

Prescribing Patterns for Upper Respiratory Tract Infections: A Prescription-Review of Primary Care Practice in Kedah, Malaysia and the implications

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Abstract

Introduction and aims: It is necessary to ascertain current prescribing of antibiotics for upper respiratory tract infections (URTIs) to address potential overuse. A retrospective analysis was conducted of all prescriptions for URTIs among ten public primary healthcare centres in Kedah, Malaysia from 1st January to 31st March 2014. Results: A total of 123,524 prescriptions were screened and analysed. Of these, 7129 prescriptions were for URTI, with 31.8% (n=2269) containing antibiotics. Macrolides were the most commonly prescribed antibiotic constituting 61% (n=1403) of total antibiotics prescribed. There was a statistically significant association between different prescribers and diagnoses ($p=0.001$) and a weak positive trend suggesting family medicine specialists are more competent in antibiotic prescribing, followed by medical officers and assistant medical officers ($\tau=0.122$). Conclusions: Prescribing practices of some prescribers were inconsistent with current guidelines encouraging resistance development. National antimicrobial stewardship programmes and further educational initiatives are ongoing in Malaysia to improve antibiotic use

Key words: Inappropriate use of antibiotics; upper respiratory tract infections; primary healthcare centres; guidelines, antibiotics stewardship programmes; Malaysia

Introduction

Upper respiratory tract infection (URTI) is a non-specific term used to describe acute infections involving nose, paranasal sinuses, pharynx, larynx, trachea, and bronchi caused by several viruses, predominantly rhinovirus [1, 2]. A small proportion of cases (0.5-10%) are sometimes accompanied by bacterial complication, usually from Group A Streptococci [1, 3]. Consequently routinely prescribing antibiotics to treat URTIs is not justified as they have very limited clinical benefit. However, they are frequently prescribed in situations where they are not indicated such as in infections with uncertain bacterial or viral aetiology [4-7]. Hence, URTIs represent a major burden to healthcare systems, especially when inappropriate antibiotic treatment leads to clinical failure and/ or increase in antibiotic resistance. Clinical

failure happens when the prescribed treatment fails to treat the existing infections and patients do not improve or deteriorate [8].

Overall, the majority of antibiotics prescribed in ambulatory care are typically to treat respiratory tract infections [9], with acute upper respiratory illnesses accounting for the highest proportion of ambulatory antibiotic prescriptions [10]. However, the inappropriate prescribing of antibiotics in ambulatory care is a long-standing issue. For example in 1992, ambulatory care physicians in the United States wrote almost 12 million of prescriptions for URIs and acute bronchitis [11]. Of these, 51% of adults with colds were prescribed an antibiotic, 52% in non-specific upper respiratory infections, and 66% in acute bronchitis [11]. Uncontrolled and indiscriminate use of antibiotics in ambulatory care increases the risk of resistance development, augmented by their low cost and easy accessibility despite concerns [11-14].

The World Health Organisation (WHO) warned that the rates of resistance among nosocomial and community-acquired infections are high and need to be addressed [15]. In fact, common infections are now becoming more difficult to treat with standard antibiotics, forcing a shift to newer generations of antibiotics, which are more specific and targeted, but more expensive, and with a higher level of side-effects [15-18]. There is, however, limited number of antibiotics for second-line and third-line therapy particularly in low- and middle- income countries (LMICs), resulting in a greater potential for resistance to first-line antibiotics [19]. In addition, there are concerns with the decline in the number of newly approved antibiotics due to barriers including resource concerns [17, 20, 21]. This will make managing infections increasingly difficult in future years especially among LMICs.

