Research Article

Antibiotic Prescribing Practice for Paediatric Outpatients across Non-specialised Regional Hospitals in Kedah State, Malaysia.

Guo Hong Tan[1], Huan Keat Chan[2], Linda Mohd Jamal[3], Muhammad Hazwan Hamidon[3], Aun Chyi Oi[4], Yae Tyug Yap[4], Yu Hsuan Khoo[5].

Received on:
09-Aug-2018

Accepted for Publication:
23-Aug-2018

Correspondence to:
Huan-Keat CHAN
huankeat123@yahoo.com

Author's Affiliation:
1. Pharmacy Department, Sik Hospital
2. Clinical Research Centre, Sultanah Bahiyah Hospital
3. Pharmacy Department, Yan Hospital
4. Pharmacy Department, Baling Hospital
5. Pharmacy Department, Kuala Nerang Hospital

ABSTRACT

Background

The Malaysia National Antibiotic Guidelines (NAG) is used to guide antibiotic prescribing, especially among public healthcare facilities without an in-house infectious disease specialist, setting-based antibiotic guidelines and clinical microbiology services.

Aims

To explore the patterns of antibiotic utilisation in children, and to assess the adherence level of antibiotic prescribing to NAG.

Methods

A three-month cross-sectional study was undertaken at four non-specialised regional hospitals in Kedah State, Malaysia. All prescriptions which contained at least one oral antibiotic for outpatients below 13 years-old were reviewed. The information including patient demographics, diagnosis, and type and dosage of antibiotics prescribed were recorded. The antibiotic regimens were then compared to NAG.

Results

Of 3,359 paediatric prescriptions reviewed, 909 prescriptions (27.1%) contained at least one oral antibiotic and were analysed. The antibiotics were most commonly prescribed for otorhinolaryngology infections (73.6%), followed by skin and soft tissue infections (13.1%), and community acquired pneumonia (4.6%). The most frequently prescribed antibiotics were amoxicillin (34.9%), phenoxymethylpenicillin (25.6%), and cloxacillin (15.3%). Non-adherence to the NAG's recommendations was found in 71.8% (653) of the prescriptions, particularly in the drug selection (35.8%) and the dosage used (64.1%).

Limitations

The information used for the analysis was based solely on what was written on prescriptions. Furthermore, nearly a quarter of the prescriptions received were excluded from the analysis due to insufficient information on the diagnosis.

Conclusion

Majority of the antibiotics prescribed were discordance with the NAG recommendations. This suggests potential inappropriate antibiotic use and warrants approaches to improve the paediatric antibiotic prescribing practice among the non-specialised hospitals.

Key words: Antibiotic, Outpatients, Paediatrics, Inappropriate Prescribing, Malaysia.

Introduction

Children constitute 26% of the world population, and therefore their health and well-being have been an area of concern.[1] It is noteworthy that the majority of paediatric patients presenting to the hospitals have been seeking treatment for acute infections, entailing a high usage of antibiotics.[2-4] Despite the introduction of the Antimicrobial Stewardship Program worldwide, inappropriate antibiotic utilisation was still commonly reported.[5-8] This has resulted in increasingly severe antimicrobial resistance in paediatric patients,[9,10] which eventually leads to treatment failure and increased medical costs.[11-12]

Hence, in order to promote the rational use of antibiotics in public health care centres, the National Antibiotic Guideline (NAG) was launched in Malaysia in 2008.[13,14] It has since then been used by physicians as the most important guide for antibiotic prescribing, particularly in hospitals and health clinics where in-house infectious disease specialists, local antibiotic guidelines and clinical microbiology services are unavailable. As the previous studies related to antibiotic prescribing in Malaysia focused mainly on the adult patients and practices in health clinics,[15-17] the current study was designed to specifically assess the antibiotic prescribing patterns in paediatric outpatients, and to investigate the level of adherence to the NAG among the prescribers in public secondary hospitals.

Methods

This cross-sectional study was undertaken between 1st January and 31 March 2017 at the outpatient departments of four selected secondary hospitals in Kedah state, Malaysia, which were operated by 27 medical officers and 10 medical assistants. The study proposal was registered with the National Medical Research Register, Malaysia (NMRR-17-910-35784), and was approved by the Medical Research Ethics Committee, Malaysia.

