AMJ
ISSN: 0005-2523

ISSN: 0005-2523
Volume 63, Issue 01, May 2023

CLINICAL COMPARATIVE OF SAFETY AND EFFICACY OF MACROLIDES AND ORAL CEPHALOSPORIN IN TREATMENT OF DIFFERENT INFECTIONS

Zina Tahsin Ali
Al-Muthanna University, College of Pharmacy, Clinical pharmacy Department.
Email: dr_zta@mu.edu.iq

Abstract:

Most bacterial infections can be successfully treated with antibiotics, although this must be balanced against potential side effects and worries about the emergence of bacterial resistance to antibiotics, which would diminish their efficacy. Bacterial infections can be dangerous and very contagious. to clarify the efficacy and safety of macrolides against different bacterial infection in contrast with oral cephalosporin.the study start from April 2021 to October 2022 in Almuthanna/ Iraq,The trial was continued with 500 patients: (i) patients whom taking macrolide A group (n=250), and (ii) whom taking cephalosporin B group (n=250). Both received the full pharmaceutical care then collect data and evaluate it after taking treatment by 5,10 and more than 10 days, the Patients medications adherence and antibiotics resistance were valuated. the results revealed that the efficacy of both groups was very close in similarity and only (5.2% of patients taking macrolide vers 4.4% taking cephalosporin)not improved due to low patient medication adherence or antibiotics resistant, also A group had more side effect in contrast with B group.

Key words: macrolide, oral cephalosporin, efficacy, safety, patients medication adherence

Introduction :

Bacterial infections can be harmful and highly contagious ,Most of it can be effectively treated with antibiotics which must be weighed against potential side effects and concerns over the development of bacterial resistance to treatment with antibiotics that reduces their effectiveness so should prescribed it only for serious conditions(1,2).

The cephalosporins are a large group of related β-lactam antimicrobial agents ,a low rates of toxicity, a fairly wide range of activity, and convenience of administration are positive characteristics of cephalosporins. Many illnesses can be successfully treated with different cephalosporins, including meningitis, skin and soft tissue infections, bacteremia, and pneumonia. The various cephalosporin antimicrobial drugs have a variety of small variances, but understanding these differences is crucial for the best usage of these agents. Bacterial resistance to cephalosporins is becoming more prevalent as a result of their extensive use, For the treatment of infections brought on by some drug-resistant germs, new, fourth-generation medications (such cefepime) provide an option(3).

Risk of adverse reaction to cephalosporin is controversial,a greatest with first- or second-generation drugs, Mild gastrointestinal problems are the most typical response to oral dosage. One to three percent of treatment courses experience hypersensitivity reactions, which might include pruritus, urticaria, and morbilliform rash. Cephalosporin administration has been linked to drug fever. Cephalosporin use can result in non-specific antibiotic-associated diarrhea and, less

frequently, C. difficile toxin-mediated colitis .Other side effects are uncommon, and some are specific to one or a few cephalosporins, such as bleeding, Coombs-positive hemolytic anemia, and reversible neutropenia, which can happen after long-term usage of high-dosage cephalosporins. Any cephalosporin with a methylthiotetrazole side chain may produce altered hemostasis due to hypoprothrombinemia (cefamandole, cefotetan, and moxalactam) (4,5).

In addition to having antimicrobial properties, macrolides like erythromycin, clarithromycin, and azithromycin also have widespread anti-inflammatory and immunomodulatory effects. The antimicrobial effects of macrolides include direct bacterial killing, the prevention of biofilm formation by interfering with microbial quorum sensing, and the stimulation of phagocytosis of bacteria by macrophages. Chronic use of macrolides, on the other hand, has been linked to the development of macrolide-resistant bacteria in the commensal flora of the pharynx of individual patients and also raises the possibility of an increase in antibiotic resistance among the general population(6). Users of macrolide antibiotics run the risk of developing side effects such nausea, diarrhea, or dermatitis (7).

