

Journal of Clinical Medicine and Research

Volume 6 Number 1 January, 2014

ISSN 2141-2235



*Academic
Journals*

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Mussel RL, De Sa Silva E, Costa AM, Mandarim-De-Lacerda CA (2003). Mast cells in tissue response to dentistry materials: an adhesive resin, a calcium hydroxide and a glass ionomer cement. *J. Cell. Mol. Med.* 7:171-178.

Booth M, Bundy DA, Albonico P, Chwaya M, Alawi K (1998). Associations among multiple geohelminth infections in school children from Pemba Island. *Parasitol.* 116: 85-93.0.

Fransiscus RG, Long JC, (1991). Variation in human nasal height and breath, *Am. J. Phys. Anthropol.* 85(4):419-427.

Stanislawski L, Lefeuvre M, Bourd K, Soheili-Majd E, Goldberg M, Perianin A (2003). TEGDMA-induced toxicity in human fibroblasts is associated with early and drastic glutathione depletion with subsequent production of oxygen reactive species. *J. Biomed. Res.* 66:476-82.

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Full Length Research Paper

Epistaxis in Kaduna, Nigeria: A review of 101 cases in a resource constrained setting

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Accepted 17 December, 2013

Epistaxis is defined as hemorrhage from the nostril, nasal cavity, or nasopharynx. Sufferers and clinicians may develop significant anxiety despite the fact that majority of patients may be treated successfully by the first attending physician. The objective of this study was to review the incidence, common etiological factors and management modalities of epistaxis in a resource constrained setting. It is a retrospective review of 101 patients seen with epistaxis over 7 years at National Ear Care Centre, Kaduna from January 2002 to December 2008. The age of patients reviewed ranged between 2 and 75 years. An incidence of 0.5% was recorded and slight male preponderance with a male:female ratio of 1.4:1. Dry-hot and cold harmattan weather had the highest prevalence. Trauma and infections were the main etiological factors identified, but over 40% had no discernable cause. About 25% presented with active bleeding and 10.98% required admission. All were managed conservatively. Less than 2% had blood transfusion. Epistaxis is a common rhinological emergency that requires prompt intervention to reduce morbidity and prevent mortality. Conservative intervention was a satisfactory approach in this study.

Key words: Epistaxis, resource constrained, conservative management.

INTRODUCTION

Bleeding from the nose and nasopharynx is a common symptom of diverse conditions which may present as mild recurrent bleeds or severe life threatening rhinological emergency and may pose a challenge to even a skilled otolaryngologist (Nnnennia, 2004).

Globally, the true incidence remained unknown, but it is estimated that 60% of the population will at least have an episode of epistaxis in their life time and 6% of them will seek medical attention (Saubrah and Saxena, 2005). A slight male preponderance with 55% male and 45% female has been reported (Nnnennia, 2004; Saubrah and Saxena, 2005; Gerald, 2008). It is rare in neonates but common among children and young adults and peaks in the sixth decade giving a bi-modal age presentation (Saubrah and Saxena, 2005; Gerald, 2008). Epistaxis is said to be commoner in the cold winter and during the hot

dry climate.

The nasal mucosa is richly supplied by branches of both the external and internal carotid arteries with rich anastomoses. The Kiesselbach's plexus is responsible for most anterior epistaxis accounting for 85 to 95%, but easy to identify and treat. Posterior epistaxis which constitute 5 to 15% are often more severe, difficult to locate and treat.

A structured clinical classification into either primary or secondary, childhood or adult and anterior or posterior epistaxis is preferred over the traditional classification based on local and systemic causes (Gerald, 2008). This is because majority of cases have no identifiable cause.

The goals of therapy in epistaxis are to control haemorrhage, reduce hospital stay and limit complications in a cost effective way. The best treatment modality to