In several countries including Australia, Chile, Europe and Korea, interventions involving key stakeholder groups, including physicians, pharmacists, infection control team as well as managerial staffs have been successfully undertaken [22]. These multifaceted campaigns and interventions have resulted in a significant reduction in antibiotic use as well as expenditures across those countries [22-29]. However, antibiotic consumption continues to be a concern among Asia Pacific countries, where reported rates of antibiotic prescription in ambulatory care centres vary from 11.6% to as high as 82% [30-35]. Malaysia was ranked within the top eight consumers of antibiotics per person in 2010 [36]. Expenditure on systemic antibiotics was the largest expenditure group in 2008 at 433 million Ringgit (US\$121 million) vs. 217 million Ringgit (US\$60.6 million) for medicines to treat diabetes and 191 million Ringgit (US\$53.3 million) for calcium channel blockers. There was also high utilisation of antibiotics in Malaysia's private ambulatory care clinics (third highest category), although lower in public primary healthcare centres [7]. Antibiotic expenditure in Ministry of Health (MOH) primary care centres is steadily increasing and represented 10% of the total drug primary care spending in Malaysia in 2011 [37]. These concerns resulted in multiple initiatives across Malaysia by the government and other bodies. This included the publication of national antibiotic guidelines for infections including URIs and more recently the launch of the Protocol on Antimicrobial Stewardship Programme (ASP) in 2014. These include developing Antimicrobial Stewardship Teams (AMS Teams), engaging both hospitals and primary care centres (Box 1) [37]. Updated national antibiotic guidelines have just been launched (May 2015) in Malaysia, which include a mobile phone application to facilitate and promote access among prescribers as well as the public [38]. In addition, there are also strict instructions regarding the issuing of prescriptions among healthcare professionals within primary healthcare centres in Malaysia. Restrictions on the prescribing of certain antibiotics among the healthcare professionals have also been emphasized in the national antibiotic guidelines (Box 1).

Box 1 – Current situation and initiatives for improving antibiotic prescribing for URTIs among physicians and other professionals including those in primary healthcare centres

A) Prescribing guidance for URTIs in primary healthcare centres in Malaysia

Medicines in the Ministry of Health (MOH) Drug Formulary are listed according to the category of prescriber-authorization (Dental Consultant, Dental specialist and Dental Officers are also included in these categories but only for medicines used in dental treatment):

| Category | Prescribers |
|----------|--|
| A* | Consultant/specialists for specific indications only |
| A | Consultant/specialists |
| A/KK | Consultant/specialists/family physician specialists |
| B | Medical officers |
| C | Paramedical staff |
| C+ | Paramedical staff doing midwifery |

| | | | Category of Prescribers** |
|----------------|---------|-------------------------|---------------------------|
| Macrolides | J01FA | Erythromycin | B |
| | | Cloxacillin | B |
| Penicillins | J01CA | Penicillin V | C |
| | | Amoxicillin | B |
| | | Amoxicillin+Clavulanate | A/KK |
| Cephalosporins | J01DB/C | Cefuroxime | A/KK |
| | | Cephalexin | B |
| Tetracyclines | J01AA | Doxycycline | B |
| Sulfonamide | J01EE | Co-Trimoxazole | B |
| Others | | Others | |

** MoH Drug Formulary No.1/2015

Summary:

- FMS can prescribe all categories (A/KK, B and C) of drugs
- MOs only can prescribe category B and C , need approval and countersigned from FMS if they want to prescribe category A/KK drugs
- AMOs can only prescribe category C, need approval and countersigned from MO or letter of authorization if they want to prescribe category B drugs

B) Current regulations for the prescribing of antibiotics for URTIs

- FMS – All available suggested antibiotics for URTIs including: Tetracyclines (J01AA) –doxyxcline; cephalosporins (J01DB/C) – Cefuroxime and cephalexine; penicillins (J01CA) – penicillin V, amoxicillin and amoxicillin + clavulanate, cloxacillin; Sulfonamides (J01EE) – co-trimoxazole; macrolides (J01FA) – erythromycin. Quinolones are not on the formulary for URTIs (FMS physicians manage referral patients from MOs, i.e. typically more complex cases)
- MOs: Penicillins – Penicillin V and amoxicillin; macrolides - erythromycin
- AMOs– penicillin V. AMOs can also issue repeat prescriptions but these must be counter-signed/ letter of authorisation by a physician including the MO in the primary health centre. Each AMO has a Diploma of Medical Assistant. They are seen as an efficient method to enhance access to healthcare professionals given often the limited number of MOs and FMS within public healthcare system and the large number of patients seeking medical help.

C) Key goals/ initiatives under the Antimicrobial Stewardship Programme (ASP)

a) General

- To improve patient outcomes (e.g. reduce morbidity and mortality from infection)
- To optimize antimicrobial therapy, by promoting judicious use of antimicrobials, optimizing

antimicrobial selection, dosing, route and duration of therapy in order to maximize clinical cure or prevent infections.