Aim of study :

to clarify the therapeutic effects of macrolides (erythromycin, azithromycin and clarithromycin) against different bacterial infection include(respiratory tract infections, urinary tract infections and gastro tract infections) in contrast with oral cephalosporin(cephalexin, cefixime and cefopodoxime) also quantify the incidences of reported adverse events for both groups clinically.

Patients and Methods:

Patients:

from April 2021 to October 2022 in Almuthanna/ Iraq,The trial was continued with 500 patients with different bacterial infections among those visiting privet internal medicine clinic before going to pharmacy to receiving the treatment .

Included patients:

1. Patients were prescribed macrolide antibiotics (azithromycin, clarithromycin, and erythromycin) or oral cephalosporins (cephalexin,cefixime and cefopodoxime) after being diagnosed with various bacterial illnesses (RTI, UTI, and GTI)
2. Patients who can verbally communicate and are between the ages of 17 and65.

Excluded patients

1.Patients who were pregnant.
2.patients have history of renal or liver diseases.
3.patients who had used antibiotics previously in the week prior to the research..
2. Patients who are not educated or live in remote rural areas because it is difficult to communicate with them.

Method

Study design:

The study was a prospective, randomized trial in which patients were have close differences for both groups in term of demographics and pre-treatment clinical presentation and patients

medications adherence (table .1).

In cooperation with the specialist physician, It was conducted with 500 patients : (i) patients whom taking macrolide A group (n=250), and (ii) whom taking cephalosporin B group (n=250). Both received the full pharmaceutical care which included individual education to increase patients medications adherence . Face to face interviews (for approximately 10 min) at baseline then all patients asked to visit the pharmacy to collect data and evaluate it after taking treatment by 5,10 and more than 10 days ;telephone calling for check and evaluation to whom can't coming to pharmacy.

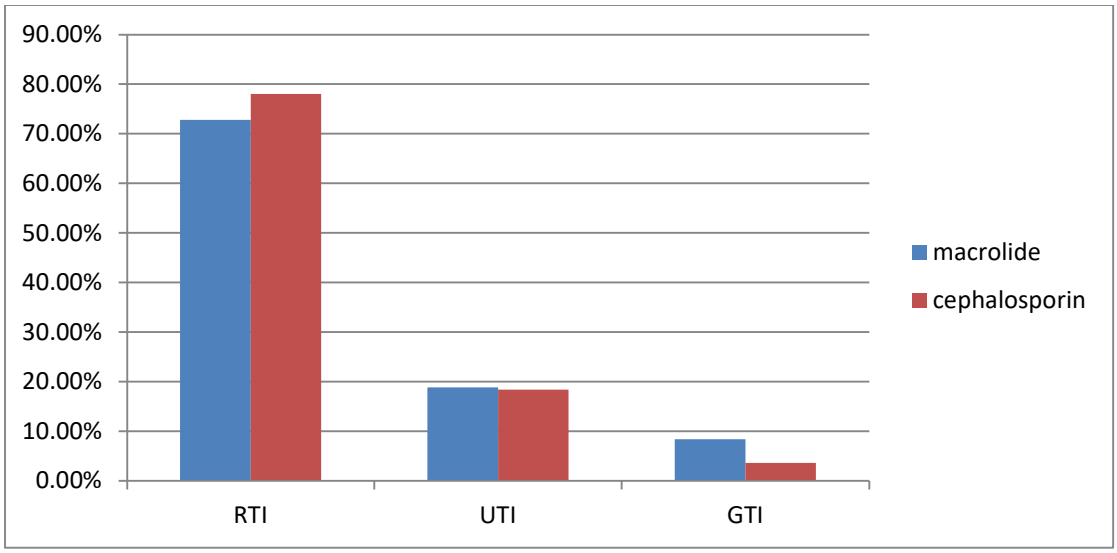
Collected data included age,gender, types of bacterial infections, patients medications adherence ,efficacy and safety of medications

Patients medications adherence was evaluated by specific questionnaire contained 9 questions (8) and evaluation based on: Six or more answers with "yes" mean high adherence, four or five answers with "yes" mean intermediate adherence and three or less answers with "yes"=low adherence.

