Research Article

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Antibiotic usage for rotaviral diarrhea among children in Libya

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ABSTRACT

Background: In Libya, routine access to rotavirus testing is not available and clinicians treat presumptively, leading to inappropriate treatments. This study describes the management of rotavirus infection among Libyan children in public hospitals.

Methods: A prospective cross-sectional study was conducted to describe the management of rotavirus among children in three public hospitals in Libya from August 2012 to April 2013. We reviewed internal documents to determine if protocols were in place to guide management of diarrheal illness. Children under five presenting with diarrhea had stool samples collected and tested for rotavirus. Comparisons of treatments were made by rotavirus status and level of dehydration; mild, moderate and severe.

Results: A total of 545 diarrhea patients below 5 years of age were enrolled in the study. Of those, 311 (57%) cases were infected by rotavirus. Treatment was administered without investigating the cause of diarrhea. Intravenous fluids (IVF) treatment was the most common treatment for rotavirus cases and was administered to 306 (98%) of cases. Antibiotics were administered to about 137 (44%) of rotavirus cases. Antibiotics were more likely to be administered with more severe dehydration.

Conclusions: Presumptive treatment with antibiotics was very common in Libyan. Protocols for management of diarrheal illness and rotavirus cases in children need to be established for effective treatment.

Keywords: Medication, Antibiotics, Diarrhea, Rotavirus, Libya

INTRODUCTION

Rotavirus is a common cause of diarrhea among children below 5 years old, with approximately 110 million cases and 600,000 childhood deaths each year worldwide.^{1,2} It accounts for approximately 40% of diarrheal illness under 5 years old.³ Children below two years of age are particularly vulnerable to rotavirus infection. Dehydration is a potentially dangerous complication of rotavirus infection, which can be measured on a scale from mild, to moderate to severe.⁷⁻¹⁰ Therapy for rotavirus patients is

intended to reduce symptoms and prevent complications. Oral rehydration therapy (ORT) is recommended for mild to moderate dehydration, while intravenous fluids (IVF) therapy should be given immediately to severely dehydrated patients. ^{7,8,11,12} Rotavirus is not susceptible to antibiotic therapy. ^{10,13} Unwarranted use of antibiotics has the potential to increase the development of drug resistance, can lead to side effects of the antibiotic and adds an unnecessary cost to treatment of viral diarrhea. ¹⁴

In Libya, most health service sectors are publicly owned and provide preventive, curative and rehabilitation services to all citizens free of charge under supervision of

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Ministry of Health.¹⁵ As in the rest of the world, rotavirus is a frequent cause of diarrhea among Libyan infants and young children, causing an estimated 44% of all diarrhea cases in children under 5 years of age.^{16,17} Rotavirus vaccine was only incorporated into the childhood immunization schedule in October 2013.^{15,18} Mortality rates from rotavirus are low in Libya indicating they are likely receiving adequate treatment.^{6,19} However, there has been no previous investigation into the use of antibiotics to treat rotavirus in Libyan hospitals. In this study we describe the spectrum of rotavirus diarrhea in children attending public hospitals in Libya, ascertain the types of treatment being used by dehydration status.

METHODS

In this cross-sectional study, data were collected prospectively from diarrhea patients under 5 years of age in three public hospitals and out-patient clinics in the cities of Zliten and Khoms in northwest of Libya from August 2012 to April 2013. The three hospitals have a total of 962 therapy beds, and provide health services for about 475,754 people. Outpatient clinics were co-located with the hospitals.

Data collection

Data was collected from medical records and laboratory data. All patients presenting with diarrhea had a stool sample collected according to standard laboratory protocols for rotavirus. As on-site testing was not available, specimens were shipped to the Libyan National Center for Diseases Control (NCDC) laboratory for testing by technicians trained by the World Health Organization (WHO) using an enzyme immunoassay (ProSpect Rotavirus Test, Oxoid Ltd, UK) supplied by WHO. Patient data extracted from charts included medications administered, age, season, gender dehydration status, mortality.

Case definition

Each diarrhea patient aged under 5 years, regardless of other symptoms such as fever, vomiting or dehydration, admitted to the pediatric ward or presenting at an outpatient clinic visit was included in this study. The standard definition for diarrhea was three times or more instances of liquid stool in a day.