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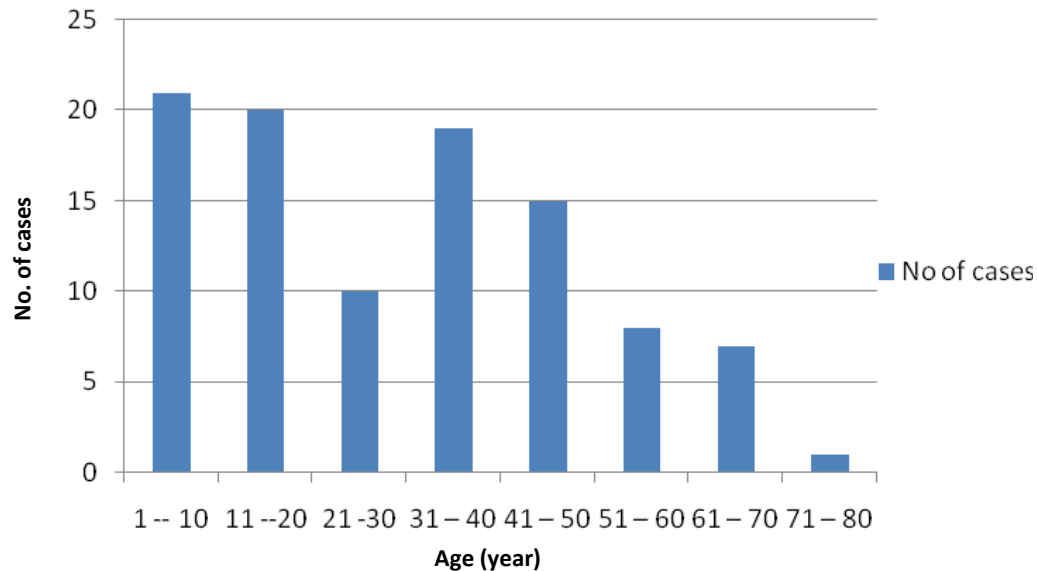


Figure 1. Age distribution.

achieve these goals is however a matter of great debate (Nnnennia, 2004; Saubrah and Saxena, 2005). Resuscitation where indicated is mandatory. Specific treatment can be conservative or surgical. Conservative methods include cauterization and nasal packing. Surgical methods involve ligation of feeding vessels and septoplasty. However, modern approaches include endoscopic ligation and embolization. This study presents our experience in managing epistaxis in a resource constrained setting.

MATERIALS AND METHODS

This is a retrospective review of 101 patients seen over a period of 7 years at the National Ear Care Centre, Kaduna from January 2002 to December 2008. This period coincided with the time when the centre used one site for administration, another hospital for clinics and admission and yet another hospital for theatre space.

Out-patient and in-patient registers were used and medical records of patients seen during the period under review were retrieved. Parameters extracted include demographics, concomitant medical conditions, drug history, month of presentation, trigger of bleeding, treatment modality, complications, length of hospital stay and examination findings. The data was analyzed using simple statistical methods.

RESULTS

A total of 20,308 patients were seen at the centre during the period under review. Of this number, 101 patients (0.5%) had epistaxis as a presenting complaint.

Figure 1 shows age distribution of patients with epistaxis. Age ranged from 2 to 75 years, with mean of 30.4 years. Peak presentations were recorded among age groups 1 to 10 years (40.6%) and 31 to 40 years

(33.6%). Only 11 patients (10.89%) required admission. Of this number, 2 had blood transfusion. Hospital stay ranged 2 to 4 days with an average of 3 days.

Table 2 shows the associated aetiological factors. Idiopathic causes accounts for about 46% and trauma (15.8%), while infections constitute 11.9%.

Table 3 shows treatment modalities offered to the 25 cases with active epistaxis at presentation. Of this number, 52% had anterior nasal pack, 16% had both anterior and posterior nasal packs, while 32% benefitted from cautery.

DISCUSSION

In spite of the anxiety generated by nose bleeding, cure can be achieved by the first attending physician if prompt and appropriate intervention is made. Epistaxis is a common symptom in ENT practice (Nnnennia, 2004; Saubrah and Saxena, 2005; Gerald, 2008; Ijaduola and Okeowo, 1983). In this study, its incidence was 0.5%. The age ranged from 2 to 75 years with mean age of 30.49 years and male to female ratio of 1.4:1. These findings agree with that of Mgbor (2004) who also reported similar findings in a study carried out in Enugu, South Eastern Nigeria. Bimodal age presentation with peaks at age groups 1 to 20 and 31 to 40 years was observed. Adult epistaxis has been reported to be commoner in the sixth decade of life (Saubrah and Saxena, 2005; Gerald, 2008); this is in contrast with the findings in this study of fourth decade. Perhaps this may be due to small proportion of the aged in this environment owing to low life expectancy. Increased incidence in cold harmattan months and the hot/dry months have been reported (Gerald, 2004) which agrees with the findings of

Table 1. Distribution by month of presentation.

