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Comparison the Effect of Ceftriaxon and Ampiclox Product by Different Available Companies in Iraq Pharmacies

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Abstract : Aims : In the last years, Iraq became open market to different unguaranteed antibiotics companies, and the local pharmacies arefull of cheateddrug and antibiotics.Most these antibiotics are ineffective. In Iraq, about 50% of patients take the drugs randomly without physician's prescription, without any test and take antibiotics depending onpharmacists.This study sheds light on this matter.

Methods : All productive companies of antibiotics in Iraq were admitted in this study.Twelve of different Ceftriaxone and seven of different Ampiclox(Ampicillin/Cloxacillin) were produced by companies which available in Iraq pharmacy. Those antibiotics were tested usingbroth dilution method.

Results : The resultsof ceftriaxone screening showed that (acino and Roth) companies which produce these antibiotic are the most antimicrobial effect, whereunto their minimum inhibitory concentration (MIC)=8μg/ml, followed by (REX,Bili, LDP and PHIL.GMP) companies,their MIC= 16μg/ml while (SANAVITA, Ronly, Pharma International, United, BRAWN and LG life sciences) companies, the MIC= 32 μg/ml, are the lowest antimicrobial effect.

Ampiclox screening revealed that (TROGE, SANAVITA and CCM) companies are the most antimicrobial effect,their MIC= 256 μg/ml, followed by (BRAWN and LDP) companies, the MIC= 512μg/ml, followed by (LG Life Sciences) the MIC= 1024 μg/ml, while (Natural Pharma Limited) companies, the MIC = 2048 μg/ml, are the lowest antimicrobial effect.

Conclusion: This study indicates that the productive companies (acino and Roth)of ceftriaxone are good options, following by (REX, Bili, LDP, GMP and PHIL). While all ampiclox options are not efficient because their MIC are very high.

Keywords : Iraq Pharmacies, Antibiotics, Determining Minimum Inhibitory Concentration (MIC).

1. Introduction

The phenomenon of cheated drug is the most serious problems that faces the people health all over the world. This problem doesn't cause side effect only, but record high ratio of deaths. According to American reports (WHO and FDA), the trade of cheated drug increases in the world to more than 50 billion dollar yearly. This rate is in 2007 and may rise to 75 billion dollar in 2012. The problem of cheated drug is wide spread in developing and unstable countries as in Iraq [1]. Antibiotics are one of the most commonly prescribed drugs

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today and widespread access to antibiotic without prescription, with resultant inappropriate use may lead to increase development of resistant strain [2,3].About 50% of patients in Iraq take the drugs randomly without physician's prescription, without any test and take antibiotics depending on pharmacists. Rational use of antibiotics is extremely important as injudicious use can adversely affect the patient, cause emergence of antibiotic resistance and increase the cost of health care [4,5].

In local pharmacies, most available drugs contain antibiotics concentrations lower than written information [1]. As known, most bacteria can develop the mechanisms resistance to antibiotics when exposure to low concentrations, so the emergence and spread of resistance to some antibiotics are threatening to create species resistant to all currently available agents [6].

Material & Methods

This study was performed in the department of microbiology from October,2017 till April, 2018. Twelve different sources of ceftriaxon and seven of ampiclox powderwere produced by different companies and used in this study (Table-1& 2), Mueller-Hinton broth, sterile tubes, sterile and distilled water containing suspension of(128μg/ml of ceftriaxon and ampiclox), tubes of sterile saline (5.0 and 9.9 ml per tube), millipore filter 0.45μm and overnight plate culture of *Pseudomonas aeruginosa* isolated from Otitis medium.

Table – 1. Ceftriaxone companies produced.

Company	Country
Acino	Switzerland
REX	Budapest Hungary
Roth	Germany
Bili	Samsun-Istanbul
SANAVITA	Germany
LDP	Torlan-Spain
United	Amman- Jordan
PHIL.GMP	USA
Pharma International	Amman-Jordan
Ronly	London.UK.
BRAWN	India
LG Life Sciences	India

Table – 2. Ampiclox companies produced.

Company	Country
TROGE	Hamburg-Germany
SANAVITA	Werne-Germany
CCM	Duopharma-Malaysia
BRAWN	India
LG Life Sciences	India
LDP	Spain
Natural Pharma Limited	China

Determining Minimum Inhibitory Concentration (MIC):

This test was performed according to Tim Sandle (2016) and Frankline *et al*,(2010).

1. All antibiotics solutions were sterilized using 0.45 μm millipore filters.
2. Nine steriled tubes were labeled and placed in a rack.
3. 0.5 ml of sterile broth was added to each tube.
4. 0.5 ml of the ceftriaxon and ampicloxbroth were added to the first tube, then the pipette was discarded. The concentration of ceftriaxon in this tube is 128μg per ml, and 4096 μg per ml of ampiclox respectively.