Evaluation of ;efficacy was depend on completely resolve of clinical presentation of bacterial infection and make sensitivity culture test to whom not improved ,while safety was depend on recording each side effect concomatly appearing during medications taking.

(Table-1):Demographic data of the two groups.

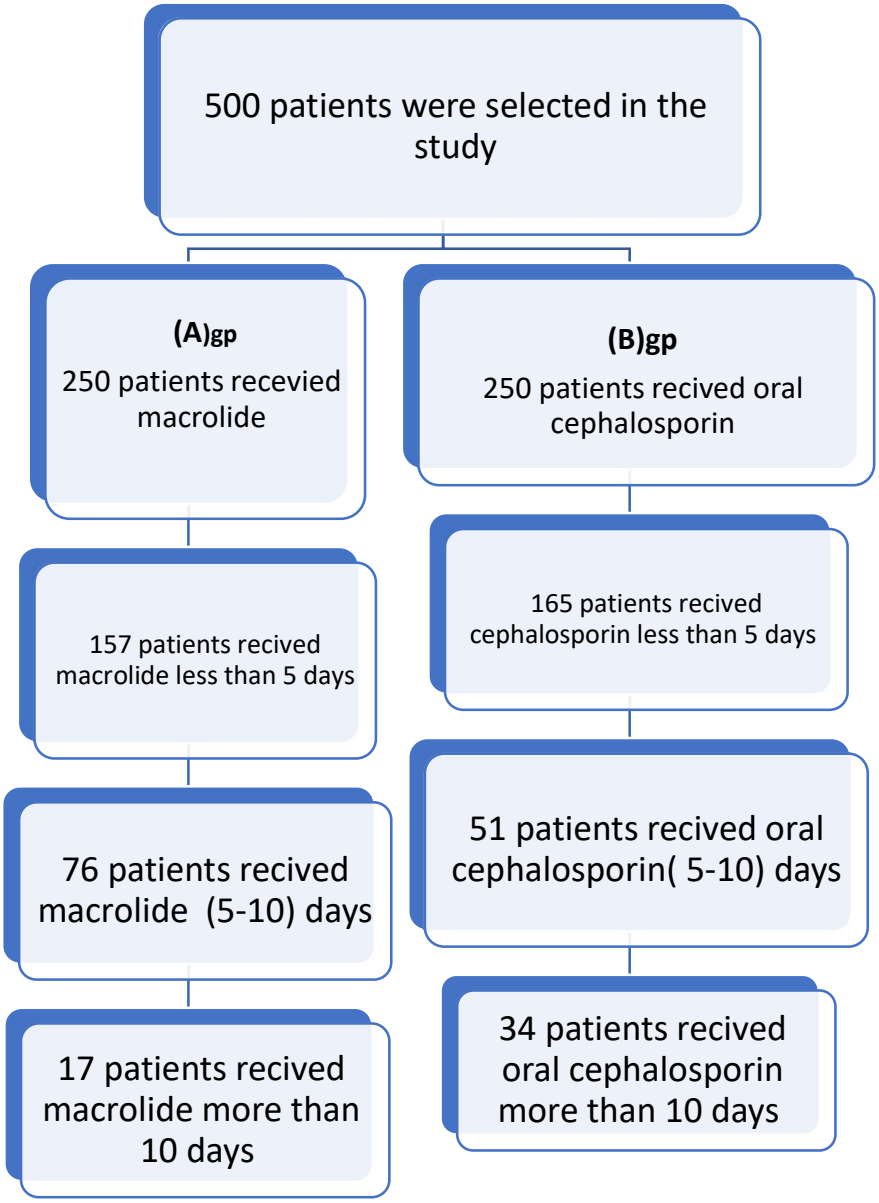
		gp A n=250 (%) Taking Macrolide	**gp B n=250 (%) Taking Cephalosporin**
Age (years)	17-45	203 (81.2%)	198 (79.2%)
	45-65	47 (18.8%)	52 (20.8%)
gender	Female	177 (70.8%)	190 (76%)
	Male	73 (29.2%)	60 (24%)
Type of infections	RTI	182 (72.8%)	195 (78%)
	UTI	47 (18.8%)	46 (18.4%)
	GTI	21 (8.4%)	9 (3.6%)
Patients medications adherence	High adherence	241(96.4%)	234(93.6%)
	Intermediate adherence	7(2.8%)	7(2.8%)
	Low adherence	2(0.8%)	9(3.6%)