- To limit unintended consequences of antibiotic prescribing such as the emergence of antimicrobial resistance and adverse drug events.
 - To reduce healthcare cost without adversely impacting quality of care.
- b) For Primary Healthcare Centres
- Ensure implementation of ASP strategies and activities.
 - Establish formulary restriction and approval systems especially for broad-spectrum antimicrobials.
 - Ensure implementation of *National Antibiotic Guideline*, treatment guidelines and clinical pathways for common infections (updated in 2015)
 - Ensure necessary action is taken based on surveillance findings.
 - Educate the public, physicians, pharmacists and paramedics about good antimicrobial prescribing practice and antimicrobial resistance
 - Evaluate and report surveillance and clinical audit findings and future audit meetings discussing future management approaches

NB: FMS = Family Medicine Specialist; MO = Medical Officer and AMO = Assistant Medical Officer

We have recently published a systematic review regarding the knowledge, perceptions, and behaviour of physicians concerning antibiotic prescribing to guide future strategies [22]. We also recently published a study describing the prescribing of antibiotics for patients with URTIs among private physicians in Malaysia [39]. We found that when assessed against antibiotic knowledge assessment criteria, most general practitioners (GPs) had a moderate level of knowledge of prescribing for URTIs. However, antibiotic prescriptions could be appreciably reduced as a large number of GPs (85.5%) reported that they could reduce antibiotic prescriptions by more than 25% without jeopardizing the outcome of the URTIs. As a result, helping to reduce future development of antibiotic resistance [39].

We are aware there is paucity of data on antibiotic prescribing rates among primary healthcare centres in the public healthcare system in Malaysia. These data are important as a baseline for assessing the influence of the recently updated national antibiotic guidelines as well as the recent Antimicrobial Stewardship Programmes in Malaysia. Consequently, we undertook a prescription analysis to document URTI-specific antibiotic prescription rates in public primary healthcare settings in Malaysia prior to these recent initiatives. Furthermore, we aimed to investigate the choice, proportion, and adherence to the guidelines of oral antibiotics prescribing in patients diagnosed with URTIs among the different healthcare professionals in the public sector. Future interventions, if needed, can be planned under the new antimicrobial stewardship programme and the national antibiotic guidelines.

Methods

Study design and prescription selection criteria

A retrospective prescription analysis was conducted whereby all prescriptions from 1st January 2014 to 31st March 2014 were screened and retrieved for further investigation. Prescriptions with diagnosis of 'URTI', 'tonsillitis', 'pharyngitis', 'rhinitis', 'common cold', 'sore throat', 'cough', or 'otitis media' were included in the study. Incomplete prescriptions, missing diagnosis, or prescriptions with more than one infection were excluded from the study. This was done to avoid or minimize uncertainty of the diagnosis and the purpose of antibiotics in the prescription.

Identification of URTI diagnosis

All prescriptions were in hard copies, retrieved manually from the pharmacy units from each clinic. The selection of prescriptions to be included in the study was based solely on the written diagnosis on the prescription, i.e. the written diagnosis and prescribed treatment. We did not verify the validity and accuracy of the diagnosis as we did not have access to specific clinical data for each patient diagnosed with a URTI including their symptomatology or laboratory results. . URTIs were defined, similar to several studies in literature, as any encounter with the diagnosis of upper respiratory tract infection including pharyngitis, acute tonsillitis, acute sinusitis, rhinitis and otitis media. Other diagnosis and symptomatic

encounters such as cough and sore throat were also included as separate diagnosis based on their frequent encounters at the healthcare clinics and strong association with respiratory complaints [34,39,40-43]. The prescriptions were screened manually by a trained data collector, who is a qualified and practicing pharmacist and has a considerable experience and competence in this regard.

Classification and appropriate prescribing of antibiotics

We reviewed the appropriateness of the antibiotic prescribing based on the recommendations contained in the Malaysian National Antibiotic Guidelines. Subsequently, we evaluated prescribers' conformity to the guidelines before the implementation of the more comprehensive surveillance programme in conjunction with the launch of the ASP protocol among the healthcare centres in Malaysia [44]. The classification of antibiotics used in this study was adapted from WHO Action Programme on Essential Drugs, International Network for the Rational Use of Drugs, and the Malaysia National Antibiotic Guideline 2008. The antibiotics included in the study were oral antibiotics listed in the formularies of the primary healthcare clinics (Box 1). Patient's age, diagnosis, choice of antibiotics (if prescribed) and the type of prescriber were reported on Microsoft Excel spread sheet.

