

PDF hosted at the Radboud Repository of the Radboud University Nijmegen

The following full text is a publisher's version.

For additional information about this publication click this link.

<http://hdl.handle.net/2066/88335>

Please be advised that this information was generated on 2019-04-18 and may be subject to change.

SHORT COMMUNICATION

Assessment of antibacterial sale by using the Anatomic Therapeutic Chemical classification and Defined Daily Dose methodology in Moshi Municipality, northern Tanzania

J. VAN DEN BOOGAARD^{1,2*}, H.H. SEMVUA², M.J. BOEREE^{1,3}, R.E. AARNOUTSE¹
and G. S. KIBIKI²

¹Radboud University Nijmegen Medical Centre, P.O. Box 9101, 6500 HB, Nijmegen, The Netherlands

²Kilimanjaro Clinical Research Institute, Kilimanjaro Christian Medical Centre, P.O. Box 2236, Moshi, Tanzania

³University Centre for Chronic Diseases Dekkerswald, Nijmeegsebaan 31, 6561 KE, Groesbeek, The Netherlands

Abstract: This study aimed at evaluating the sale of antibacterials for systemic use to outpatients in Moshi Municipality, northern Tanzania. Trained pharmacy assistants of all fourteen pharmacies in Moshi that are authorized to sell antibacterials for systemic use (part I pharmacies), recorded the sales of antibacterials to outpatients by using the Anatomic Therapeutic Chemical (ATC) classification and Defined Daily Dose (DDD) methodology, during a two-months period. The unregulated availability of antibacterials in drug outlets that are not authorized to sell antibacterials was assessed in 15 randomly selected outlets. The total sale of antibacterials was 4.99 DDDs per thousand inhabitants per day (DID). The penicillins were sold most frequently (2.18 DID; 44%), followed by the quinolones (0.63 DID; 13%), macrolides, lincosamides and streptogramins (0.61 DID, 12%), and the tetracyclines (0.57 DID, 11%). The sale of amoxicillin, the individual drug sold most frequently, was 1.28 DID. Ciprofloxacin was available in all unauthorized drug outlets. Given their wide availability in unauthorized drug outlets, the sale of antibacterials by authorized pharmacies is probably an underrepresentation of the total sale of antibacterials in Moshi. Regulatory measures to control the availability of antibacterials in Tanzania are warranted. Repetition of the study in different seasons and in consecutive years, could reveal highly relevant data on antibacterial consumption trends, which, especially if correlated to data on antibacterial resistance, could help to control communicable diseases.

Key words: Antibacterial sale, Anatomic Therapeutic Chemical (ATC) classification, Defined Daily Dose (DDD) methodology, Tanzania

In developing countries, where the main causes of death continue to be community-acquired infections, the occurrence of antibacterial resistance is a great concern (Okeke *et al.*, 2005a; WHO, 2001). It is widely agreed that antibacterial consumption is the single most important factor responsible for the development of resistance as it induces selective pressure for resistant micro-organisms to multiply (Byarugaba, 2004; Okeke *et al.*, 2005b). The control of antibacterial use in developing countries is hampered by various factors such as immature health care systems, limited diagnostic facilities and unregulated access to drugs. In addition, many developing countries lack surveillance systems for antibacterial use and resistance (Byarugaba, 2004; Radyowijati & Haak, 2003). The wide range of formal and informal drug outlets through which antibacterials are usually available and the

* Correspondence: Jossy van den Boogaard; Email: jossyvandenboogaard@gmail.com

unregulated sale of antibacterials with and without prescription, challenge the systematic monitoring of antibacterial consumption in developing countries (Radyowijati & Haak, 2003). However, health care programmes are being strengthened, the availability of drugs is being regulated more extensively, and policy makers are increasingly aware of the need of improved drug prescription behaviour (WHO, 2001). Adopting a surveillance system for antibacterial use has therefore become a more realistic priority in developing countries.

The monitoring of antibacterial use could be of help in developing interventions for antibacterial drug prescribers, dispensers and users, especially when compared to data on antibacterial resistance (Okeke *et al.*, 2005b). Moreover, the evaluation of antibacterial use over time and between regions can direct the development and adaptation of rational drug use guidelines (Hutchinson *et al.*, 2004; Okeke *et al.*, 2005b; WHO, 2003).

The World Health Organization (WHO) promotes the use of the Anatomic Therapeutic Chemical (ATC) classification and Defined Daily Dose (DDD) system for drug utilization studies (WHO, 2003). The ATC/DDD methodology is based on a standardized drug classification system (ATC) in which drugs are grouped according to their therapeutic, pharmacological and chemical properties, and the use of an 'assumed average maintenance dose per day for a drug used for its main indication in adults' (DDD) as a fixed measurement unit for drug consumption (www.whocc.no/atcddd). Data on drug prescription or sale are usually presented as numbers of DDDs per 1000 inhabitants per day (or, in case of inpatient drug use, as DDDs per 100 bed-days) (WHO, 2003). Provided that there is consistency in applied methodology, the ATC/DDD system is a valuable tool to monitor drug use over time and to compare between regions (Hutchinson *et al.*, 2004).

