutions (5 hospitals, 16 health centres, 2 specialty centres, 60 clinics), 18 hospice centers providing palliative care for terminally ill persons and 5 HIV/AIDS counselling and social service centres. Fifty-two of these centres have a pharmacy department (4 hospitals, 16 health centers and 32 clinics). In September 2016, 23 pharmacists and pharmacy technicians (hereafter referred to as Pharmacy Providers PP) attended the Essentials of Pharmacy Practice course provided by the ECC-SDCO and EPN. Course invitations were based on the population serviced by the different hospitals and health centres and included a random sample of other clinics. All attendees were invited to complete an anonymous written questionnaire regarding their experience with dispensing methotrexate for the treatment of rheumatic conditions. Areas addressed by the questionnaire included local drug availability, MTX counselling practises and personal confidence with counselling patients taking MTX. Descriptive statistics are reported as obtained using SPSS 24 (IBM Software).

Semi-structured interview: To learn about the experience of dispensing MTX pharmacists (n=2) working at the country's sole public hospital with a rheumatology clinic (TASH), we conducted a 45-minute semi-structured interview. TASH is a teaching hospital under Addis Ababa University, College of Health Sciences. In TASH there are approximately 73 PP and 13 dispensaries supplying the emergency department, intensive care units, inpatient wards and outpatient clinics. Both PP had experience working in the inpatient wards and outpatient clinics at TASH and provided written informed consent. Both rheumatologists conducting the interview were familiar with the inpatient medicine wards and the rheumatology clinic at TASH. Interviews were audio recorded and transcribed verbatim. After defining relevant thematic codes, transcripts were reviewed and coded for themes separately by the two rheumatologists who conducted the interviews. Discrepancies usually due to elements fitting more than one theme,were resolved by consensus. Themes related to MTX dispensing patterns and barriers to dispensing were identified. The content of each theme was summarized qualitatively and informative quotations highlighted.

Ethics: The study was approved by the Institutional Review Boards of participating universities. Participants provided informed consent.

Results

Pharmacy providers survey: Twenty-three PP (18 pharmacy technicians; 5 pharmacists; 65% male) from hospitals and health centers of 9 regional states and 2 chartered cities of Ethiopia completed the survey [18/23 (78%) were located outside Addis Ababa]. Seven PP (30%) worked in a hospital-based pharmacy, 12 (52%) in a health center pharmacy and 4 (17%) in other areas (i.e. clinic pharmacy). The number of years of practice[median (range)] was less for pharmacy technicians compared to pharmacists[4 (1-8) vs 10(6-15) $p<0.0001$]. MTX was available in only 3/23 (13%) pharmacies (2 were hospital pharmacies) and only as oral tablets. Five PP reported that MTX was available in the hospital pharmacy of their region. Only 2/23 (9%) PP had dispensed MTX for rheumatic conditions. Only 3(13%) PP reported feeling comfortable educating/instructing patients on how to take MTX, (2 had counseled on MTX, 1 had not). Counselling included need for blood work (n=3), folic acid supplementation (n=3) and restricted alcohol intake (n=1). No PP reported counselling on contraception.

Semi-structured interview: The two interviewed pharmacists worked in the nephrology and rheumatology clinics at TASH for 2-3 years. Both had experience with MTX use mainly for haematology/oncology disorders, the primary reason for prescribing MTX in Ethiopia, but also for rheumatic diseases. Four major themes were identified from the interview:(i) access to MTX for rheumatic disease patients at TASH, (ii) barriers to prescribing MTX, (iii) MTX counselling, and (iv) patient related factors affecting MTX acceptance. Themes and representative quotations are shown in Table 1.

Table 1: Themes and representative quotations from the semi-structured interview

Access to MTX for rheumatic disease patients at TASH
"For patients in this hospital to access MTX the hospital has to buy this medication through open tender…, So even the hospital cannot buy this medication, why, because … since [the] Ministry of Health had a mandate to buy MTX for oncology patients, the hospital doesn't have a chance to buy this medication in the open bid or open tenders."
"If the department - the rheumatology, the renal/ rheumatology department - states that MTX is vital and critical for the management of … RA patients the hospital has to accept this…it is professional judgement and anyone can say this so the hospital … will buy that medication."
"Last year I think … there was a catastrophe. All MTX in the country was out of stock. Most MTX available in [the] market in the community pharmacies is counterfeit or … came into the country in the black market. So we now made it a vital medication for oncology maintenance or for the rheumatic patients but for continuity, there is a sustainability problem… So we are not sure how much or how long the patient can access the medication, even if they are oncology patients."
Additional barriers to prescribing MTX at TASH
"…since [TASH] was the only outpatient oncology centre in [the] country, patients come from all over [the] countryside and from far away so they are given a 4-6 month supply of oral MTX and so [TASH pharmacy] runs out of stock."
MTX counselling practices of PP at TASH
"Pregnancy is a sensitive issue. So first of all, before I try to ask about pregnancy I create a good atmosphere to make the communication easy, then it is easy to ask whether you are pregnant or plan to be."
"…[patients] challenge me because I make the communication easy, I tell them 'I am a pharmacist, don't worry, ask me anything… what you feel'. So they tell me whatever they feel."
Patient factors affecting MTX acceptance
"… most of the patients in our country …their health literacy is poor."
"… there is also in our country cultural and social worries …. In our country, there are adherence issues".