Study settings and sampling

The study targeted all primary public healthcare centres (n=10) in the district of Kota Setar in the State of Kedah, Malaysia. Health care in Malaysia is provided through both the public and private sector. The public health care system provides services through a network of tertiary care centres, general hospitals, district hospitals, and primary health clinics [45]. All of these centres are centrally administered by the Ministry of Health (MoH) and fully subsidised by the government [45]. In total, there are 897 healthcare clinics in Malaysia scattered throughout the country [46]. In every district, there are health district offices managing a number of primary health clinics. Kota Setar is the second largest district in Kedah with a total population of 366,787 [47], with one major hospital as a referral centre and 10 healthcare clinics, serving patients for their primary medical care needs..

Multiple services are provided at these clinics, including general outpatient services, maternal and child health services for the urban and sub-urban population of Kota Setar. Other services include family health, dental, dietetics and nutrition, health education and promotion, home nursing, radiology, pharmacy, adolescent health and community mental services. During this study period, eighty-three prescribers were attached to the general Outpatient Department (OPD) and Maternal Child Health Clinic (MCH) in all centres. These include 43 medical officers (MOs), 36 assistant medical officers (AMOs) and 4 family medicine specialists (FMSs) (Box 1). Total patient attendance at all healthcare clinics in Kota Setar District during the study period was 135,320 cases. All of the cases presented at the clinics were attended by these prescribers. Nurses who see the large portions of patients at the MCH clinics were excluded from the study as they were not allowed to prescribe antibiotics.

The age of the patients in this study were divided into age groups of ten years for consistency as we were not looking specifically at children versus adults but the general prescribing of antibiotics for URTIs.

Statistical analysis

The data was entered into Microsoft Excel spread sheet, and then exported to the Statistical Package for the Social Sciences (SPSS), version 20 for further analysis. The Kolmogorov-Smirnov test was used for testing the normality of the sample distribution. Both descriptive and inferential statistics were used for data elaboration. Frequencies and percentages were used to summarize the data. The Jonckheere–Terpstra test was used to evaluate the trend of association between the tendencies of different group of prescribers; i.e. the FMS with the higher qualified education compared to MOs and AMOs with lower qualifications towards prescribing antibiotic according to the national antibiotic guideline. Where significant associations were reported, effect size was calculated by using Kendall tau correlation coefficient. P value of <0.05 was considered to be of statistical significance.

Ethical approval

The Medical Research and Ethics Committee Ministry of Health, Malaysia approved the study. The study was registered with National Medical Research Register of Malaysia under identity number: NMRR-13-1231-16769.

Results

Over the three months, 123,524 prescriptions were screened and analysed according to the established inclusion and exclusion criteria. 49,251 prescriptions were excluded as they were appointment-based prescriptions mainly for chronic conditions. Others were excluded due to criteria as mentioned above. A total of 7129 (5.8%) URTI prescriptions met the inclusion criteria, of which 2269 (31.8%) prescriptions contained antibiotics. Among the ten centres, four clinics with the highest number of patients' attendance (Clinic 2, 4, 6 and 9) contributed to 58.8% of all URTI attendances as shown in Table 1.

Table 1: Prescribing activities at the 10 clinics of District Kota Setar, Malaysia

| Clinics | Screened prescriptions | Prescriptions with diagnosis of URTI (%) |
|----------------|-------------------------------|---|
| Clinic 1 | 8736 | 783 (11.0) |
| Clinic 2 | 20652 | 1011 (14.2) |
| Clinic 3 | 10243 | 591 (8.3) |
| Clinic 4 | 12359 | 1073 (15.0) |
| Clinic 5 | 9683 | 411 (5.8) |
| Clinic 6 | 26662 | 1135 (15.9) |
| Clinic 7 | 6884 | 353 (4.9) |
| Clinic 8 | 8522 | 365 (5.1) |
| Clinic 9 | 12962 | 654 (9.3) |
| Clinic 10 | 6821 | 753 (10.6) |
| Total | 123,524 | 7129 |

As seen in Table 2, 3445 (48.3%) prescriptions with URTI symptoms were filled for patients (20 years old or below) compared with older patients (21 years or above). Little variation was reported between the proportion of cases attended by medical officers (n=3946, 55.3%) and assistant medical officers (n=3117, 43.7%) with equal tendency among both to prescribe antibiotics (34.0% and 29.5% respectively). Tonsillitis, otitis media and pharyngitis were listed as major conditions for which antibiotics were prescribed (91.3%, 89.8%, and 84.2% respectively).