In this study, the ATC/DDD methodology was used to evaluate the sale of antibacterials for systemic use to outpatients by pharmacies in Moshi Municipality. Moshi is the capital of Tanzania's northern Kilimanjaro Region and has a population of 170500 (Moshi Urban Municipality, 2009). The town is host to one of Tanzania's four university teaching hospitals, a governmental regional hospital, and several private and public clinics and dispensaries. Drug sale is covered by fourteen part I pharmacies that are run by a registered pharmacist and allowed to sell both prescription-only and over-the-counter drugs, and 105 part II pharmacies, or so called *maduka ya dawwa baridi* (literally: shops for cold drugs), that are allowed to sell drugs for minor conditions, but no prescription-only drugs such as antibacterials for systemic use (Center for Pharmaceutical Management, 2003). The sale of antibacterials is not systematically recorded by pharmacies in Moshi. Therefore, little is known about the extent of antibacterial consumption in this part of the world where the burden of infectious diseases is high and the occurrence of antibacterial resistance a serious concern (Blomberg *et al.*, 2004). Data from the current study will help to fill this gap. The data on fluoroquinolone sales in Moshi, which forms part of the data included here, have already been published (Van den Boogaard *et al.*, 2010). Fluoroquinolones are of particular concern in light of their role in anti-tuberculosis treatment regimens.

Data were collected from February 1st 2009 until March 31st 2009 from all fourteen part I pharmacies in Moshi. Pharmacy assistants were trained to document the following on pre-designed and pre-tested forms: generic name of each antibacterial of the ATC J01 class (antibacterials for systemic use, excluding antifungals, antibacterials for tuberculosis and topical antibiotics (www.whocc.no/atcddd)) sold to children and adults during the study period (with and without prescription), the amount, and strength per unit dose. The investigators visited the participating pharmacies frequently (daily in the first week of data

collection and at least once weekly during the remaining study period) in order to monitor the data collection process closely and to assist in case of queries.

The number of DDDs per antibacterial was obtained by: (i) calculating the amount in grams of each dose dispensed (for example, a dose of 14 amoxicillin capsules of 250 mg each corresponds to a total amount of 3.5 gram); (ii) summing the total amount in grams per antibacterial in all fourteen pharmacies; and (iii) dividing this total by the DDD conversion factor obtained from the ATC/DDD index 2009 (available from: www.whocc.no/atcddd). DDDs per 1000 inhabitants per day (DID) were calculated by dividing the number of DDDs per antibacterial by 59 days (the study period) and by 170500 inhabitants, and multiplying by 1000.

To evaluate whether antibacterials for systemic use were indeed *not* available from part II pharmacies, fifteen part II pharmacies were visited by one of the investigators who asked for a dose of ciprofloxacin for systemic use in each pharmacy. The part II pharmacies were randomly selected by using a map of Moshi town and picking three pharmacies from each of five different areas of Moshi.

The study was approved by the Institutional Review Board of the Kilimanjaro Christian Medical Centre, Tanzania.

The DDDs per 1000 inhabitants per day (DID) of the antibacterial chemical subgroups and individual chemical substances are shown in Table 1. In total, the antibacterial sale to outpatients by part I pharmacies in Moshi was 4.99 DID. The penicillins accounted for the largest sale (2.18 DID; 44% of total sale). The quinolones were second most frequently sold (0.63 DID, 13%), followed by the macrolides, lincosamides and streptogramins (0.61 DID, 12%), and the tetracyclines (0.57 DID, 11%). Amoxicillin was the individual chemical substance sold most frequently (1.28 DID). Other frequently sold antibacterials were doxycycline (0.50 DID), ciprofloxacin (0.46 DID), co-trimoxazole (0.33 DID), azithromycin (0.30 DID), metronidazole (0.29 DID), cloxacillin (0.28 DID), and erythromycin (0.26 DID). Ciprofloxacin was available without prescription in all visited part II pharmacies.

To our knowledge, this is the first study in sub-Saharan Africa in which the ATC/DDD methodology was used systematically to evaluate the sale of antibacterials to outpatients. The penicillins accounted for the largest part of antibacterial sale by part I pharmacies in Moshi (44%), and amoxicillin was responsible for more than half of the total sale of penicillins. Other frequently sold broad-spectrum antibacterials were doxycycline, ciprofloxacin, co-trimoxazole, azithromycin and erythromycin.