All the prescriptions of outpatients below 13 years of age received by the four hospitals during the study period were screened by the investigators (pharmacists). The prescriptions containing at least one oral antibiotic were retained for further analysis, except for those of the patients referred from other health care centres. The information on each of the prescriptions, including patients' age, gender, body weight, diagnosis, and the types and dosage of antibiotics prescribed, was recorded in a data collection form. Subsequently, the prescribing patterns of antibiotics were investigated, while the drug selection and dosage in each of the cases were compared with the NAG's recommendations. The data analysis was performed using the Microsoft Excel 2010 (Microsoft, Washington), and the results were presented as frequencies and percentages.

Results

Over the three-month study period, the pharmacy departments received a total of 3359 prescriptions of paediatric outpatients, 1194 (35.5%) of which contained at least one oral antibiotic. The patients receiving antibiotics were mostly male (53.1%), with a mean age of 5.52 ± 3.44 years. The majority of the prescriptions (99.7%) contained only one oral antibiotic, while the rest contained two oral antibiotics. The most frequently prescribed antibiotic was amoxicillin (34.9%), followed by phenoxymethylpenicillin (25.6%), and cloxacillin (15.3%). Of all the antibiotic-containing prescriptions, 285 (23.9%) were not included in the subsequent analysis, mainly due to an unclear or unspecified diagnosis (16.5%), a diagnosis for which recommendation was not made in the NAG (5.2%) and multiple diagnoses (2.1%).

In the 909 prescriptions (27.1%) included in the final analysis, antibiotics were most commonly prescribed for otorhinolaryngology infections (73.6%) which included tonsillitis/pharyngitis (428 prescriptions), unspecified upper respiratory tract infections (188 prescriptions), otitis media (49 prescriptions), and otitis externa (4 prescriptions). This was followed by skin and soft tissue infections (13.1%) which consisted of cellulitis (38 prescriptions), impetigo (30

prescriptions), unspecified skin and soft tissue infections (21 prescriptions), scabies (12 prescriptions), abscess (12 prescriptions), and animal bite (6 prescriptions). Meanwhile, there were 42 prescriptions (4.6%) with the diagnosis of community acquired pneumonia. However, it is found that both the antibiotic selection and dosage in only 256 (28.2%) of the prescriptions were consistent with the NAG's recommendations. Inappropriate antibiotic selection was detected in 35.8% of the prescriptions. Meanwhile, 64.1% of the antibiotics were prescribed out of the recommended dosage range.

Of all the antibiotics used, amoxicillin (59.7%), phenoxymethylpenicillin (24.5%) and cloxacillin (11.2%) were most frequently underdosed. On the other hand, overdosing most commonly involved phenoxymethylpenicillin (2.9%) and amoxicillin (2.0%) (Table 1).

Furthermore, unnecessary antibiotic use was noticed in a number of diseases for which it was not commonly indicated, including acute gastroenteritis, otitis externa, fungal infections, and viral fever (Table 2). Besides, inappropriate antibiotic choice was found to be particularly common in animal bites (100.0%), conjunctivitis (80.0%), and pneumonia (54.8%).

Antibiotic Class	Name of Antibiotic	ATC Code	Number of Prescriptions (% of total)	No. of prescriptions with inappropriate antibiotic use (% of total)	
				Antibiotic Selection	Dosage
Penicillins	Amoxicillin	J01CA04	418 (34.9)	8 (3.4)	242 (57.8)
	Phenoxymethylpenicillin	J01CE02	306 (25.6)	43 (18.3)	118 (28.2)
	Cloxacillin	J01CF02	183 (15.3)	7 (3.0)	42 (10.0)
	Amoxicillin/ clavulanic acid	J01CR02	107 (8.9)	49 (20.9)	10 (2.4)
	Ampicillin/ sulbactam	J01CR01	2 (0.2)	0 (0)	0 (0)
Macrolides	Erythromycin ethylsuccinate	J01FA01	128 (10.7)	112 (47.7)	0 (0)
Cephalosporins	Cefuroxime	J01DC02	37 (3.1)	8 (3.4)	7 (1.7)
Imidazole derivatives	Metronidazole	J01XD01	8 (0.7)	5 (2.1)	0 (0)
Tetracycline	Doxycycline	J01AA02	5 (0.4)	1 (0.4)	0 (0)
Sulfonamide	Sulfamethoxazole/ trimethoprim	J01EE01	3 (0.3)	2 (0.9)	0 (0)
Total			1194 (100)*	234 (100)**	419 (100)

Table 1: Inappropriate antibiotic use by pharmacological classes.

* Three prescriptions contained two antibiotics.