Month of the year	No. of cases	Percentage
January	8	7.92
February	6	5.94
March	8	7.92
April	11	10.89
May	2	1.98
June	5	4.95
July	9	8.91
August	7	6.93
September	6	5.94
October	13	12.87
November	14	13.86
December	10	9.90

Table 2. Distribution by aetiologic factor.

Aetiological factors	No. of patients	Percentage
Idiopathic	45	45.55
Trauma	16	15.84
Hypertension	13	12.87
Infections	12	11.88
Tumours	5	4.95
Blood dyscrasias	4	3.96
Chronic liver disease	3	2.97
Foreign Body	1	0.99
Drug induced	1	0.99
Deviated nasal septum	1	0.99
Total	101	100

Table 3. Treatment modalities.

Treatment modality	No. of cases	Percentage
Anterior nasal packing	13	52
Anterior and posterior nasal packing	4	16
Cauterization	8	32
Total	25	100

this study as shown in Table 1. This also agrees with the report of Bhatia and Varughese (1987) in Jos who attributed the increased incidence to high wind velocity and dryness which favour crust formation in the nasal cavity.

There must be a committed search for the bleeder as well as a deliberate effort to find the cause of epistaxis (Gerald, 2008; Dounil et al., 1999; Jeselius, 1974), because too many cases of epistaxis are grouped as idiopathic or primary which may not necessarily be so. In this study, 45.55% of the cases were idiopathic. This is similar to findings of Mgbor (2004). With more resources/

better equipment and careful examination, this figure may likely decrease. Trauma, infections and tumours were noted as shown in Table 2. Varshney and Saxena (2005) however reported cardiovascular diseases (including hypertension and arteriosclerosis), infection and trauma in decreasing importance as leading cause of secondary epistaxis in their study. In this series, about 13% of patients had hypertension without any identifiable cause of epistaxis, but it was observed that 3 patients who had epistaxis secondary to trauma and 1 patient due to blood dyscrasias also had hypertension. Bleeding was also more severe among the hypertensives. It is possible that

with committed search one could find the real cause of epistaxis in these hypertensives. Elima and Knopfholz (2000) reported that epistaxis is unlikely to be a hypertensive emergency. Also, a number of large studies have failed to show causal relationship between hypertension and epistaxis (Lubianca-Neto et al., 1998).

The bleeding point if found is cauterized either with silver nitrate or electro cautery. Failure to find the bleeding point leads to anterior nasal pack with paraffin gauze, gloved finger or rarely merocel when available. Fifty two percent were successfully managed with anterior nasal packs alone, 16% with posterior nasal pack using Foleys catheter inflated with air in addition to anterior nasal pack with paraffin gauze under local anaesthesia. All patients with nasal packs were given prophylactic antibiotics. Nasal packs were removed between 24 and 48 h. Most patients were discharged home on the third day of admission. There was no mortality recorded and this is similar to Urashi et al. (2004).

Epistaxis is a common symptom which presents often as recurrent minor bleeds, but not infrequently as acute severe episode requiring emergency care. Thorough patient evaluation is mandatory for appropriate management. More purposeful search for etiological factors by the attending surgeon and identification of bleeding point must be encouraged. Conservative management was very effective despite resource constrain.

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Full Length Research Paper

Comparative *in vitro* potency of four fluoroquinolones on clinical isolates over a year period

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Accepted 16 December, 2013

This study aimed at evaluating the efficacy of four common fluoroquinolone drugs over a year period on some clinical isolates. It also aimed at comparing statistically the average effects of each drug on the isolates. Five different clinical samples (urine, sputum, wound, blood and high vaginal swab [HVS]) from patients attending a university medical centre (between June 2011 and May 2012) were analysed for the purpose of bacteria isolation. The isolates were tested with commonly used fluoroquinolones: pefloxacin (30 µg), ofloxacin (30 µg), sparfloxacin (10 µg), and ciprofloxacin (10 µg). Each sensitivity test was done in duplicate and a mean average of zone of inhibition was recorded. One hundred and eighty eight bacteria were isolated: *Staphylococcus aureus* (44.7%), *Streptococcus pyogenes* (6.4%), *Escherichia coli* (28.2%), *Pseudomonas aeruginosa* (8.5%), *Klebsiella pneumonia* (8.0%), and *Proteus mirabilis* (4.3%). All drugs were equally potent against the isolates, but a higher potency was seen in ofloxacin against *P. mirabilis*. The fluoroquinolones are a group of broad spectrum drugs effective in clinical cases. Their efficacy should be preserved by ensuring strict compliance to local drug policies.