Table 2: Study characteristics by age, prescriber status and diagnosis

| Characteristics | Number of prescriptions | Prescription with antibiotics N (%) |
|-------------------------------|-------------------------|--|
| Patients' age (years)* | | |
| 1-10 | 1968 | 644 (32.7) |
| 11-20 | 1477 | 498 (33.7) |
| 21-30 | 916 | 314 (34.3) |
| 31-40 | 673 | 219 (32.5) |
| 41-50 | 562 | 185 (32.9) |
| 51-60 | 631 | 165 (26.1) |
| >60 | 685 | 165 (24.1) |
| Prescriber status | | |
| Family Medicine Specialists | 66 | 7 (10.6) |
| Medical officers | 3946 | 1341 (34.0) |
| Medical assistants | 3117 | 921 (29.5) |
| Diagnosis | | |
| Nonspecific URTI | 6398 | 1752 (27.4) |
| Tonsillitis | 264 | 241 (91.3) |
| Pharyngitis | 209 | 176 (84.2) |
| Rhinitis | 37 | 11 (29.7) |
| Common Cold | 79 | 18 (22.8) |
| Sore Throat | 36 | 14 (38.9) |
| Cough | 57 | 13 (22.8) |
| Otitis Media | 49 | 44 (89.8) |

*Missing values=217

Table 3 presents the frequency of antibiotics prescribed to patients. Among all antibiotics, macrolides (erythromycin ethyl succinate) were the most commonly prescribed antibiotic, constituting of 61% (n=1403) of total antibiotics prescribed for all cases, followed by the penicillin group 790 (34.8%). The range of preferred antibiotics among the different groups of prescribers did not vary. However, more than half of patients were prescribed macrolides after consultations with AMOs (55.2%), compared to 44.2% and 0.5% following MO and FMS consultations respectively.

Table 3: Choice of antibiotics prescribed for URTIs

| Antibiotic class | ATC Code | Name of antibiotic | Prescriptions for URTIs | Prescribed by FMSs N (%) | Prescribed by MOs N (%) | Prescribed by AMOs N (%) |
|------------------|----------|-------------------------|-------------------------|--------------------------|-------------------------|--------------------------|
| Macrolides | J01FA | Erythromycin | 1403 | 7 (0.5) | 621 (44.2) | 775 (55.2) |
| | | Cloxacillin | 31 | 0 (0) | 14 (45.2) | 17 (54.8) |
| Penicillins | J01CA | Penicillin V | 20 | 0 (0) | 15 (75.0) | 5 (25.0) |
| | | Amoxicillin | 698 | 0 (0) | 582 (83.4) | 116 (16.6) |
| | | Amoxicillin+Clavulanate | 41 | 0 (0) | 37 (90.2) | 4 (9.8) |
| Cephalosporins | J01DB/C | Cefuroxime | 53 | 0 (0) | 51 (96.2) | 2 (3.8) |
| | | Cephalexin | 11 | 0 (0) | 10 (90.9) | 1 (9.1) |
| Tetracyclines | J01AA | Doxycycline | 2 | 0 (0) | 2 (100) | 0 (0) |
| Sulfonamide | J01EE | Co-Trimoxazole | 2 | 0 (0) | 2 (100) | 0 (0) |
| Others | | Others | 8 | 0 (0) | 7 (87.5) | 1 (12.5) |

ATC: Anatomical Therapeutic Chemical

Among all URTI cases, erythromycin was the most favoured antibiotic in more than 50% of cases, except for otitis media. Amoxicillin was preferred as the treatment of choice in otitis media (68.2%). The choice of prescribed antibiotics is described in Table 4.