5. A fresh pipette was introduced into the first tube (128μg per ml of ceftriaxone and 4096 μg per ml of ampiclox), andthe contents were mixed thoroughly, then 0.5 ml was transferred from this tube into the second tube (64 and 2048μg per ml respectively).
6. The dilution processes were continued through tube number (7). The eighth and ninth tubes receive no antibiotic.
7. After the contents of the seventh tube are mixed, 0.5 ml of broth was discarded, so that the final volume in all tubes is 0.5 ml.
8. Suspension from the plate culture of *P. aeruginosa*wasprepared. A suspension of the organism in 5 ml of saline equivalent to a McFarland 0.5 standard.
9. 0.1 ml of the *P. aeruginosa* suspension transferred into a tube containing 9.9 ml of saline. The pipette was discarded.
10. With a fresh pipette, the contents of the tube well were mixed. 0.1 ml of this organism suspension was added to the antibiotic-containing broth tubes 1 through 7 and to the growth control tube.
11. The rack was shacked gently to mix the tube contents and the tubes were placed in the incubator for 18 to 24 hours.
12. After incubation overnight, the tubes were examined for turbidity produced by bacterial growth. The first tube in which visible growth is absent (clear) is the MIC for that organism.

Results

Table 3 and 4, show Determining Minimum Inhibitory Concentration (MIC) results profiles of ceftriaxone and ampiclox.According to the presented results, *P. aeruginosa* isolate is resistant to all ampiclox which produced by different companies, whereunto the MIC value reached up to 2048 μg/ml. While, the produced ceftriaxoneby different companies are more active than ampiclox, though there are variation in MIC values,

Table-3. MIC of all available ceftriaxone.

Ceftriaxoneproducers	MIC
Acino - Switzerland	8 μg/ml
Roth- Germany	8 μg/ml
REX- Budapest Hungary	16μg/ml
Bili- Samsun-Istanbul	16 μg/ml
LDP- Torlan-Spain	16 μg/ml
PHIL.GMP - USA	16 μg/ml
SANAVITA- Germany	32μg/ml
United- Amman- Jordan	32μg/ml
Pharma International- Amman-Jordan	32μg/ml
Ronly- London.UK.	32μg/ml
BRAWN- India	32μg/ml
LG Life Sciences- India	32μg/ml

Table -4. MIC of all available of ampiclox

Ampiclox producers	MIC
TROGE- Hamburg-Germany	256μg/ml
SANAVITA-Werne-Germany	256μg/ml
CCM- Duopharma-Malaysia	256μg/ml
BRAWN- India	512μg/ml
LDP- Spain	512 μg/ml
LG Life Sciences- India	1024μg/ml
Natural Pharma Limited- China	2048μg/ml

Discussion

This study is new and significant because there are no previous researches that deal this topic. So, the discussion of our results is authentic and has no similar written researches in Iraq.

An Minimum Inhibitory Concentration (MIC) is generally regarded as the most basic laboratory measurement of the activity of an antimicrobial agent against an organism[9,10]. This study used *P. aeruginosa* strain which is very notorious for its resistance to antibiotics [9], though many of used antibiotics are very effective against this bacteria.

Table-3, shows moderate variation in MIC scoresof ceftriaxone antibiotics producers. MIC of ceftriaxone was produced by acino and Roth companies are low value 8 μg/ml. Because a lower MIC value indicates that less of the drug is required in order to inhibit growth of the organism, drugs with lower MIC scores are more effective antimicrobial agents [11,12].So,ceftriaxone that produced by acino and Roth companies aremore effective than others, followed by REX, Bili, LDP and PHIL.GMP are MIC score 16 μg/ml, followed by SANAVITA, United, Pharma International, Ronly, BRAWN and LG Life Sciences , are MIC score 32 μg/ml.

According to (performance standards for antimicrobial susceptibility testing, twentieth informational supplement) which refer that MIC testing acceptable limits (μg/ml) of ceftriaxone and ampiclox for quality control *P. aeruginosa* strain used to monitor accuracy using Mueller-Hinton medium without blood or other nutritional supplements is (**8- 64**) and (**2- 8**) μg/ml respectively [8]. So that all ceftraxion sources which admitted in this study are good options and acceptable.

Table-4 showresults of ampiclox screening companies, andits reveal that these antibiotics were loses effective against *P. aeruginosa*,since theMIC score ofTROGE, SANAVITA and CCM companies 256 μg/ml, followed by BRAWN and LDP 512 μg/ml, followed by LG Life Sciences 1024 μg/ml, followed by Natural Pharma Limited 2048 μg/ml.

According to (Frankline *et al*, 2010) these MIC values of ampicloxare very highand very surprise, so these values are unacceptable. (Al-Bakri *et al.,* 2005;Oyetunde *et al.,* 2010) refer that ampiclox is the most commonly purchased antibiotic without prescription, with resultant inappropriate usemay lead to increase development of resistant strain. In Nigeria, many studies refer that in the last years most bacterial strains became resistant to ampiclox [13,14].

Some companies produced both used antibiotics which admitted in this study, but there varying in activity against *P. aeruginosa* isolate. For example, ceftriaxone produced by LDP- Spain company is effective and its MIC scorewas 16 μg/ml, while ampiclox was produced by same company is inefficient effect and its MIC is 512 μg/ml.

Conclusion :

This study indicates that the productive companies (acino and Roth) are good options, following by (REX, Bili, LDP, GMP and PHIL). While all ampiclox options are not because their MIC scores are very high and discordant to international standards scores.

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