Key words: Clinical, fluoroquinolones, efficacy.

INTRODUCTION

The health and well-being of human populations relies, in large, on the control of communicable diseases, as well as the availability of efficient and potent drugs for treatments of such diseases. Infectious diseases continue to take a toll, especially in most developing countries, accounting for nearly 50% of all deaths. The introduction of antimicrobial agents in the early 20th century brought a great relief in medicine; however, this relief was not to endure a while, especially due to the indiscriminate and uncontrolled use of these agents. Resistance, an unfriendly term in medicine, became a global problem when frequently used antimicrobials in human and veterinary medicine were observed to be impotent against known bacterial infections (Smith,

1999). Serious infections, notably in hospitals and other health care facilities are associated with the emergence of antibiotic-resistant organisms, and these organisms appear to be biologically competent to cause serious threat to life (Schwartz et al., 1997; Spellberg et al., 2008; Mulvey and Simor, 2009; Sibi et al., 2011; Taddele et al., 2012). The principal area of concern to this has been the increasing emergence of resistant phenotypes in both clinically relevant strains and normal commensal microbiota (Chikwendu et al., 2008).

Fluoroquinolones, as a class of drugs, have gained some importance during the last two decades because of their potent antibacterial activity against wide varieties of Gram positive and Gram negative pathogenic bacteria

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Table 1. Isolates per clinical sample.

Isolate	Urine	Sputum	Wound	Blood	HVS	Occurrence (% , n = 188)
<i>E. coli</i>	36	-	08	-	09	28.2
<i>S. aureus</i>	52	04	-	08	20	44.7
<i>P. aeruginosa</i>	04	04	08	-	-	8.5
<i>K. pneumoniae</i>	08	-	07	-	-	8.0
<i>P. mirabilis</i>	04	-	-	-	04	4.3
<i>S. pyogenes</i>	04	-	04	-	04	6.4

with minimum toxic side effects and a different mechanism of action than other available antibacterial drugs (Talah and Gadad, 2006). To date, many fluoroquinolones have been introduced into clinical use with significant improvement in antibacterial spectrum and activity, thus forming an invaluable part of the present anti-infective armoury of the clinicians. This group of drugs are increasingly being used in both the hospital and community sectors to treat a broad range of infections (Bhanot et al., 2001). However, increased use has led to recent emergence of fluoroquinolone-resistant bacteria which has necessitated the search for newer drugs worldwide (Shindikar and Viswanthan, 2005; Foroumadi et al., 2006). Along with known mechanisms of resistance is the presence of fluoroquinolone resistant proteins (Qnr), codified by transmissible genes by means of plasmids, especially in *Enterobacter* species, *Escherichia coli*, and *Klebsiella pneumonia* (Luzzaro, 2008). Additionally, new specific resistance mechanisms have been described. AAC(6')-Ib-cr represents the first enzyme able to inactivate, by acetylation, antimicrobials of two different classes, aminoglycosides and fluoroquinolones; and an efflux-pump plasmid-mediated, codified by the QepA gene, acts as a selective mechanism (Luzzaro, 2008). In an over nine years of study, Adam et al. (2009) identified a significant strong relationship between increase in fluoroquinolone usage and rise in ciprofloxacin resistance in *Streptococcus pneumonia* from 0 to 4.5% in children (0 to 15 years), 0.2 to 5.4% in adults (16 to 64 years), and 1.4 to 11.6% in the elderly (≥ 65 years). In the last several years, resistance to fluoroquinolone has remained very high among methicillin-resistant *Staphylococcus aureus* (MRSA) strains in intensive care unit (ICU) patients, and it has increased among nosocomial isolates of *K. pneumonia*, *Serratia marcescens* and *Pseudomonas aeruginosa*. More worrisome are reports of an overall increase in resistance to fluoroquinolone among bacteria of community-acquired infections such as *E. coli*, *Salmonella* species, *Campylobacter* species and *Neisseria gonorrhoeae* (Acar and Goldstein, 1997). A research carried out in Imo State, Nigeria reports a high occurrence of resistance to ciprofloxacin in *S. aureus* isolated from medical samples (Ugbogu et al., 2007). In the same vein, Lamikanra et al. (2011) confirmed that the increase and uncontrolled use of fluoroquinolones paved

