# Five Days azithromycin is more efficient than ten Days Erythromycin for the Treatment of pertussis

## Baha D. Moohy Alosy

**Departments of Pediatrics, Collage of Medicine, University  of Tikrit, Tikrit, Iraq**

## Abstract

Whooping cough (pertussis) is a highly contagious caused by Bordetella pertussis. During the last decade three Bordetella pertussis isolates have been found to be resistant to erythromycin, the azithromycin are used for treatment of pertussis. Sixty Child as 31 (5-day group) and 29 (10-day group) with pertussis in private clinic were evaluated for more efficiency of a 5-day course azithromycin in compares to a 10-day course erythromycin therapy. Treatment outcomes were stand on rates of bacteriological cure. Participants were randomized to receive 5 Days azithromycin (10 mg/kg/d) once a day or 10 Days Erythromycin 40 -50 mg/kg/ d in 4 divided doses, Bacteriological persistence did not happened for azithromycin ( 0% ) But  for erythromycin ( one =3.44 %). Bacteriological failures occurred with azithromycin treatment ( one =3.22%)while in Erythromycin (two  =7.40 %) the estimates of bacterial cure were elevated for azithromycin 96.77% in   compares for erythromycin 93.10% the bacterial cure rate time was 16.48 days for azithromycin less than for erythromycin 24.2625 days. The Variance in clinical manifestation duration for azithromycin 36.6 days less than for erythromycin 47.5 days for that our study recommended that 5-day azithromycin is more efficient than 10-day erythromycin in the treatment of pertussis in children.

كفاءة أستخدام ا ازيثرومايسين لمدة خمسة أيام بدلا من أستخدام ارثرومايسين لمدة عشرة أيام في علاج السعال الديكي

بهاء ضياء محي

### المستخلص

السعال ديكي  مرض معدي جداً سببه بكتريا سعال (Bordetella )ألديكي. أثناء العقد الأخير ثلاثة أنواع سـعال Bordetella ألديكي عُزلتْ ووُجدَت مقاومة إلى ارثرومايسين ، ازيثرومايسين اسُتعمل لمعالجةِ السعال ألديكي. ستون طفل ٣١ (مجموعة ٥ أيام) و٢٩ (مجموعة ١٠ أيام) بالسعال ألديكي في العيادةِ الخاصةِ قيّمتْ للكفاءة الأكثر فصل ٥ أيام ازيثرومايسين يُقارنُ إلى فصل ١٠ أيام ارثرومايسين علاج . نتائج معالجةِ كانتْ جناحَ على نِسَبِ العلاج البكتريولوجي. المشاركون عُشوائيا لاستلامَ ٥ أيامَ (ازيثرومايسين (١٠) mg/ كيلوغرام /اليوم) مرة كل يوم أو ١٠ أيام ارثرومايسين ٤٠ -٥٠ mg / كيلوغرام / d في ٤ جُرَع منقسمة، إصرار بكتريولوجي لمْ يحَدثْ لازيثرومايسين لكن لارثرومايسين (واحد =٣,٤٤). حالات الفشل البكتريولوجية حَدثتْ بمعالجةِ لازيثرومايسين (واحد =٣,٢٢%) بينما في لارثرومايسين (اثنان =٧,٤٠ %) تخمينات العلاج الجرثومي رُفِعتْ لـ لازيثرومايسين ٩٦,٧٧ بينما في المقارنة لارثرومايسين (٩٣,١٠)كذالك معدل وقت العلاج القضاء الجرثومي كَانَ ١٦,٤٨ يومَ لازيثرومايسين أقل مِنْ لارثرومايسين٢٤,٢٦٢٥ يوم. إنّ الخَلافَ في مدَة التوضيح السريرية لازيثرومايسين36.6 يوم أقل مِنْ لارثرومايسين47.5 يوم. لذالك فأنّ دراستِنا أوصتْ بأنّ لازيثرومايسين5 أيام أكثر كفاءة مِنْ لارثرومايسين10 أيام في معالجةِ السعال ألديكي في الأطفال.