(Figure-1):types of infection treated by macrolide&cephalosporin

Results and discussion :

500 patients were enrolled in two groups (A gp contain 250patients whom taking macrolide while Bgp contain 250patients whom taking oral cephalosporin).the results revealed that the end point when resolved all bacterial infection clinical presentation for Agp was during 5 days for 157 patients,10 days for 76 patients and more than 10 days for17 patients while to Bgp was during (5,10 and more than 10) days for (165,51 and 34) patients respectively (figure-2).



(Figure-2):distribution of population according to the end point of the study

This results explain the improvement of most patients taken different types of antibiotics at certain duration ,since (62%) of patients in Agp whom taking macrolide was improved in less than (5) days, (30.4%) during (5-10) days , (1.6%) in more than(10)days while the remaining (5.2%) not improved.

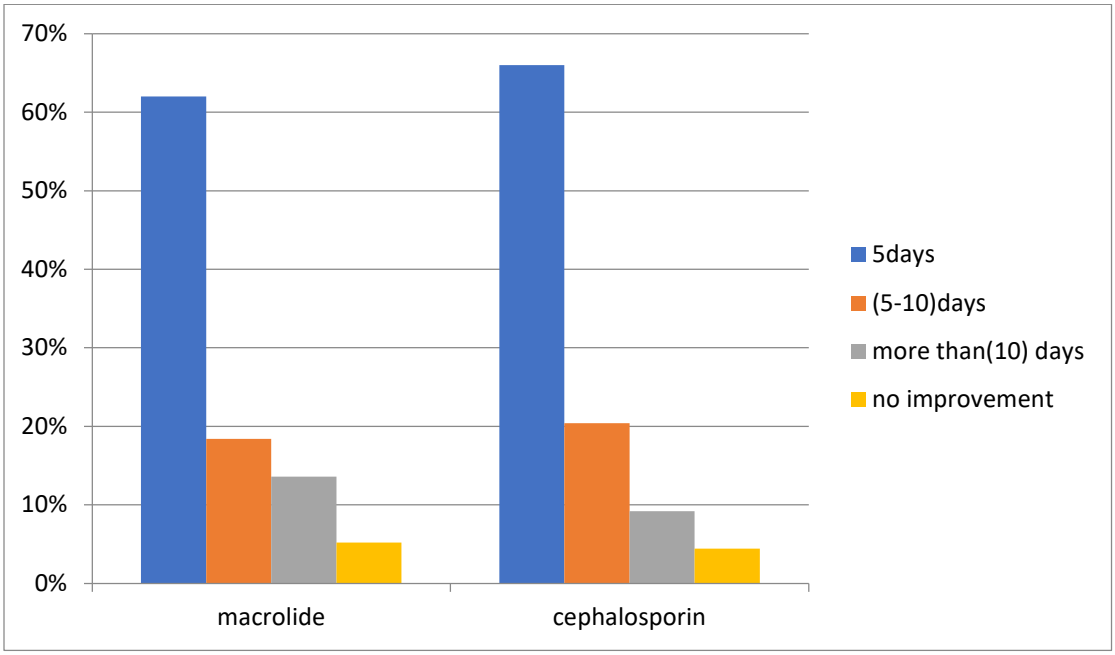
In B gp whom taking oral cephalosporine (66%) of patients was improved in less than (5) days, (20.4%) during (5-10) days , (9.2%) in more than(10)days while the remaining (4.4%) not improved.(table-2)&(figure-3)

the above results show good efficacy for both groups which resemble to results of similar studies (9) and low percentage only of patients was not improved and that may be due to low

medications adherence or antibiotics resistance . Antibiotic resistance leads to failed treatments (10).

