Therapeutic study of rosacea by Azithromycin and Metronidazole

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Summery:

Background: Rosacea is a chronic disease that requires long-term systemic and or local therapy, which carries risk for systemic complications and adverse reactions and high recurrence rate.

Patient and methods: Two groups of rosacea patient with at least 8 inflammatory papules and pustules, moderate to severe facial erythema (22 patient treated with oral azithromycin versus 18 patient treated with oral metronidazole) were studied at single medical center (medical city of Baghdad: department of dermatology and venereology , both for 60 days, Subjects were evaluated monthly for up to three months to determine the relapse rate. Main outcome measures: Inflammatory papules and pustules were counted at each visit, relapse were determined by the appearance of a clinically significant increase in number of papules and pustules. Erythema were classified to three grades: - 0=Nil, 1=mild to moderate, 2=severe. Patient satisfaction also classified to three grades: 0=no satisfaction, 1=partial satisfaction, 2=full satisfaction.

Results: Most of the patients respond to treatment measured by at least 70% reduction in the number of inflammatory lesions. (21 patient versus 14 patient) completed the study and compare by assessing:- erythema improvement and papule and pustule count reduction and percentage of occurrence of side effects and relapse, and subjective assessment of the degree of patients satisfaction with their treatment Erythema were reduced after two months of treatment:- (56.6% to 33.3% for azithromycin group versus 43.5% to 66.7% for metronidazole group).Mean papules count reduced from (36.9 to 10 for azithromycin group versus 25.8 to 11 for metronidazole group). Mean pustule count reduced from (2.95 to 0.33 for azithromycin group versus 2.92 to 0.5 for metronidazole group). The percentage of relapse was 16.7% versus 83.3% for azithromycin and metronidazole group respectively. Complete satisfactions were 70% versus 30% and side effect were 20% versus 80% for azithromycin and metronidazole group respectively.

Conclusion: For the above results treatment of rosacea by azithromycin is more effective, safer thanmetronidazole, although the coast is little higher.

Key Words: Azithromycin , Rosacea .

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Introduction:

Rosacea is a chronic acne form disorder of the facial pilosebacous units, coupled with an increase activity of capillaries to heat leading to flushing and ultimately to telangactasia. The disease was previously called “acne rosacea”,(1). Rosacea is not uncommon problem in Iraqi patients. M.mosbahi and co workers in study done at 1996, find that the mean age 42.5 years which is comparable to other studies (2). Rosacea is characterized by episodic flushing of the affected area, which may be associated with the consumption of alcohol, hot drinks, or spicy foods, and swelling,, papules and pustules. The skin lesions are notable for the absence of commedones, which distinguishes this disorder from acne vulgaris, Rhinophyma is a late finding (3) Ocular rosacea is a spectrum of eye findings associated with skin involvement. Occasionally, the ocular manifestation may precede skin involvement, delaying the diagnosis (4) . Rosacea is mainly disease of females and this similarly was confirmed by mosbahi study, as female to male ratio was 4:1. Propagating factors were studied in all patients and were mainly: emotional tension, heat exposure, [mainly cooking fire, hot foods and drinks] and sun light exposure.

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Alcohol consumption has not found to be an aggravating factor as the entire patient were not alcoholics. Etiology of rosacea is still not well determined although many theories have been postulated. Demodex follicularum was found in 41% of patients in contrast to acne vulgaris, which is devoid of this microorganism. (5).

Patients and Methods:

Clinical study was carried out for a period of 17 months from July 2002 to December 2003 in the Department of Dermatology and Veneriology, Baghdad teaching hospital (Baghdad). The study was performed after receiving the agreement from health authorities including Baghdad University medical college council, and from the medical city ethical committee. An interventional clinical trial to compare: efficacy, safety and cost benefit of Azithromycin versus Metronidazole in the treatment of acne rosacea. 40 patients, with moderate to severe papulo-pustular rosacea were treated as two groups of treatments; One with the new azalide antibiotic azithromycin capsule 250 mg /day for 59 days after loading dose of 500 mg in the day one, The other with metronidazole tab 500 mg twice daily as comparative therapy for a total of 60 days.

Table1: the two samples used in clinical trials.