way for resistance among *E. coli* in Nigeria. However, Olufunmilola et al. (2012) established the efficacy of fluoroquinolones in the treatment of typhoid fever in Ibadan despite evidence of emerging resistance. This study aimed at evaluating the efficacy of four common fluoroquinolone drugs over a year period on some clinical isolates.

METHODOLOGY

Five different clinical samples (urine, sputum, wound, blood and high vaginal swab [HVS]) from patients being attended to at a university medical centre (between June 2011 and May 2012) were analysed for the purpose of bacteria isolation on CLED, Mannitol salt, McConkey, EMB and Nutrient agars. A total of one hundred and twenty eight samples in all were analysed; thirty two samples per quarter. Isolates were characterised and identified in reference to Cowan and Stell (1993).

All isolates, suspended in normal saline at a density in comparison to 0.5 McFarland standard were subjected to antibiotic sensitivity test using disc diffusion method on Mueller Hinton agar (Oxoid, UK) (CLSI, 2006). The isolates were tested with commonly used fluoroquinolones; pefloxacin (30 μ g), ofloxacin (30 μ g), sparfloxacin (10 μ g), and ciprofloxacin (10 μ g). Each sensitivity test was done in duplicate and a mean average of zone of inhibition was recorded.

Statistical analysis

Analysis of variance (ANOVA) was applied to compare the average effect of the four fluoroquinolones on all isolates at 5% significant level.

RESULTS

From all the samples analysed, a total of one hundred and eighty-eight bacteria was isolated. Ninety six (96) were Gram positive isolates, while ninety two (92) were Gram negative isolates. Isolates were mostly of six species; *S. aureus* (44.7%), *Streptococcus pyogenes* (6.4%), *E. coli* (28.2%), *P. aeruginosa* (8.5%), *K. pneumonia* (8.0%), and *Proteus mirabilis* (4.3%). Urine samples had the highest number of isolates at 57.5%, while sputum and blood samples equally yielded the least number of isolates at 4.3% (Table 1 and Figure 1).

The antibiotic sensitivity test (AST) for the period of the study showed varying sizes of zone of inhibition in

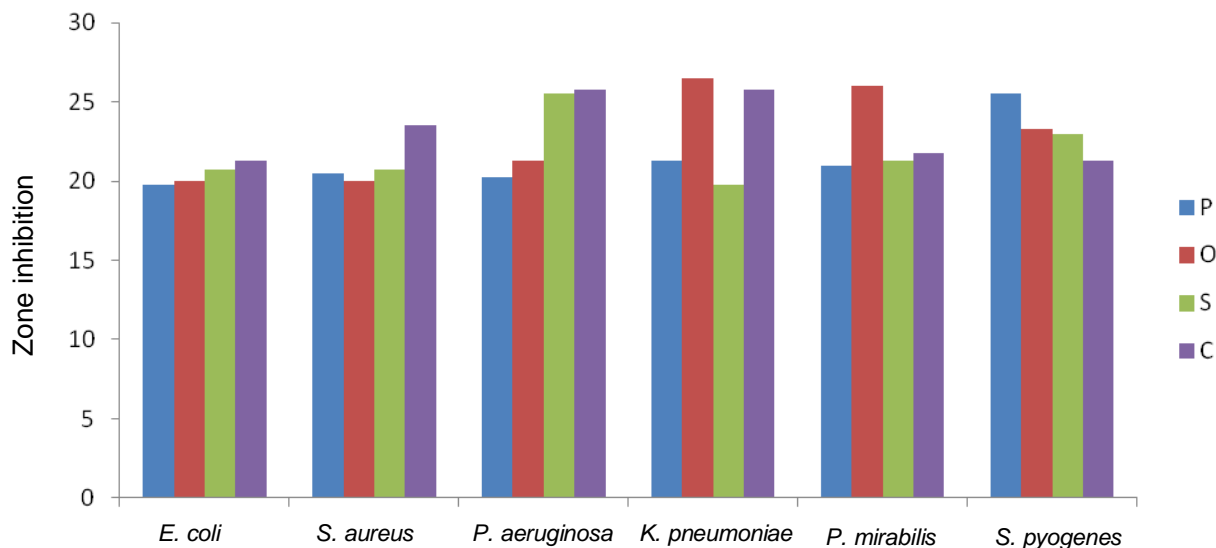


Figure 1. Overall average zone of inhibition. P: Pefloxacin; O: ofloxacin; S: sparfloxacin; C: ciprofloxacin.n

Table 2. The overall average zone of inhibition in millimetres (mm).