(Table-2):efficacy of macrolide &cephalosporin during different duration.

medications	Duration to improvement N=250(%)			
	(5) days	**(5-10) days**	**More than (10)days**	**No improvement**
gp(A): taking macrolide	157 (62%)	76 (30.4%)	4 (1.6%)	13 (5.2%)
gp(B):taking cephalosporin	165 (66%)	51 (20.4%)	23 (9.2%)	11 (4.4%)



(figure-3):efficacy of macrolide &cephalosporin during different duration.

During clinical side effect evaluation, results revealed that (140out 172,43out 65 and 7 out 13) of patients whom taking (azithromycin, clarithromycin and erythromycin)respectively suffered from gastric upset,(17 and 3 out 172)of patients whom taking azithromycin suffered from(headache and cardiac arrhythmia)respectively. the remaining patients (12 out 172, 22 out 65 and 6 out 13) respectively did not suffered from any clinical side effect.

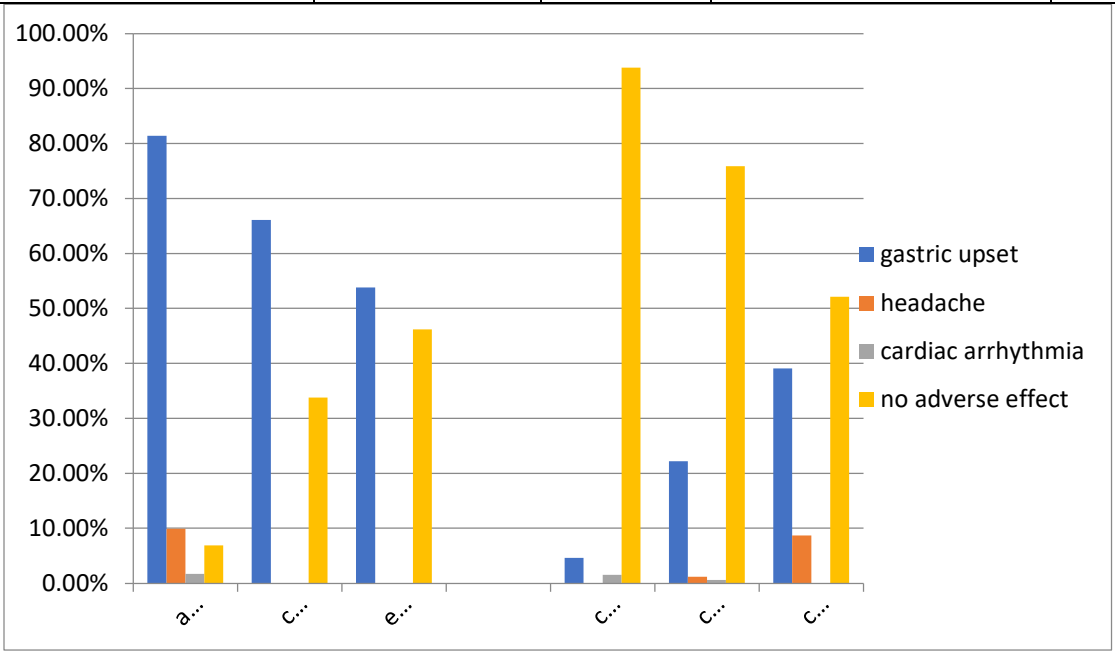
For patients whom taking oral (cephalexin,cefixime and cefopodoxime) (3 out 65,36 out 162 and 9 out 23)respectively suffered from gastric upset,(0 out 65,2 out 162 and 2 out 23)respectively suffered from headache and (1 out 65,1out162 and 0 out 23)respectively suffered from skin rash. while the remaining patients(61out 65,123 out 162 and 12 out23) respectively did not suffered from any clinical side effect (table-3& figure-4).