Patient group	start treatment	continue treatment	defaulter
Azithromycin	(22)	(21)	(1)
Metronidazole	(18)	(14)	(4)
Total	(40)	(35)	(5)

Clinical evaluation On day 15 to point out control of the disease by monitoring the appearance of new groups of papules and pustules. At days 0,30 ,60 for assessment of the clinical response of patients by evaluating erythema state and papules and pustules counts . At day 90 to label relapse if happened or not. Photo for the patient in day 0,30,60,90. Erythema Graded as 0= (null) , 1=(mild to moderate-pinkish color) , 2 =(sever-purplish color),Papules and pustules was counted and compared Self satisfaction subjective scale Graded as 0 = (Patient is not satisfied). 1= (Partial satisfaction), 2 = (Complete satisfaction) , Side effects positive or negative at visits of 30 and 60 days., Relapse at day 90 by appearance groups of papules or pustules or both, erythema is not involved ; usually it remains after the treatment.

Results:

After one month of treatments severe erythema was remarkably reduced in the Azithromycin group (14.3% versus 85.7%) while mild to moderate erythema present more frequently in the Azithromycin group (71.4% versus 28.6%)in Metronidazole group. After two months of treatments erythema resolution still higher in Azithromycin group of treatments, regarding severe erythema (33.7% versus 66.7%) and also for mild to moderate erythema, (61.3% versus 38.7%), and only one patient was erythema free in Azithromycin group.

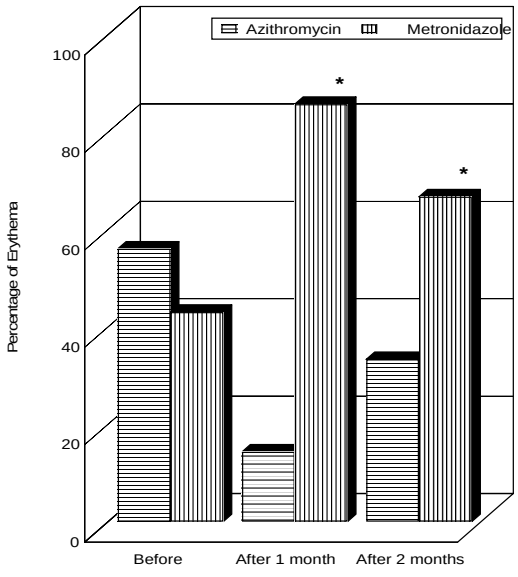

Figure-1 Percentage of erythema in rosacea patient ,in both drug groups .

There were prominent reduction in both groups of treatments regarding papules and pustules counts,(Figure 2 and 3) ; the mean papule count were 36.9 and 25.8 for azithromycin and metronidazole respectively at the beginning of the treatment and become 10 and 11 patients with end point present changes of 64% and 58% respectively, while mean pustules count is reduced from 2.95 and 2.92 to 0.33 and 0.5 for the azithromycin and metronidazole treatment groups respectively with end point present changes of 89% and 82% for azithromycin and metronidazole treatment groups respectively.

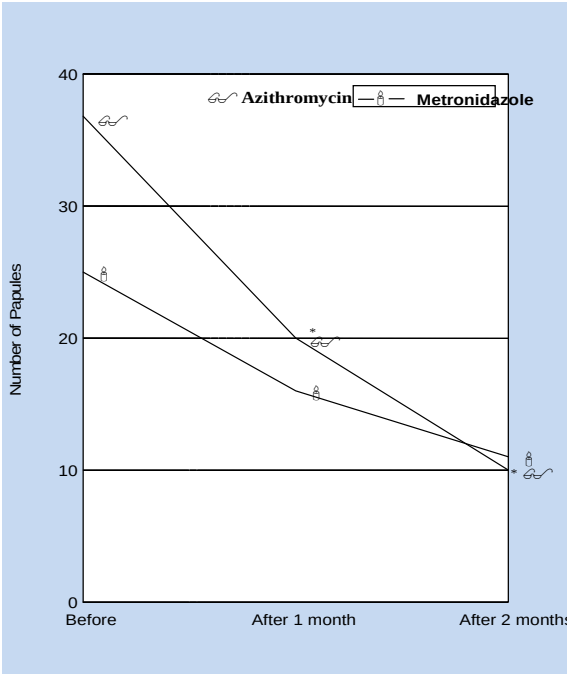

Figure -2 Mean + SD papule number comparison, in both drug groups.