Access to MTX for rheumatic disease patients at TASH: At the time of the interview, all medications for the country were purchased through a central national agency (Pharmaceutical Supply and Funding Agency, PSFA) and regulated by the Federal Food Medicine Health Care Administration and Control Agency. Relevant to MTX, the Ethiopian Ministry of Health has a mandate to purchase oncology medications nationally by the PSFA (including MTX) and covers 50% of their cost for oncology patients. Access to this national supply of MTX is restricted to oncology patients and only accessible in hospitals with oncology programs (6 in Ethiopia including TASH). Further, national MTX supply is often inconsistent with intermittent availability. A second route to accessing MTX exists at TASH if the drug is considered a 'priority medication'. Recently, MTX was included as a "priority medication"primarily for oncology although rheumatology patients can sometimes access this. A third route for rheumatology patients to access MTX is through community pharmacies however, supply is often limited, not available or of uncertain quality, and more expensive.

Parenteral MTX can be prescribed when available however, due to limited experience with using parenteral MTX for rheumatic disease, oral MTX is usually prescribed. Folic acid is readily available and usually co-prescribed. In contrast to the limited availability of MTX, oral corticosteroids are readily available from community pharmacies even without prescriptions. Patients with inflammatory arthropathies can obtain and often take corticosteroids unsupervised for disease management.

Additional barriers to prescribing MTX at TASH: The pharmacists reported that the majority of patients in the rheumatology clinic are not prescribed MTX but instead receive NSAIDs and oral corticosteroids. When prescribed, because of inconsistent supplies, MTX is often only dispensed for short intervals (i.e. a few months). Refills require repeated hospital visits which are not feasible for patients travelling extended distances and/or with financial limitations. This was felt to contribute to treatment nonadherence. Those patients depend on community pharmacies many of which do not stock MTX and if stocked the cost is much higher than at TASH. Some patients resort to obtaining their MTX from unregulated sources at even higher cost.

MTX counselling practices of PP at TASH: At TASH, pharmacists participate in patient counselling and may advise prescribers at the rheumatology clinic regarding medication options. The interviewed pharmacists estimated they identify and counsel approximately 10-20% of clinic patients about MTX. They review the patient's chart for working diagnosis, medication history, and prescribed medications, however they do not check laboratory reports. The pharmacists report that mostly low dose MTX is used however rarely doses up to 20 mg/week are prescribed ('2.5 mg/3x per week or 7.5 mg/ week up to 20mg/week'). Pharmacists discuss indications for using MTX with the prescribing physician according to the patient's medical situation, recognizing that MTX is first line therapy for RA. The pharmacists acknowledge the limited time of the patient-physician encounter and the lack of private areas for physician counselling on MTX at TASH. They emphasized the need to consider cultural and social aspects as well as patients' beliefs while providing MTX counselling. Further they suggest that information

is provided in a simple, culturally appropriate way and reinforced by confirming patients' understanding of the discussion. They indicate that when they counsel, they include a discussion of the benefits and risks of MTX compared to other drugs that patients commonly use for arthritis (i.e. steroids and NSAIDs). The MTX side effects discussed by the pharmacists include haematological myelosuppression, hepatotoxicity, skin rash, central nervous system symptoms (i.e. confusion dizziness), GI side effects and alopecia (temporary).At the same time, patients are reassured about the benefit of MTX, and are encouraged to contact the pharmacists with further questions or concerns if needed. However, in reality there is limited opportunity for follow-up counselling.

Patient factors affecting MTX acceptance: According to the pharmacists, the level of health literacy among the population is generally poor even for otherwise educated individuals. The clinic environment for counselling is suboptimal thus restricting effectiveness of counselling provided by physicians. Despite fear of experiencing adverse effects, patients are generally reluctant to ask questions or address their concerns regarding medications with their physician providers. These concerns, combined with inadequate counselling and lack of clinical improvement when taking MTX (e.g. related to low medication dosing), may lead to unrecognized nonadherence. Cultural and social practices also affect adherence particularly relating to religious fasting days which impact dosing schedules.

Discussion

The survey and interview conducted with PP identified several key aspects limiting the use of MTX for treating rheumatic diseases in Ethiopia. These include availability of the drug in hospitals and pharmacies, experience and confidence of designated pharmacists in supplying and counselling rheumatic disease patients on MTX, and patients' social and cultural concerns related to taking the medication.

A key limiting factor for the use of MTX in Ethiopia is maintaining a consistent availability of regulated MTX for rheumatology patients. While systems are being implemented to address this supply gap for rheumatic disease patients attending TASH, improved availability in hospitals and clinics outside of TASH remains a challenge that will hopefully be improved with increased rheumatic disease awareness.