Isolate	P	O	S	C
<i>E. coli</i>	21.3	21.6	23.1	20.4
<i>S. aureus</i>	22.6	23.1	23.8	22.6
<i>P. aeruginosa</i>	21.9	22.0	22.2	23.6
<i>K. pneumoniae</i>	24.4	23.1	19.4	22.5
<i>P. mirabilis</i>	21.3	25.6	22.3	22.5
<i>S. pyogenes</i>	22.0	22.8	22.6	21.4

P: Pefloxacin; O: ofloxacin; S: sparfloxacin; C: ciprofloxacin.

millimetre (mm). The least zone of inhibition was 13 mm, recorded in the first quarter by sparfloxacin against *P. aeruginosa*, and in the fourth quarter by pefloxacin and sparfloxacin against *S. aureus* and *K. pneumoniae*, respectively. The largest zone of inhibition recorded was at 35 mm in the first quarter by ciprofloxacin against *S. aureus* and in the second quarter by ciprofloxacin and pefloxacin against *K. pneumoniae* and *E. coli*. The overall average zone of inhibition by each drug on each of the six isolates tested is as shown in Table 2 and Figure 2.

Statistical analysis showed that the average effect of all four drugs in comparison had no significant difference at 5% significant level against *S. aureus*, *S. pyogenes*, *E. coli*, *P. aeruginosa*, and *K. pneumoniae*. However, there was a significant difference in the average effects of the drugs on *P. mirabilis*. Multiple comparisons (using LSD test) showed that ofloxacin had a significant effect at 5% significant level on *P. mirabilis* unlike other drugs.

Of all the samples analysed, urine consistently had all test isolates analysed in this study. Independently of other sample isolates, statistical analysis of the average effect of the drugs on the urine isolates showed no significant difference at 5% significant level.

DISCUSSION

The six species isolated in this study are very common clinical isolates implicated in various clinical diagnoses. In virtually all these isolates, resistance to the first line drugs have been reported in different research works, which may have prompted the use of fluoroquinolones in empirical treatments. Many research works have been published in relations to resistance in these bacteria against the fluoroquinolones both from in-patients and out-patients. The most commonly prescribed of the fluoroquinolones is ciprofloxacin. Resistance to this drug was discovered in the mid-1990s, and it increased slowly from 1.2% in 1998 to 2.5% in 2001 (Kalowsky et al., 2002). The North American Urinary Tract Infection Collaborative Alliance (NAUTICA) study revealed that ciprofloxacin resistance increased to 5.5% in 2004 (Zhanet al., 2006). Uropathogens studied between the years 1996 and 2009 in the province of British Columbia demonstrated an increase in fluoroquinolone resistance. The resistance rates in *E. coli* and *K. pneumoniae* increased from <2% in 1996 to ≥20% in 2009; the resistance rates of fluoroquinolones for *P. mirabilis*