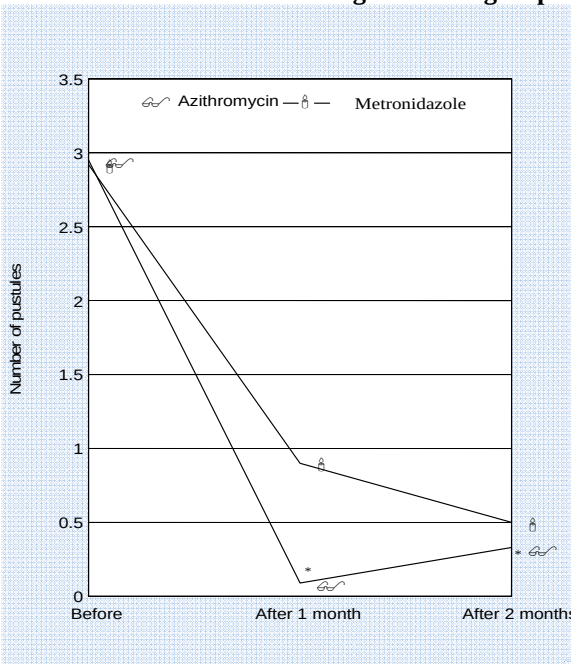

Figure -3 Mean + SD pastule number comparison, in both drug groups.

Relapse rate was estimated after one month of cessation of treatment and were less often to occur in Azithromycin group (16.7% versus 83.3%) in Metronidazole group. See table No-2 :

Table2: Relapse rate in Azithromycin and Metronidazole groups.

DRUG	RELAPSE	
	+ ve	- ve
Azithromycin	16.7%	82.6%
Metronidazole	83.3%	17.4%

Patient satisfaction after one month of the treatments were more in Azithromycin group (77.85 versus 22.2%) After two months of treatment 70% in azithromycin versus 30% with Metronidazole group as in Table No-3 :

Table 3: treatment satisfaction rate in the two groups

DRUG	Satisfaction after 1 month		
	Grade 0	Grade 1	Grade 2
Azithromycin		50.0%	77.8%
Metronidazole	100.0%	50.0%	22.2%

DRUG	Satisfaction after 2 months		
	Grade 0	Grade 1	Grade 2
Azithromycin	40.0%	50.0%	70.0%
Metronidazole	60.0%	50.0%	30.0%

Safety of the two drugs was studied by comparing side effects rate which were more frequent in Metronidazole group than in Azithromycin group (80% versus 20%) respectively. and the degree of satisfaction of patient to the drug safety, table No- 4:

Table 4: side effects rate.

DRUG	Side Effect	
	+ ve	- ve
Azithromycin	20.0%	90.0%
Metronidazole	80.0%	10.0%

Discussion:

Systemic therapy are associated with excellent safety profiles, especially considering there wide spread use over many years ,it must be considered that when these antibiotics are used for the treatment of rosacea there use is on long term bases rather than their typical short coarse regimen for most infectious diseases, as result, dermatologist need to be aware of potential adverse reactions that may be associated with the usage of these drugs, in addition ,potentially significant drug interactions may occurs also.(6) In order to reduce the incidence of these problems and also to overcome the microbial resistance that fluctuate globally, azithromycin, a new generation macrolide antibiotics, presents pharmacokinetic and pharmacodynamic advantages that allow for simple dosing regimen with minimal side effects.(7) Metronidazole were used systemically for moderate to severe rosacea by Mark V Dahl and co-workers.(8) Most of patients on azithromycin treatment were more satisfied about their treatments to be more safe and more effective as compared to metronidazole group, but still Azithromycin Treatment cost is more than metronidazole .see figure -4;

BEFORE AFTER

BEFORE AFTER

Figure 4: Photographic comparison therapy before and after azithromycin .

Conclusion:

This study is probably the first study in Iraq to compare the effectiveness and safety of azithromycin and metronidazole in the treatment of rosacea., Both drugs where safe and effective but azithromycin seems to be safer and more effective

than metronidozel , Azithromycin treatment still more expensive than metronidazole.

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