PP play a key role in counselling patients regarding medication use and monitoring and are important partners in providing medical care, particularly in settings where physician resources are limited[12,13]. Even in North American rheumatology clinics, the degree to which medication risks are discussed by physicians is limited[14,15]. Patients frequently desire additional information regarding their medications yet are often reluctant to discuss their concerns. This hesitation can be even greater in settings where physicians are deemed less accessible due to clinic volume, lack of privacy, or where frequent physician turnover limits the development of patient–physician alliances. The result can be medication nonadherence particularly for patients with low health literacy[16.] Patient education has been identified as one means to improve poor medication adherence in patients with arthritis and other chronic diseases in Africa and globally[17,18]. Pharmacists in Ethiopia recognize their role in providing accurate and appropriate counselling regarding medication use and monitoring[19] and the openness of the TASH pharmacists to address patient concerns is fundamental as physicians are perceived to be less accessible. This pharmacist-directed education is a critical adjunct to physician-provided counselling.

Clear, balanced discussions of risk and benefit are particularly relevant when counselling patients regarding MTX. Common misconceptions often arise regarding the toxicity of low dose compared to high dose MTX. Discussions of potential MTX toxicity that are based on the degree of risk associated with high doses used for oncology create unnecessary concern for patients, families, and care providers potentially leading to nonadherence and reluctance to take the medication even at doses needed for treating rheumatic diseases[20]. At the same time, low dose MTX does require appropriate monitoring to ensure safety as serious toxicity can occur with misuse[5,21]. It is critical that pharmacists provide balanced information on the specific benefits versus toxicity and need for appropriate monitoring. Our survey of Ethiopian PP found, at least for community pharmacists, limited experience with dispensing MTX, and a low level of confidence in counselling patients who are taking or starting MTX particularly for rheumatic diseases. While the TASH pharmacists had more experience, confidence and knowledge regarding the use of low dose MTX, they also recognized the need for specialty-specific treatment recommendations to increase their confidence and that of MTX prescribers. Recommendations on pre-MTX screening and surveillance of patients on MTX, as well as a system to ensure adequate review of monitoring investigations were identified as interventions to increase the safe use of this drug among rheumatology patients.

To be effective, education and counselling methods must acknowledge and incorporate cultural beliefs and practices. This is particularly relevant in Ethiopia where there is a rich history of traditional healing practices and holistic approaches to health and wellness often linked with spirituality[22]. The majority of the population, particularly in rural areas, seek health care from traditional healers and many prefer to use traditional remedies over "Western medicines". This is combined with severely limited formal "Western" health care resources including infrastructure and medication access (or affordability). Importantly for rheumatology, the safety of combining a rheumatologic medication such as methotrexate with traditional therapies is under-studied and open dialogue with patients is needed to monitor for potential unexpected adverse effects.

The pharmacists acknowledged difficulty seeing patients for follow-up counselling. Ethiopia has one of the lowest density of pharmacists per population globally[23] with less than 500 community pharmacists in the country[24]. While individual counselling enables patient-specific information to be provided and concerns addressed, additional patient education tools could contribute to increasing acceptance and adherence to MTX[25]. To be effective, culturally appropriate patient-oriented educational tools, suitable for environments with limited access to modern technology are needed. Strategies and education or counselling programs such as those endorsed by the World Health Organization that safely incorporate traditional practices with "Western medicine" are most likely to be successful[26,27].

The societal impact of RA and rheumatic conditions in Ethiopia is under-recognized. Musculoskeletal conditions are among the leading causes of global physical disability and the burden to individuals and society may be especially acute in LHDI countries due to increased reliance on physical labour[1,28]. In southern Ethiopia, musculoskeletal disorders were the most common chronic medical conditions identified in patients attending outpatient clinics[29]. Although epidemiological data on RA prevalence is lacking for Ethiopia, the prevalence of RA in Africa has been estimated at 0.36% of the population (thus potentially affecting several million population) but varies widely based on region[30]. Since there is no practicing rheumatologist in Ethiopia, the number of undiagnosed (or untreated) RA patients is likely substantial. As awareness of rheumatic conditions increases, the number of individuals prescribed medications such as MTX will also increase highlighting the importance of developing strategies to facilitate optimal care delivery[31]. Care delivery models incorporating pharmacy-physician partnerships similar to those successfully implemented in other chronic diseases are one option.

Improving outcomes for patients with rheumatic disease, particularly in resource limited settings such as Ethiopia, requires a multidisciplinary approach that includes PP. Enhancing access to MTX and promoting training of health care professionals in patient counselling are key measures to optimize the treatment of rheumatic patients in LHDI. Increasing the number of rheumatologists (or other trained clinicians) to identify and accurately diagnose rheumatic diseases, institute and monitor appropriate treatment, and importantly provide patient counselling and support would improve patient acceptance and adherence to MTX. Establishing consistent access to a regulated supply of medication is critical for the effective and safe management of rheumatic diseases. Actionable goals include the development of culturally appropriate educational resources for patients and providers. These measures may ultimately lead to improved outcomes for rheumatology patients in Ethiopia, a country with significant needs, and can potentially be adapted for use in other LHDI African countries.

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