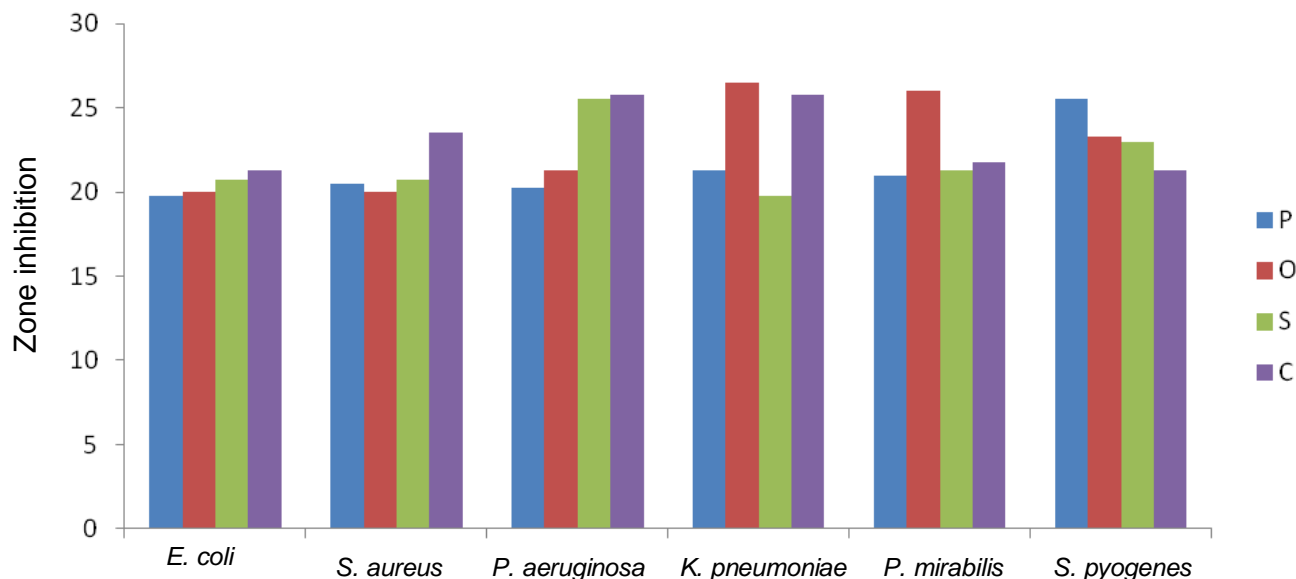


Figure 2. Overall average of drugs on urine isolates only. P: Pefloxacin; O: ofloxacin; S: sparfloxacin; C: ciprofloxacin.

remained almost constant throughout the years at $\leq 2\%$. *Enterococci* demonstrated frequently resistance against fluoroquinolones although resistance rates decreased between 2002 and 2009 (AMR Report, 2009). The Antimicrobial Resistance Epidemiological Survey on Cystitis (ARESC) study revealed that in uropathogens collected in nine European countries and Brazil from 2003 to 2006 ciprofloxacin resistance in *E. coli* was recorded in $>10\%$ of all the isolates in Brazil, Spain, Italy, and Russia; in the remaining European countries, ciprofloxacin resistance ranged from 1.4% in France to 6.7% in Poland (Naber et al., 2008; Schito et al., 2009; Neuzillet et al., 2012). Though extended spectrum beta-lactamase production was not verified in our isolates, it has been however reported that increase to fluoroquinolone resistance is aided by its production (Azap et al., 2010). Increasing fluoroquinolone resistance in pneumococci paralleled increased usage of fluoroquinolones in general or 2nd generation quinolones in particular (Chen et al., 1999; Waites and Brown, 2003; Bhavnani et al., 2005; Pletz et al., 2011). Occasionally, fluoroquinolone resistance resulted in clinical failures in patients with pneumococcal pneumonia having been previously treated empirically with oral fluoroquinolones (Ho et al., 1999; Urban et al., 2001; Davidson et al., 2002; Pottumarthy et al., 2005; Fuller and Low, 2005). In total, there were 20 ciprofloxacin and levofloxacin treatment failures reported till January 2005 and reviewed by Fuller and Low (2005). Susceptibility testing of *P. aeruginosa* isolates from cystic fibrosis (CF) patients revealed that ciprofloxacin resistance in Europe ranged from 13.7% in Bulgaria (Strateva et al., 2009) to approximately 30% in the UK, Spain, Germany, and Italy (Schulin, 2002; Pitt et al., 2003; Morosini et al., 2005; Manno et al., 2005);

37.4% of the US isolates were ciprofloxacin-resistant (Burns et al., 2000). One of the most important features of bacterial resistance to fluoroquinolones is the ability to accumulate several mutations, affecting both DNA gyrase and bacterial permeability and resulting in strains associated with very high MICs (e.g. MICs of ciprofloxacin of 32 to 1,024 $\mu\text{g/ml}$). Such strains have been observed among isolates of *S. aureus*, Enterobacteriaceae species, and *P. aeruginosa* (Truong et al., 1995; Lehn et al., 1996). Widely varying percentages of resistance to fluoroquinolones have been associated with particular bacterial species, clinical settings, origin of strains, geographic locations, and local antibiotic policies (Acar and Goldstein, 1997). The continued increase in fluoroquinolone resistance rates affects patient management and necessitates a change in some current guidelines for the treatment of, for example, urinary tract infections (Peterson, 2004; Han et al., 2010; Wagenlehner et al., 2011).