From above results, the majority of side-effects involve the gastrointestinal disturbance in both

groups and this similar to previous studies(11). In general results revealed that the patients whom taking macrolide suffered from different side effect more than patients whom taking oral cephalosporin.

(Table-3): clinical Side effects of treatment for two (A and B) groups.

Macrolide gp	**Gastric upset**	**headache**	**Cardiac arrhythmia**	**No adverse effect**
Azithromycin 500 mg N=(172)	140(81.4%)	17(9.9%)	3(1.7%)	12(6.9%)
Clarithromycin 500 mg N=(65)	43(66.1%)	-	-	22(33.8%)
Erythromycin 500 mg N=(13)	7(53.8%)	-	-	6(46.2%)
Cephalosporin gp	**Gastric upset**	**headach**	**Skin rash**	**No adverse effect**
Cephalexin 500 mg N=(65)	3(4.6%)	-	1(1.5%)	61(93.8%)
Cefixime 400 mg N=(162)	36(22.2%)	2(1.2%)	1(0.6%)	123(75.9%)
Cefopodoxime 200mg N=23	9(39.1%)	2(8.7%)	-	12(52.1%)



(Figure-4):clinical Side effects of treatment for two (A and B) groups.

Conclusion:

Both groups (macrolide& oral cephalosporin) had very close result in efficacy ,but oral cephalosporin had less side effects reported by the patients participated in the study.

More studies with larger numbers of samples are needed to further evaluation.

References:

1- https://www.healthdirect.gov.au/bacterial-infections.
2- Kaehne A, Milan SJ, et al.cochrane.org/CD012590/AIRWAYS_how-do-different-antibiotics-compare-terms-safety-and-treatment-effectiveness people-bronchiectasis ,5 September 2018.
3- Christopher A. Crutchfield, Mark A. Marzinke, Bioanalytical development and validation of liquid chromatographic–tandem mass spectrometric methods for the quantification of total and free cefazolin in human plasma and cord blood, Practical Laboratory Medicine, Volume 1,2015,Pages 12-21.
4- ames W. Little DMD, MS, ... Nelson L. Rhodus DMD, MPH, in Little and Falace's Dental Management of the Medically Compromised Patient (Eighth Edition), 2013.
5- Ian C. Michelow, George H. McCrackenJr., in Feigin and Cherry's Textbook of Pediatric Infectious Diseases (Sixth Edition), 2009.
6- Brusselle GG Are the antimicrobial properties of macrolides required for their therapeutic efficacy in chronic neutrophilic airway diseases? Thorax 2015;70:401-403.
7- Hansen MP, Scott AM, McCullough A, Thorning S, Aronson JK, Beller EM, Glasziou PP, Hoffmann TC, Clark J, Del Mar CB. Adverse events in people taking macrolide antibiotics versus placebo for any indication. Cochrane Database of Systematic Reviews 2019, Issue 1. Art.
8- Ali ZT, Al Saadi MTA, Al Saadi NTA (2019): Incidence of stroke with uncontrolled DM: effect of pharmaceutical care intervention to DM type-2 patients in Iraqi hospitals, Ann Trop & Public Health; 22(8): S226.
9- Williams DJ, Edwards KM, Self WH, et al. Effectiveness of β-Lactam Monotherapy vs Macrolide Combination Therapy for Children Hospitalized With Pneumonia. JAMA Pediatr. 2017;171(12):1184–1191. doi:10.1001/jamapediatrics.2017.3225.
10- (Gyssens IC. Antibiotic policy. Int J Antimicrob Agents. 2011 Dec;38 Suppl:11-20. doi: 10.1016/j.ijantimicag.2011.09.002. Epub 2011 Oct 21. PMID: 22018989.)
11- G.D.Williams: Evaluation of the safety of macrolides ,international journal of antimicrobial agents.https://www.sciencedirect.com/journal/international-journal-of-antimicrobial-agents, volume 18,supplement.1 September 2001, Pages 77-81