Statistical analysis

Data were analyzed using SPSS version 16. Summary descriptive statistics were calculated to describe age, seasonal distribution, gender, dehydration status and mortality by rotavirus infection. Treatments used for cases were determined and stratified by dehydration status (severe, moderate or no dehydration). Differences in treatment by dehydration status and rotavirus testing result (positive/negative) were determined using chisquare testing.

Ethical issues

Consent was obtained orally from patient's parents after informing them on the purpose of the study. The study was approved by the University of Malaya Medical Ethics Committee (IRP - 908.6). In addition, approval to conduct the study was obtained from the national laboratory and managements of the study hospitals in Libya.

RESULTS

Description of rotavirus diarrhea

The study enrolled 545 diarrhea patients among children under 5 years of age during the study period. The basic epidemiology of rotavirus cases has been described previously (cite other paper). Briefly, 57% (n = 311) cases were confirmed as positive rotavirus diarrhea. Most rotavirus cases were under 2 years of age (n = 266, 86%), had symptoms less than one week (n = 255, 82%) and nearly all cases of rotavirus presented with dehydration (n = 302, 97%). There were no deaths due to diarrheal disease over the study period.

Medication for rotavirus diarrhea

Most rotavirus cases (306/311, 98%) were given intravenous fluids (IVF) therapy, while (11/311, 4%) cases were given oral rehydration therapy (ORT) with 6 rotavirus cases receiving both IVF and ORT. All rotavirus cases with fever were provided fever medication (n = 216/311, 69%). Nearly half of rotavirus cases were administered an antibiotic (n = 137/311, 44%). Of those receiving antibiotics over a third received more than one antibiotic (n = 54/137, 39%). A range of antibiotics were given and included in order from most used: Metronidazole (66/311, 21%), Ceftriaxone (51/311, 16%), Penicillin (31/311, 10%), Ampicillin (24/311, 8%), Augmentin (15/311, 5%), Gentamicin (9/311, 3%) and Septrim (co-trimoxazole) (5/311, 2%). Other treatment drugs to treat the rotavirus patients included Zinc sulfate for (41/311, 13%) cases and Lacteol fort for (39/311, 13%). Medications administered to rotavirus patients are shown in Figure 1.

Medications for patients testing positive or negative for rotavirus

Medications for diarrheal patients were classified according to whether the patient tested positive or negative for rotavirus infection (Table 1). Fifty-seven percent of all diarrheal patients were positive for rotavirus (311/545). IVF was prescribed to most cases, whether positive or negative for rotavirus, while ORT was given to very few (11/311, 4%) positive rotavirus cases and slightly more (31/234, 13%) with diarrhea from other causes. Fever reduction medication was given to both groups equally (70%), p = 0.874 as were antibiotics (137/311, 44% rotavirus vs. 114/234, 49% other cause; p

= 0.479). Zinc sulfate was administered in a relatively small proportion of both rotavirus cases and those due to other causes (41/311, 13% and (20/234, 9%). Lacteol fort medication was given to both groups as similar percent to Zinc sulfate.

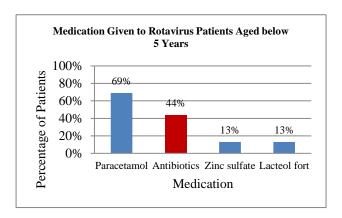


Figure 1: Medications administered to rotavirus patients five years and under.

Table 1: Medications for diarrhea patients based on positive or negative rotavirus.

Drugs	Positive- Rotavirus N = 311		Negative- Rotavirus N = 234		Chi- square test	
	No. of patients	%	No. of patients	%	(p-value)	
IVF	306	98	218	94	0.002	
ORT	11	4	31	13	0.001	
Paracetamol	216	69	164	70	0.874	
Antibiotics	137	44	114	49	0.326	
Zinc sulfate	41	13	20	9	0.090	
Lacteol fort	39	13	20	9	0.138	