** One prescription contained both cefuroxime and erythromycin ethylsuccinate.

Diagnosis	Name of Antibiotic	No. of prescriptions with inappropriate antibiotic use (% of total)	
		Antibiotic Selection	Dosage
Tonsilitis/Pharyngitis	Amoxicillin	0 (0)	119 (28.4)
	Phenoxymethylpenicillin	0 (0)	87 (20.8)
	Amoxicillin/ clavulanic acid	45 (19.2)	0 (0)
	Erythromycin ethylsuccinate	52 (22.2)	0 (0)
	Cefuroxime	3 (1.3)	0 (0)
Unspecified Upper Respiratory Tract Infection	Amoxicillin	0 (0)	92 (22.0)
	Phenoxymethylpenicillin	0 (0)	31 (7.4)
	Amoxicillin/ clavulanic acid	0 (0)	1 (0.2)
	Erythromycin ethylsuccinate	45 (19.2)	0 (0)
Otitis Media	Amoxicillin	0 (0)	28 (6.7)
	Phenoxymethylpenicillin	1 (0.4)	0 (0)
	Amoxicillin/ clavulanic acid	0 (0)	9 (2.1)
Otitis Externa	Amoxicillin	2 (0.9)	0 (0)
	Amoxicillin/ clavulanic acid	2 (0.9)	0 (0)
Skin and soft tissue infections	Amoxicillin	1 (0.4)	3 (0.7)
	Phenoxymethylpenicillin	4 (1.7)	0 (0)
	Cloxacillin	5 (2.1)	42 (10.0)
	Amoxicillin/clavulanic acid	1 (0.4)	0 (0)
	Erythromycin ethylsuccinate	12 (5.1)	0 (0)
	Cefuroxime	1 (0.4)	0 (0)
	Doxycycline	1 (0.4)	0 (0)
Community acquired pneumonia	Phenoxymethylpenicillin	20 (8.5)	0 (0)
	Erythromycin ethylsuccinate	1 (0.4)	0 (0)
	Cefuroxime	3 (1.3)	0 (0)
Gastrointestinal Infections	Amoxicillin	2 (0.9)	0 (0)
	Phenoxymethylpenicillin	17 (7.2)	0 (0)
	Erythromycin ethylsuccinate	1 (0.4)	0 (0)
	Metronidazole	5 (2.1)	0 (0)
Urinary Tract Infections	Amoxicillin	1 (0.4)	0 (0)
	Amoxicillin/clavulanic acid	1 (0.4)	0 (0)
	Cefuroxime	0 (0)	7 (1.7)
	Sulfamethoxazole/ trimethoprim	2 (0.9)	0 (0)
Viral fever	Cloxacillin	1 (0.4)	0 (0)
	Erythromycin ethylsuccinate	1 (0.4)	0 (0)
Fungal Infections	Cloxacillin	1 (0.4)	0 (0)
Ocular Infections	Amoxicillin	2 (0.9)	0 (0)
	Phenoxymethylpenicillin	1 (0.4)	0 (0)
	Cefuroxime	1 (0.4)	0 (0)
Total		234 (100)*	419 (100)

Table 2: Inappropriate antibiotic use by diseases.

*One prescription contained both cefuroxime and erythromycin ethylsuccinate.

Discussion

The current study is, to our best knowledge, the first study to review the antibiotic use in paediatric outpatients among the secondary hospitals in Malaysia. It is important to note that these hospitals have been highly dependent on the NAG to guide the antibiotic prescribing, unlike the tertiary health centres which commonly have an in-house infectious disease specialist and are well equipped with facilities to enable the implementation of individualized antimicrobial therapy. Therefore, by comparing how the drugs were used in these hospitals with the recommendations of the NAG, the findings could be useful in disclosing the weaknesses in the current antibiotic prescribing practice. Furthermore, the current study evaluated the antibiotic use in children, adding to the existing literature in Malaysia which have been focusing primarily on adults.[15]

However, despite the findings on the appropriateness of antibiotics use, it is noted that more than one-third of the paediatric outpatients received at least one oral antibiotic. Similar to a number of previous studies, the antibiotic prescribing rate in paediatric patients shown in this study was relatively high as compared with the recommendation of the WHO (no more than 30%).[18-20] This would be expected, as children are generally more prone to infections due to their exploratory behaviours, lack of prior exposure to various infectious agents, and association with other children.[21] In addition, in comparison with adults, children more commonly seek medical treatment for acute infections.[20,22]