The use of the ATC/DDD methodology allows for comparison of data between regions. The total sale of antibacterials in Moshi by authorized pharmacies was 4.99 DID; twice as low as in the Netherlands, the European country with the lowest antibacterial use (9.8 DID in 2003) (Ferech *et al.*, 2006). Considering the high burden of infectious diseases in Tanzania (Byarugaba, 2004; Okeke *et al.*, 2005a; Radyowijati & Haak, 2003), the total DID of antibacterials sold in Moshi is surprisingly low. Our study covered all pharmacies in Moshi that are authorized to sell antibacterials for systemic use (part I pharmacies), but did not include pharmacies that are not authorized to sell antibacterials for systemic use (part II pharmacies). Our attempts to buy ciprofloxacin (without prescription) in part II pharmacies were successful in all pharmacies that we visited, suggesting that antibacterials are more widely available in Moshi than from authorized drug outlets only. Therefore, our findings are likely to be an underestimation of the total sale of antibacterials in Moshi.

Table 1: Defined Daily Doses (DDDs) per 1000 inhabitants per day (DID) of antibacterial chemical subgroups and substances (in accordance with the Anatomic Therapeutic Chemical (ATC) coding system) sold in Moshi Municipality

<i>Antibacterial chemical subgroup</i>	<i>DID</i>	<i>Chemical substance</i>	<i>DID</i>
J01AA Tetracyclines	0.57	Doxycycline	0.50
		Tetracycline	0.07
J01BA Amphenicols	0.11	Chloramphenicol	0.11
J01CA Penicillins with extended spectrum	1.39	Ampicillin	0.11
		Amoxicillin	1.28
J01CE B-lactamase sensitive penicillins	0.14	Benzylpenicillin	0.03
		Phenoxymethylpenicillin	0.09
		Benzathine benzylpenicillin	0.01
		Procaine benzylpenicillin	0.01
J01CF B-lactamase resistant penicillins	0.29	Cloxacillin	0.28
		Flucloxacillin	0.01
J01CR Combinations of penicillins	0.36	Amoxicillin/clavulanate	0.03
		Amoxicillin/bromhexin	0.06
		Co-fluampicil	0.06
		Ampicillin/cloxacillin	0.21
J01DB First-generation cephalosporins	0.09	Cefalexin	0.09
		Cefadroxil	<0.01
J01DC Second-generation cephalosporins	0.03	Cefuroxime	0.03
J01DD Third-generation cephalosporins	0.08	Ceftriaxone	0.06
		Cefixime	0.01
		Cefpodoxime	0.01
J01EE Combinations of sulfonamides and trimethoprim	0.33	Co-trimoxazole	0.33
J01FA Macrolides	0.61	Erythromycin	0.26
		Clarithromycin	0.05
		Azithromycin	0.30
J01FF Lincosamides	<0.01	Clindamycin	<0.01
J01GB Other aminoglycosides	0.05	Gentamycin	0.05
J01MA Fluoroquinolones	0.62	Ofloxacin	0.03
		Ciprofloxacin	0.46
		Pefloxacin	<0.01
		Norfloxacin	0.04
		Lomefloxacin	0.04
		Sparfloxacin	<0.01
		Levofloxacin	0.04
J01MB Other quinolones	<0.01	Nalidixic acid	<0.01
J01XD Imidazole derivatives	0.30	Metronidazole	0.29
		Tinidazole	0.01
J01XE Nitrofurantoin derivatives	0.01	Nitrofurantoin	0.01
J01XX Other antibacterials	<0.01	Spectinomycin	<0.01
Total	4.99		4.99

Inadequate control of antibacterial consumption is a known risk factor for the emergence of drug resistance (Byarugaba, 2004). Unfortunately, no data are available on antibacterial resistance in northern Tanzania, but limited data are available from the Dar es Salaam region. The university teaching hospital in Dar es Salaam (Muhimbili National Hospital)

implemented an antibacterial resistance surveillance programme in 1998, and findings of the first 18 months after implementation have been published (Blomberg *et al.*, 2004). High rates of resistance of gram-positive and gram-negative bacteria were found to ampicillin, co-trimoxazole, tetracycline, penicillin, and sulfonamides. The wide, unregulated availability and low cost of these drugs are thought to have contributed to high rates of resistance (Blomberg *et al.*, 2004).

Clearly, regulating the availability of antibacterials is an important strategy in the control of antibacterial use and resistance (Okeke *et al.*, 2005b; WHO, 2001). The Tanzanian Food and Drugs Authority and the Ministry of Health have adopted a plan to replace the part II pharmacies by accredited drug dispensing outlets (ADDOS) in which essential drugs (including some antibacterials for systemic use) are sold by trained dispensers who are under regulatory supervision (Center for Pharmaceutical Management, 2003; Mbwasi & Mlaki, 2008). In the Kilimanjaro Region the process of phasing out the part II pharmacies will start in 2010 (personal communication with Regional Pharmacist).