Treatment by rotavirus status

Treatment given to rotavirus patients varied by dehydration status (Table 2). A total of 97 rotavirus patients were classified as severely dehydrated (97/311, 31%), 205 cases were moderately dehydrated (205/311, 66%) and 9 cases in the study group had no dehydration (9/311, 3%). IVF was given to all cases with severe dehydration (97/97, 100%) and most moderate dehydration cases (203/205, 99%), as well as to about two-third of cases without dehydration. However, a few of cases (2/97, 2%) with severe and moderate dehydration cases (5/205, 2%) were treated only with ORT, while (4/9, 44%) cases with no dehydration were given ORT. Fever reduction medication was trended to higher use in more severely dehydrated patients; severe dehydration (78/97, 80%) moderate dehydration (132/205, 64%) and no dehydration (6/9, 67%) cases (p for trend = 0.009). Zinc sulfate was prescribed to a small proportion of patients without relation to dehydration status; 9% (n = 9/97) of rotavirus patients with severe

dehydration, 15% (n = 31/205) of cases with moderate dehydration and 11% (n = 1/9) of patients without dehydration. Lacteol fort medication was administered in the same percentages as Zinc sulfate.

Antibiotic therapy use was also associated with more severe dehydration; 55% of patients with severe dehydration (n = 53/97), 40% with moderate dehydration (n = 83/205) and 11% without dehydration (n = 1/9) and (p-value for test for trend = 0.003). The most common antibiotics used were Ceftriaxone and Metronidazole. Ceftriaxone was administered, respectively, to (24/97, 25%), (26/205, 13%) and (1/9, 11%) of rotavirus cases with severe, moderate and no dehydration; while Metronidazole was given to (25/97, 26%) of rotavirus cases with severe dehydration, to (40/205, 20%) of cases with moderate dehydration and (1/9, 11%) case with no dehydration. Other antibiotics were given to rotavirus cases with severe and moderate dehydration such as Augmentin, Penicillin, Gentamicin and Ampicillin. Septrim was the least frequently used antibiotic to treat rotavirus patients which was given to (1/97, 1%) and (4/205, 2%) of severe and moderate dehydration patients, respectively.

Table 2: Medications for rotavirus patients based on dehydration status.

Rotavirus Patients											
Variable -	Severe Dehydration n = 97		Moderate Dehydration n = 205		No Dehydration n = 9		Chi- square test for				
	No. of Patier	0/0	No. of Patient	% %	No. of Patients	s %	trend (p- value)				
IVF	97	7 100	203	99	6	67	0.001				
ORT	2	2	5	2	4	44	0.002				
Paracetam	ol 78	80	132	64	6	67	0.009				
Antibiotic	s 53	3 55	83	40	1	11	0.003				
Zinc sulfa	te 9	9	31	15	1	11	0.238				
Lacteol fo	rt 9	9	29	14	1	11	0.310				

Note: percentages are not mutually exclusive.

Diarrheal protocol review

There were no standard protocols or procedures for diarrheal treatment at any of the in-patient or out-patient facilities. Clinicians made individual decisions for all patients treated.

DISCUSSION

There was no standard treatment or guidelines to treat diarrhea patients in the study hospitals and outpatient clinics despite clear WHO guidelines established for treating diarrhea in young patient.²³ Pediatricians prescribed medications for diarrhea cases on an individual basis without set criteria and with almost no laboratory confirmation of the infectious agent causing the diarrhea. This led to an over-prescription of antibiotics to individuals with rotaviral diarrhea which

has limited efficacy in treating rotavirus and can increase both cost and risk of side effects. 9,11,13,24 Antibiotics were given to 44% (137/311) of all rotavirus cases, and 17% (52/311) of these rotavirus cases received more than one type of antibiotic. Prescribing antibiotics without determining the agent is not recommended by WHO. 12,25 Antibiotics are not effective against viruses and even most bacteria that cause diarrhea except shigellosis which is recommended to be treated by antibiotics only after confirmation from laboratory diagnosis. Not surprisingly, clinicians were more likely to prescribe antibiotic therapy when a child was severely dehydrated. Severity of illness is more likely to trigger aggressive treatment courses.

Inappropriate treatment with antibiotics can lead to increased side effects. The most common antibiotics prescribed were Ceftriaxone and Metronidazole. Administration of Ceftriaxone has been associated with the development of Clostridium difficile toxin-positive diarrhea.²⁶ Clostridium dificile diarrhea can have serious outcomes and can lead to chronic sequaleae such as arthritis.²⁷ Metronidazole, is often used as a treatment for C. dificile infection and in some instances has been shown to reduce the risk of C. dificile diarrhea when used to treat non-C. dificile infections.²⁸ Metronidazole, however, has its own set of rare but serious side effects including convulsive seizures, encephalopathy, aseptic meningitis, optic and peripheral neuropathy²⁹ though most resolve upon cessation of antibiotic therapy. Administration of these antibiotics should be based on laboratory evidence. Capacity to improve laboratory diagnosis should be a high priority to avoid unnecessary treatments that could lead to serious side effects.