When it comes to otorhinolaryngology infections, it is clear that most of the prescribers were unaware of the latest recommendations of the NAG, which were made in accordance with to the clinical evidence. Within this context, erythromycin ethylsuccinate has long been removed from the NAG and other clinical practice guidelines for the treatment of tonsillitis and pharyngitis, mainly due to the increasing resistance rate of *Streptococcus sp.* to it.[14,23-24] Apart from that, inappropriate dosing was of concern, particularly for amoxicillin. In this study, the rate of inappropriate dosing was found to be much higher than that reported by Ergül B, *et al.*[25] In fact, both inappropriate selection and dosing of antibiotics have been shown to continuously result in ineffective treatment, prolonged treatment duration, unnecessary exposure of patients to adverse drug reactions, and ultimately, the development of antimicrobial resistance. Consequently, it has increased the healthcare expenses and mortality. In response to this trend, materials to promote the rational use of antibiotics in paediatric patients, such as a simplified version of the NAG and a standard weight-based antibiotic dosing table, could be helpful to the prescribers.

Additionally, the regular use of antibiotics for both the non-bacterial infections and non-infectious diseases demonstrated in the current study was worth highlighting. A recent study in Malaysia showed that several factors such as lack of confidence in choosing the right antimicrobial treatment, patient insistence for antibiotics and low awareness of antimicrobial resistance may lead to overprescribing of antibiotics.[26] Hence, multifaceted approaches such as educational interventions and profiling report can be carried out to improve antibiotic prescribing practices.[27,28]

Nevertheless, irrespective of all the findings, the current study had several limitations. First, the information used for the analysis, particularly the diagnosis, was based solely on what was written on prescriptions. It was likely that some of the reasons that could support the use of an antibiotic were not captured in a prescription. Also, nearly a quarter of the prescriptions received were excluded from the analysis due to insufficient information on the diagnosis. Hence, further investigation on these prescriptions is recommended to determine if the antibiotics were appropriately used.

Conclusion

These findings suggest an inappropriate antibiotic use in paediatric outpatients presenting to secondary hospitals in Malaysia, as the antibiotic selection and dosage used in the majority of the prescriptions was not in line with the NAG's recommendations. While antimicrobial resistance has been posing a major challenge to the public healthcare system, a multidisciplinary approach is thus urgently required to revise the current antibiotic prescribing practice.

Acknowledgement

We wish to thank the Director General of Health, Malaysia for his permission to publish the findings for this study. Besides, all the staffs from the Sik, Yan, Baling and Kuala Nerang Hospitals, who had helped us in acquiring the data, are acknowledged.

References

1. United Nations, Department of Economic and Social Affairs, Population Division. World population prospects: The 2017 revision, key findings and advance tables. 2017. Working paper No. ESA/P/WP/248.

2. Sireesha G, Thomas JC, Patil PB, *et al.* A prospective study on medication prescribing pattern for paediatrics in a tertiary care teaching hospital. World Journal of Pharmacy and Pharmaceutical Sciences 2016;5(10):654-66.

3. Khan Z, Sharma P, Kaushal R, *et al.* Drug utilisation study in department of paediatrics of tertiary care hospital. J. Evolution Med. Dent. Sci. 2016;5(26):1372-5. doi:10.14260/jemds/2016/323.

4. Kagitapu S, Nune A, Devulapally H, *et al.* Prescribing patterns of drugs in paediatrics outpatient department in tertiary care hospital. Journal of Dental and Medical Sciences 2016;15(10):92-5.

5. Piovani D, Clavenna A, Cartabia M, *et al.* Assessing the quality of paediatric antibiotic prescribing by community paediatricians: a database analysis of prescribing in Lombardy. BMJ Paediatrics Open 2017;1:e000169. doi: 10.1136/bmjpo-2017-000169.

6. Ivanovska V, Hek K, Mantel Teeuwisse AK, *et al.* Antibiotic prescribing for children in primary care and adherence to treatment guidelines. The Journal of Antimicrobial Chemotherapy 2016;71(6):1707-14. doi: 10.1093/jac/dkw030.

7. Song YK, Han N, Kim MG, *et al.* A national pharmacoepidemiological study of antibiotic use in Korean paediatric outpatients. Archives of Disease in Childhood 2017;102(7):660-666. doi: 10.1136/archdischild-2016-310981.

8. Saleh EA, Schroeder DR, Hanson AC, *et al.* Guideline-concordant antibiotic prescribing for pediatric outpatients with otitis media, community-acquired pneumonia, and skin and soft tissue infections in a large multispecialty healthcare system. Clinical Research in Infectious Diseases 2015;2(1). pii: 1010.