Table 4: Antibiotic prescription against specific diagnosis

| Diagnosis | Cases prescribed with antibiotics | Type of antibiotic prescribed | | | | | | | | | |
|------------------|-----------------------------------|-------------------------------|-------------|--------------|-------------|---------------------------|------------|------------|-------------|----------------|---------|
| | | Erythromycin | Cloxacillin | Penicillin V | Amoxicillin | Amoxicillin + Clavulanate | Cefuroxime | Cephalexin | Doxycycline | Co-Trimoxazole | Others |
| | | N (%) | N (%) | N (%) | N (%) | N (%) | N (%) | N (%) | N (%) | N (%) | N (%) |
| Nonspecific URTI | 1752 | 1110 (63.4) | 26 (1.5) | 9 (0.5) | 526 (30.0) | 25 (1.4) | 38 (2.2) | 11 (0.6) | 1 (0.1) | 2 (0.1) | 4 (0.2) |
| Tonsillitis | 241 | 141 (58.5) | 2 (0.8) | 9 (3.73) | 72 (29.8) | 9 (3.7) | 8 (3.3) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Pharyngitis | 176 | 104 (59.1) | 0 (0.0) | 1 (0.6) | 60 (34.1) | 4 (2.3) | 7 (4.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Rhinitis | 11 | 6 (54.5) | 0 (0.0) | 0 (0.0) | 4 (36.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (9.0) | 0 (0.0) | 0 (0.0) |
| Common Cold | 18 | 14 (77.8) | 0 (0.0) | 0 (0.0) | 4 (22.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Sore Throat | 14 | 13 (92.9) | 1 (7.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Cough | 13 | 10 (76.9) | 0 (0.0) | 1 (7.7) | 2 (15.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Otitis Media | 44 | 5 (11.4) | 2 (4.5) | 0 (0.0) | 30 (68.2) | 3 (6.8) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 4(9.1) |

The Jonckheere–Terpstra test revealed a statistically significant association between the status of the prescriber and the diagnosis ($p=0.001$). Furthermore, a weak positive trend was reported with FMS physicians being more competent in antibiotic prescribing based on their diagnosis, followed by medical officers (MOs) and assistant medical officers (AMOs) ($\tau=0.122$). No significant association, however, was reported among other study variables.

Discussion

This study highlighted the frequent use of antibiotics for upper respiratory tract infections at public primary care settings in Malaysia (Table 2). The prescription rate for URTI was higher than the rate observed in another published study on primary care in Malaysia [34]. However encouragingly, the antibiotic prescribing rate in URTIs in this study appeared to be lower than reported in other recent studies. For example, antibiotics were prescribed in more than 60% for URTI cases in a Malaysian district hospital in 2011 [40], and 53% of outpatient prescriptions in China's primary healthcare facilities in 2009 through 2011 [48]. The differences in rates could be explained by different natures of the denominator used in these studies as well as the study setting, data collection period, and the difference in the types and availability of antibiotics. It was found in this study, among all screened prescriptions, 5.8% were for URTIs, of which 32% contained antibiotics principally for patients over 20 years old (Table 2).

As documented in the literature and guidelines, only a very limited number of patients with URTIs warrant antibiotic treatment [49-53]. However, this study has found antibiotics were frequently prescribed for tonsillitis, otitis media and pharyngitis (Table 2). According to the Center for Disease Control and Prevention (CDC), there are several criteria which should be taken into account when diagnosing URTIs. This include the presence of tonsillar exudates, tender anterior cervical adenopathy, history of fever, and lack of cough [38,54]. Patients with none or only one of these findings during clinical examination should not be treated with antibiotics [54]. Therefore appropriate clinical judgement is fundamental, in addition to ascertaining the bacterial aetiology before antibiotics should be prescribed [54]. This practice could be enhanced by local antibiotic guidelines, as well as up-to-date information regarding antibiotic use [22]. Prescribers should be well trained and educated regarding pertinent guidelines and initiatives to maximize the benefits of antibiotics and reduce potential resistance through making the right choices and dosing. This is especially important as successful reduction in antibiotic use could result in a rapid drop in resistance rates. This was shown in an observational Japanese study where the authors found that 62% of Group A streptococcal isolates were resistant to erythromycin when macrolides accounted for 22% of all antibiotic use in 1974 [55]. By 1988 when the prescribing of macrolides was reduced to only 8% of total antibiotic use, less than 2% of group A streptococcal isolates were resistant to erythromycin [55].