Some challenges were faced in using the ATC/DDD methodology in Moshi. Drug dispensing is documented manually and there are no electronic databases available through which data on antibacterial sale can be obtained. Calculating total DDDs and DIDs from manually collected data is a time-consuming process.

Limitations to our study include the following. The study was conducted during a single, limited period of time and in a small, urban area only. No differentiation was made between antibacterials sold by prescription and over the counter. No information was obtained on treatment indications and it is not known whether the antibacterials that were sold, were actually consumed. Nevertheless, the results of this study could serve as a starting point for monitoring antibacterial sale in northern Tanzania. Repetition of the study (by applying the same ATC/DDD methodology) in different seasons and in consecutive years, could reveal highly relevant data on antibacterial consumption trends, which, especially if correlated to data on antibacterial resistance, could be of help in the control of infectious diseases. Regulatory measures to control the unauthorized availability of antibacterials in Tanzania are warranted and the implementation of an electronic system to document drug sale by pharmacies is highly recommended.

Acknowledgements

The authors gratefully acknowledge the participation of the owners and assistants of the fourteen Part I pharmacies in this study. Financial support was obtained from the African Poverty Related Infection Oriented Research Initiative, a research network sponsored by the Netherlands-African Partnership for Capacity development and Clinical Interventions against Poverty-related Diseases.

Received 9 February 2010

Revised 26 April 2010

Accepted 27 April 2010

References

- Blomberg, B., Mwakagile, D.S., Urassa, W.K., Maselle, S.Y., Mashurano, M., Digranes, A., Harthug, S., Langeland, N. (2004) Surveillance of antimicrobial resistance at a tertiary hospital in Tanzania. *BMC Public Health* 4:45. doi: 10.1186/1471-2458-4-45.
- Byarugaba, D.K. (2004) A view on antimicrobial resistance in developing countries and responsible risk factors. *International Journal of Antimicrobial Agents* 24, 105-110.
- Center for Pharmaceutical Management (2003) *Strategies for Enhancing Access to Medicines Program. Access to essential medicines: Tanzania, 2001*. Arlington, VA: Management Sciences for Health.
- Ferech, M., Coenen, S., Malhotra-Kumar, S., Dvorakova, K., Hendrickx, E., Suetens, C. & Goossens, H. (2006) European Surveillance of Antimicrobial Consumption (ESAC): outpatient antibiotic use in Europe. *Journal of Antimicrobial Chemotherapy* 58, 401-407.
- Hutchinson, J.M., Patrick, D.M., Marra, F., Ng, H., Bowie, W.R., Heule, L., Muscat, M. & Monnet, D.L. (2004) Measurement of antibiotic consumption: A practical guide to the use of the Anatomical Therapeutic Chemical classification and Defined Daily Dose system methodology in Canada. *Canadian Journal of Infectious Diseases* 15, 29-35.
- Mbwasi, R. & Mlaki, W. (2008) Increasing access to medicines in Tanzania. *Lancet* 372, 205-206.
- Okeke, I.N., Laxminarayan, R., Bhutta, Z.A., Duse, A.G., Jenkins, P., O'Brien, T.F., Pablos-Mendez, A. & Klugman, K.P. (2005a) Antimicrobial resistance in developing countries. Part I: recent trends and current status. *Lancet Infectious Diseases* 5, 481-493.
- Okeke, I.N., Klugman, K.P., Bhutta, Z.A., Duse, A.G., Jenkins, P., O'Brien, T.F., Pablos-Mendez, A. & Laxminarayan, R. (2005b) Antimicrobial resistance in developing countries. Part II: strategies for containment. *Lancet Infectious Diseases* 5, 568-580.
- Radyowijati, A. & Haak, H. (2003) Improving antibiotic use in low-income countries: an overview of evidence on determinants. *Social Science & Medicine* 57, 733-744.
- Van den Boogaard, J., Semvua, H.H., Boeree, M.J., Aarnoutse, R.E., Kibiki, G.S. (2010) Sale of fluoroquinolones in northern Tanzania: a potential threat for fluoroquinolone use in tuberculosis treatment. *Journal of Antimicrobial Chemotherapy* 65, 145-147.
- WHO (2001) *Who Global Strategy for Containment of Antimicrobial Resistance*. WHO/CDS/CSR/DRS/2001.2a. 2001. Geneva, Switzerland.
- WHO (2003) *Introduction to Drug Utilization Research*. World Health Organization, Geneva, Switzerland.