9. Bryce A, Hay AD, Lane IF, *et al.* Global prevalence of antibiotic resistance in paediatric urinary tract infections caused by *Escherichia coli* and association with routine use of antibiotics in primary care: systematic review and meta-analysis. BMJ 2016;352:i939. doi:10.1136/bmj.i939.

10. Costelloe C, Metcalfe C, Lovering A, *et al.* Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. British Medical Journal 2010;340:c2096. doi: 10.1136/bmj.c2096.

11. Michaelidis CI, Fine MJ, Lin CJ, *et al.* The hidden societal cost of antibiotic resistance per antibiotic prescribed in the

United States: An exploratory analysis. BMC Infect Dis 2016;16:655.

12. Teillant A, Gandra S, Barter D, *et al.* Potential burden of antibiotic resistance on surgery and cancer chemotherapy antibiotic prophylaxis in the USA: a literature review and modelling study. The Lancet Infectious Diseases 2015;15(12):1429-37. doi: 10.1016/S1473-3099(15)00270-4.

13. Pharmaceutical Services Division. Protocol on antimicrobial stewardship program in healthcare facilities. 1st ed, Ministry of Health Malaysia, Kuala Lumpur, 2014.

14. Pharmaceutical Services Division. National Antibiotic Guidelines 2014. Available at://www.pharmacy.gov.my/v2/en. [Accessed February 24, 2018].

15. Tan GH, Low QW, Lim HC, *et al.* Inappropriate Antibiotic Utilization: Outpatient Prescription Review of a Regional Secondary Hospital in Kedah, Malaysia. Journal of Pharmacy Practice and Community Medicine 2017;3(4):215-9.

16. Rezal RS, Hassali MA, Alrasheedy AA, *et al.* Prescribing patterns for upper respiratory tract infections: a prescription-review of primary care practice in Kedah, Malaysia and the implications. Expert Review of Anti-infective Therapy 2015;13(12):1547-56. doi: 10.1586/14787210.2015.1085303.

17. Ab Rahman N, Teng CL, Sivasampu S. Antibiotic prescribing in public and private practice: a cross-sectional study in primary care clinics in Malaysia. BMC Infectious Diseases 2016;16:208. doi: 10.1186/s12879-016-1530-2.

18. WHO. Using indicators to measure country pharmaceutical situations: fact book on WHO Level I and Level II monitoring indicators. Available at: http://www.who.int/medicines/publications/WHOTCM2006.2A.pdf.

19. Sireesha G, Thomas JC, Patil PB, *et al.* A prospective study on medication prescribing pattern for paediatrics in a tertiary care teaching hospital. World Journal of Pharmacy and Pharmaceutical Sciences 2016;5(10):654-66.

20. Alili-Idrizi E, Malaj L, Dauti M. Spectrum of infectious diseases and antibiotic usage in a paediatric outpatient department. European Scientific Journal 2013;9(30):364-370.

21. National Research Council, Committee on Evaluation of Children's Health. Children's health, the nation's wealth: assessing and improving child health. Washington: National Academies Press; 2004.

22. Malpani AK, Waggi M, Rajbhandari A, *et al.* Study on prescribing pattern of antibiotics in a pediatric out-patient department in a tertiary care teaching and non-teaching hospital. Indian Journal of Pharmacy Practice 2016;9(4):253-259.

23. Shulman ST, Bisno AL, Clegg HW, *et al.* Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. Clin Infect Dis 2012;55:1279.

24. Ibrahim SB, El-Sokkary RH, Elhewala AA, *et al.* Emerging resistance to erythromycin and penicillin among streptococcus pyogenes isolates in Zagazig, Egypt. International Journal of Current Microbiology and Applied Sciences 2014;3(10):750–6.

25. Ergül B, Gökçek İ, Çelik T, *et al.* Assessment of inappropriate antibiotic use in pediatric patients: Point-prevalence study. Turk Pediatri Ars 2018; 53: 17-23.

26. Tan WL, Mohammed SR, Ishak S, *et al.* Knowledge, attitude and practice of

antibiotics prescribing among medical officers of public health care facilities in the state of Kedah, Malaysia. Med J Malaysia 2015;70(5):307-11.

27. Arnold SR, Straus SE. Interventions to improve antibiotic prescribing practices in ambulatory care. Cochrane Database Syst Rev 2005;4:CD003539.

28. Mohd Fozi K, Kamaliah MN. The effect of profiling report on antibiotic prescription for upper respiratory tract infection. Malaysian Family Physician 2013;8(2):26-31.