Another potential area of concern discovered in this study is the greater prescribing of antibiotics by AMOs compared with MOs and FMS physicians in the primary care centres (Table 2). This is despite the fact that AMOs should not initiate antibiotics on their own with the exception of penicillin V, but must have prescriptions countersigned by MO and FMS. However, this could be explained by the fact that the proportion of patients seen by MO and AMOs are almost equal in public primary healthcare centres. Moreover, AMOs play integral role in screening and provision of medical care to patients, including prescribing for ailments such as URTIs [40]. Because of this, in most clinics AMOs appear to prescribe antibiotics which are not in their prescription category without referring the case to the MOs or seeking approval from the MOs. This is against current guidelines, clearly explained in the MOH Drug Formulary (Box 1).

Overall, we believe from the findings that the extent of antibiotics used and the variation in prescribing between the different prescribers in the primary healthcare centres (Table 2) may be attributed to a number of factors. We know biomedical factors such as the characteristic of the disease, the clinical presentation of the patients, as well as choice of medicines and prescribers' knowledge, provided key inputs into the decision making [22]. However, other factors ranging from attitudes of the prescribers and patients, to managerial constraints and policies can also influence the prescribing decision [22]. For instance, FMS physicians only see refractory cases so may not see URTI patients initially – only when the infection persists or when cases are referred to them by the medical officers, which may be rare in practice. Variations in choice of antibiotics as well as the use of antibiotics can also be potentially explained by other factors. These include firstly, the limited selection of antibiotics that can be prescribed by an MO and AMO, if countersigned and repeated, versus the greater selection of antibiotics available to FMS physicians for prescribing (Box 1). Secondly ease of dosing, since

erythromycin is administered twice daily compared to the penicillin group, which require three to four administrations per day. Thirdly, primary care centres are busy places with long waiting times. In view of this, it may be quicker for an MO or AMO to prescribe and/ or recommend an antibiotic rather than take considerable time to explain why they are not necessary.

Consequently, health policy makers need to take steps to address these issues. Potential next steps should include provision of education among AMOs and MOs with the implementation of new antimicrobial stewardship programme and the guidelines. These include emphasizing the use of penicillins if needed as first line treatment for URTIs rather than macrolides (Box 2). In addition, greater education should be fostered among patients, that antibiotics are rarely needed for URTIs and their inappropriate use will increase antibiotic resistance, building on the current ASP initiatives (Box 1). In future, potentially greater swabbing or sensitivity testing could be done as a regular practice as testing kits become routine and inexpensive, given the number of patients typically seen each day in primary healthcare centres.

Box 2 – Updates on Antibiotic Guidelines, the Antimicrobial Stewardship Programme

A) Antimicrobial Stewardship Programme updates

- July 2015 - ASP Roadshow to all regions in the country to provide regular updates on antimicrobial prescribing, practice and usage for healthcare professionals as well as strengthening the implementation of ASP in all healthcare facilities.
- In the ASP, prescribing restrictions have again been emphasized as well as emphasizing that prescribers should comply with local as well as the national drug formularies including which antibiotics for given situations

B) The new National Antibiotic Guideline (NAG)

1. In formulating the current edition of NAG, numerous considerations were taken into account including changes in antimicrobial resistance patterns in various sectors of clinical practice, trends in antimicrobial utilization, current guidelines and new clinical data.
2. For URTIs:
 - For the general sore throat, the modified Centor score as described by McIsaac et al [56] has been introduced in the new guideline to help physicians decide which patients need no testing, throat culture/rapid antigen detection testing or empiric antibiotic therapy. This is a clinical score to reduce unnecessary antibiotic use in patients with sore throats.
 - Penicillin V is still recommended as first line treatment for tonsillitis/pharyngitis with changes in dosage frequency from 8 hourly to 12 hourly. It is in Category C, so it can be prescribed by all groups of prescribers from AMOs to FMS.
 - Erythromycin has been removed as a preferred treatment in URTIs due to high resistance patterns. Other macrolides such as Azithromycin and Clindamycin have been introduced as replacements.