Conclusion

Although all fluoroquinolones used in this study showed potency against the clinical isolates for the period of study, this does not negate the need for periodic monitoring of the efficacy of these drugs, as well as strict compliance to drug usage policies.

ACKNOWLEDGEMENT

The authors wish to thank the staff of the Babcock University Medical Centre's laboratory for making available the clinical samples used in this study.

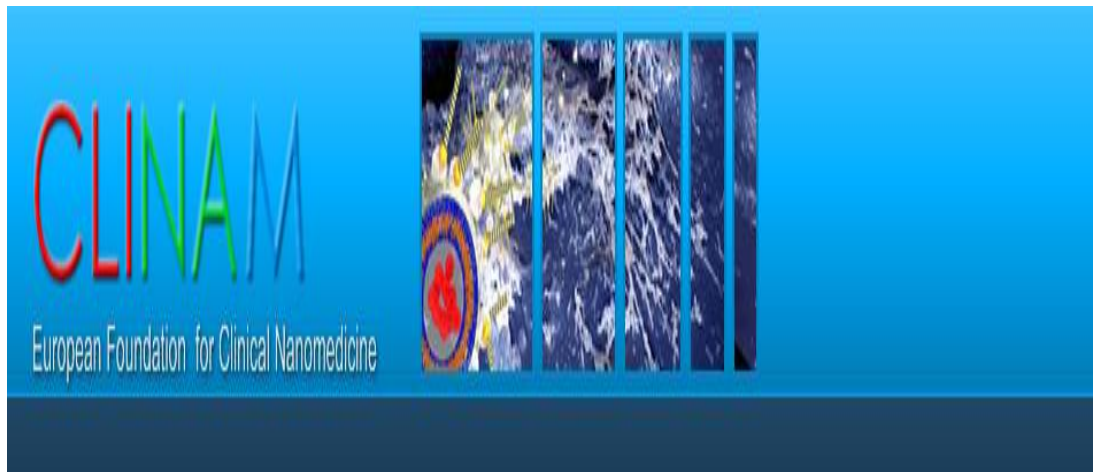
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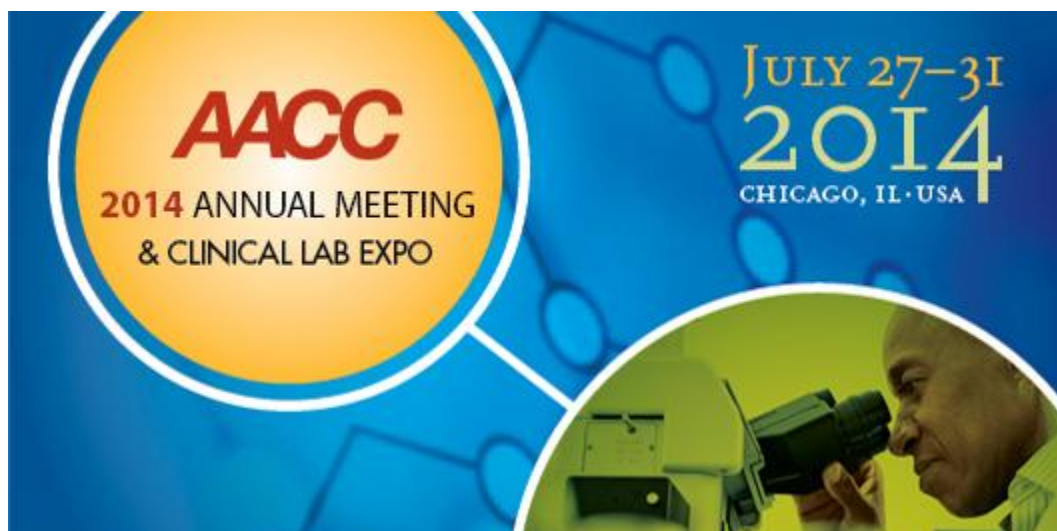
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