Rotavirus is most appropriately treated using palliative care to ensure the patient is well hydrated during the course of illness. All patients received palliative care through either intravenous fluid administration or oral rehydration therapy. However, there was an over-use of IVF therapy according to the standards of the WHO and the Centers for Disease Control and Prevention (CDC). IVF must be given to severe rotavirus cases, whereas ORT is more effective for moderate and mild dehydration status.^{8,9,12,13,30} Unnecessary IVF therapy can also increase the economic burden on health facilities. Zinc supplements were only used in approximately 13% of rotavirus cases in this study. This is a safe and effective supplement that has been shown to efficiently reduce the duration and severity of the disease for children over 6 months of age.³¹ Increasing the use of zinc in diarrheal cases should be included in treatment algorithms, while Lacteol fort drug was not recommended for diarrhea cases.23

There are strengths and limitations to this study. This study likely captured nearly all patients in the catchment area seeking treatment for diarrhea. Public hospitals are the only health institutions with the facilities to admit diarrhea patients for treatment in Libya. Private health

institutions do not have sufficient equipment or materials to treat diarrhea cases; for example to administer IVF therapy. The number of laboratory diagnostic tests carried out for diarrhea cases to determine the cause of the illness was limited to rotavirus and the appropriate medication could not be determined for non-rotavirus patients. Without on-site rotavirus testing, samples had to be shipped to the National Laboratory for testing. While this reduced the timeliness of diagnosis, it ensured standard testing across all hospitals.

Guidelines for diarrhea and rotavirus therapy for children should be established to treat rotavirus infection effectively in Libyan hospitals. WHO has developed protocols that address appropriate treatment that could be modified to local needs and capacity³², when in place these protocols should reduce the risk of unintended side effects of inappropriate antibiotic therapy and ensure the most efficient use of resources. Efforts should be made to increase the testing capacity of Libyan hospitals so that point of care diagnosis can be made to ensure appropriate therapy.

CONCLUSION

Rotavirus infection continues to be a significant health threat among young children in Libya. Antibiotic therapy was widely used to treat rotavirus cases, despite them having no effectiveness. The use of IVF when ORT would have been recommended was also common. Currently, there are no guidelines for managing diarrhea cases in the hospitals studied. Facilities for laboratory diagnosis to determine the cause of diarrhea were limited in the study hospitals; thus, pediatricians prescribed medications to diarrhea patients without any accurate diagnosis, leading to widespread use of antibiotics. The frequent use of IVF and wide use of antibiotics add additional economic burdens to the Libyan healthcare system and increases the risk of adverse events related to antibiotic therapy. Guidelines are necessary for efficient treatment for diarrhea and rotavirus patients. Systematizing the prescription of treatment such IVF, antibiotics and zinc could lead to reduced expenditures in the country's health facilities.

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REFERENCES

 Van Der A. Gastroenteritis in children. SA Pharmaceutical Journal. 2010;10.