We acknowledge that there are a number of limitations in this study. Firstly, we only carried out the study among public health centres in Kedah. However we believe for the reasons documented, including the fact that the same antibiotic guidelines and ASP are implemented throughout public health centres in Malaysia, and that these centres are centrally administered by the MOH with the same policies, that this does represent the public sector in Malaysia. In addition, we excluded antibiotic prescriptions where more than one indication, where there were incomplete prescriptions or missing diagnoses, for the reasons stated earlier. We also acknowledge that the diagnoses of URTIs were based on the written diagnosis on the prescription and we did not verify the accuracy of the clinical examination and diagnosis with the prescribers for the reasons documents. However, this is similar to a number of database studies where no additional information is included apart from the diagnosis and the prescription. Despite these limitations, we believe this is a step forward from our first paper with Private GPs in Malaysia where we were just asking them for their treatment intentions based on various scenarios. As such, this paper provides a better reflection of the current situation regarding antibiotic prescribing in Malaysia.

Finally, we acknowledge we have not undertaken interviews with the various healthcare professionals and groups to ascertain the rationale behind their prescribing of antibiotics for URTIs. Nevertheless in spite of these caveats, we believe our findings do provide an insight into the current management of URTIs among public facilities in Malaysia to help develop and refine future guidance, building on the

recent Antimicrobial Stewardship Programme and the updated version of National Antibiotic Guideline which have recently been launched in Malaysia (Boxes 1 and 2). This will be the subject of future research following dissemination of the new Antimicrobial Stewardship Programmes and guidelines (Boxes 1 and 2). The development of scoring systems such as the recently introduced scoring system for sore throats in the updated version of National Antibiotic Guidelines will also be closely monitored as part of future research projects.

Conclusion

The prescribing of antibiotics for the management of URTIs in the public sector was found to be inconsistent with current guidelines. Proper use of antibiotics is not just the professional role of doctors, but can help prevent the emergence of antibiotic resistance. Consequently a better understanding of appropriate antibiotic prescribing must be fostered among prescribers to improve their use. This includes enhancing physician adherence to standard treatment practices, including reserving antibiotic prescribing for URTIs as they are typically viral in origin, as well as prescribing penicillins first line where needed. The introduction of the national antimicrobial stewardship program and guidelines in Malaysia should help with planning future initiatives among the primary healthcare centres in Malaysia to enhance the appropriate prescribing of antibiotics. This will be the subject of future research projects, building on the current findings.

Declaration of interests

Mardhiyah Bt Kamal, Rosminah binti Mohd. Din and Dr Faridah Aryani Binti Md. Yusof are employed by the Ministry of Health in Malaysia. Otherwise, the authors have no conflict of interest to disclose. No funding was received for this study. However, there was a small grant from the Karolinska Institute to help with the writing of the paper.

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Key points

- There have been recent initiatives in Malaysia to improve the prescribing of antibiotics for upper respiratory tract infections (URTIs) among prescribers in primary healthcare centres. These include guidelines and Antibiotic Stewardship Programmes
- To assess the need for further initiatives to improve the prescribing of antibiotics for URTIs, it is necessary to ascertain current prescribing practices. Consequently, a retrospective analysis was conducted of all prescriptions for URTIs among primary healthcare centres from 1st January to 31st March 2014.
- During this period, 123,524 prescriptions were screened and analysed of which 7129 prescriptions were for URTIs, with 31.8% (n=2269) containing antibiotics
- There was appreciable tendency of medical officers and assistant medical officers to prescribe antibiotics for the management of URTIs when a prescription was issued (34.0% and 29.5% respectively) versus only 10.6% for Family Medicine Specialists. Tonsillitis, otitis media and pharyngitis were the most common indications for antibiotics
- Macrolides were the most commonly prescribed antibiotic constituting 61% of total antibiotics prescribed despite the fact that penicillins are the recommended first line treatment. Erythromycin has been removed from national guidelines due to high resistance patterns replaced by azithromycin and clindamycin
- Whilst there appears to be a reduction in the prescribing of antibiotics in primary healthcare centres in this study versus previous studies, there are areas of concern with some prescribing inconsistent with current guidelines. National antimicrobial stewardship programmes and further educational initiatives are ongoing in Malaysia to improve antibiotic use, and their impact needs to be monitored in the future.

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