- 2. WHO. Diarrhoeal Diseases. Initiative for Vaccine Research (IVR). Department of Immunization, Vaccines and Biologicals. 2009.
- 3. CDC. Rotavirus Surveillance. Worldwide, 2001—2008. Department of Health and Human Services. 2008;57(46):1255-7.
- WHO. Rotavirus Bulletin. Western Pacific Region 1, 2009.
- WHO. Rotavirus, 2009. Available at http://www.who.int/nuvi/rotavirus/en/. Accessed 15 March 2012.
- Alkoshi S, Ernst K, Maimaiti N. Dahlui M. Rota Viral Infection: A Significant Disease Burden to Libya. Iranian Journal of Public Health. 2014;43:1356-63.
- 7. Van Der A. Gastroenteritis in children. SA Pharmaceutical Journal. 2010;10.
- 8. King C, Glass R, Bresee J, Duggan C. Managing acute gastroenteritis among children. MMWR Recomm Rep. 2003;52:1-16.
- 9. Elliott E, Acute gastroenteritis in children. BMJ: British Medical Journal. 2007;334:35.
- Patient Educatiom Institute. Viral Gastroenteritis. Available at http://www.kaahe.org/en/ArabicSampleModules/modules/gastro/gefc01a1/gefc0101/gefc0101.pdf. 2013. Accessed 2 Jun 2014.
- 11. CDC. Rotavirus. 2013. Available at http://www.cdc.gov/rotavirus/index.html Accessed 15 March 2011.
- 12. WHO. Clinical Management of Acute Diarrhoea. Department of Child and Adolescent Health and Development Family and Community Health. 2004.
- 13. Shek K, Ng P, Hung C, Lam K, Lau C, Ching W. A review on the management of acute gastroenteritis in children. Hong Kong Journal of Emergency Medicine. 2004.
- 14. Kotwani A, Chaudhury R, Holloway K. Antibiotic-Prescribing Practices of Primary Care Prescribers for Acute Diarrhea in New Delhi, India. Value in health. 2012;15:S116-S119.
- 15. Alkoshi S, Leshem E, Parashar U, Dahlui M. Anticipating rotavirus vaccines—a pre-vaccine assessment of incidence and economic burden of rotavirus hospitalizations among children< 5 year of age in Libya, 2012-13. BMC Public Health. 2015;15:26.
- 16. Hanane K, Isla O, El Khoury Antoine D, Mireille G. Burden of rotavirus gastroenteritis in the Middle Eastern and North African pediatric population. BMC Infectious Diseases. 2009;11.
- 17. NCDC. Annual report for infectious disease in Libya. Surveillance department at NCDC. 2007.
- 18. IVAC. VIMS Report: Global Vaccine Introduction. 2013. Available at http://www.jhsph.edu/research/centers-and-institutes/ivac/vims/IVAC-VIMS-Report-2013-Dec.pdf. Accessed 2 June 2014.

- 19. Alkoshi S, Smeo M, Dahlui M. A Review on Gastroenteritis Infection in Libya. Advanced Science, Engineering and Medicine. 2014;6:133-6.
- 20. WHO. Generic protocols for (i) hospital-based surveillance to estimate the burden of rotavirus gastroenteritis in children and (ii) a community-based survey on utilization of health care services for gastroenteritis in children: (Vaccines and Biologicals, World Health Organization. 2002.
- 21. Neale J. Research methods for health and social care. Palgrave macmillan. 2009;10:137-48.
- 22. Masters J. Gastroenteritis and the rotavirus vaccine, Health University of Bristol. 2007.
- 23. WHO. Diarrhoea Treatment Guidelines. 2005. Available at http://whqlibdoc.who.int/publications/2005/a85500. pdf?ua=1. Accessed 2 June 2014.
- 24. WGO. World Gastroenterology Organisation practice guideline: Acute diarrhea. 2008.
- 25. Chin J. Control of communicable diseases manual. American Public Health Association Washington, DC. 2000.
- 26. Vesteinsdottir I, Gudlaugsdottir S, Einarsdottir R, Kalaitzakis E, Sigurdardottir O, Bjornsson E. Risk factors for Clostridium difficile toxin-positive diarrhea: a population-based prospective case—control study. European journal of clinical microbiology & infectious diseases. 2012;31:2601-10
- 27. Horton D, Strom B, Putt M, Rose C, Sammons J. Clostridium difficile Infection-Associated Reactive Arthritis in a Pediatric Cohort. Arthritis & Rheumatology. 2014;66:S82-S82.
- Rodriguez S, Hernandez M, Tarchini G, Zaleski M, Vatanchi M, Cardona L. Risk of Clostridium difficile Infection in Hospitalized Patients Receiving Metronidazole for a Non-C difficile Infection. Clin Gastroenterol Hepatol. 2014;S1542-3565,00445-00445.
- 29. Kuriyama A, Jackson J, Doi A, Kamiya T. Metronidazole-induced central nervous system toxicity: a systematic review. Clinical neuropharmacology. 2011;34:241-7.
- 30. Burkhart D. Management of acute gastroenteritis in children. American Family Physician. 1999;60:2555.
- 31. Lazzerini M, Ronfani L. Oral zinc for treating diarrhoea in children. Cochrane Database; Syst Rev 3. 2008.
- 32. WHO. The treatment of diarrhoea. A manual for physicians and other senior health workers. Department of Child and Adolescent Health and Development. 1995.

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