## Introduction

Whooping cough (pertussis) is a highly contagious caused by *Bordetella pertussis*. In the present vaccine era, the overall incidence of *pertussis* had reduced dramatically, but the cyclic pattern has not changed with peaks every 2 to 5 years (1-3). The incubation period is most commonly 7 to 10 days (4). The illness has three stages: catarrhal, paroxysmal, and convalescent. In the catarrhal stage, there is rhinorhea, lacrimation and mild cough, over a 7- to 14-day period (5). The paroxysmal stage characterized by repeated coughing fits with 5 to 10 or coughs that are more forceful during a single expiration (a paroxysm). At the end of a paroxysm, the classic whoop occurs. Cyanosis, bulging eyes, protrusion of the tongue, Posttussive vomiting is common, the paroxysmal episodes lasts for 2 to 8 weeks (6). The convalescent stage usually lasts for 1 to 2 weeks. The clinical diagnosis should base on the paroxysmal cough with Posttussive vomiting, whooping and absolute lymphocytosis however; the etiologic diagnosis of illness requires definitive *Culture of* Bordetella pertussis (7). The mainstay of treatment over the last 30 years has been oral erythromycin. During the last decade, *Bordetella pertussis* had found to be resistant to Erythromycin (8-9). The newer macrolides azithromycin are also effective for the treatment of pertussis (10). the dose and duration of azithromycin at 10 mg/kg on day 1 and 5 mg/kg on days 2 to 5 as a single dose for 5 days for children(11) and has been shown to be effective in eradicating *Bordetella pertussis* in 97% of cases after 2–3 days(12).

## Patients and Methods

*Aim:* Assess the efficiency of a 5-day course azithromycin in compares to a 10-day course erythromycin therapy*1*. *Bacteriologicaly:* - a. bacteriological cure rate percent.   b. frequency of bacterial persistence & relapse & failure & 95% CI Paired Differences. C. The average time was need for Bacteriological cure rate. 2. *Clinical backgrounds*: - a. the average Mean percent of cough, paroxysmal, whoop & Posttussive vomiting. B. the Mean duration of cough, paroxysmal, whoop, Posttussive vomiting.

**STUDY  DISGIN  -  CASE DEFINITION** according WHO criteria for diagnosis of pertussis by both culture-proven *B pertussis* and / or a cough illness suspected by a physician as to be pertussis. *Bacteriological cure* defined as negative cultures at both the end-of-therapy and one-week post therapy. *Bacteriological persistence* defined as a positive culture at the end-of-therapy. *Bacteriological relapse* defined as a positive culture one-week post completion of therapy after a negative end-therapy culture

**STUDY  PLACE  &  PERIOD** A prospective study executed over a period of 24 month starting from September2003 to September 2005 in my private clinic in Baghdad.

*CASESS:*A Sixty Child with pertussis in my private clinic (free of charge).(( *starting with74 cases were proved positive DFA test for pertussis, but 14casess(27 culture) did not complete with recommended timing of visit and culture for many reasons security risk, migration, So had been neglected & also excluded 16 cases had been proved negative DFA test for pertussis over a period of 24 month )) Classified as 31*

(5-*day* group) and 29 (10-day group) with positive pertussis direct fluorescent antibody test & Cultures for *Bordetella pertussis* were done in the *central health teaching laboratory in indules's square in Baghdad & private (Salam)* laboratory in Baghdad.Participants were randomized to receive 5- Days course of azithromycin (10 mg/kg/d) once a day (5) or 10 Days course of Erythromycin (samara, Iraq) were given at a dose of (40 -50 mg/kg/ d) in 4 divided doses (10) of treatment (13). All medication given free of charge to patient (cost 311 thousand I.D).*Study Procedures*; Clinical data and culturing were obtained through four visits to my private clinic (free of charge) one before definitive diagnosis and three after diagnosis. A specially designed questionnaire was used to study, Follow-up visits, and cultures were scheduled for the end of therapy (5 days OR 10 days). Moreover, for one week post therapy (12 days OR 17 days) at which time the symptom questionnaire was completed.*Laboratory Procedures*; All equipments(single use) for specimen (nasopharyngeal aspiration) collection, direct antigen detection (direct fluorescent-antibody [DFA] test) transport (regan-lowe agar) a nutritive medium that inhibits the growth of the normal nasopharyngeal flora (14)and culturing medium (Stainer-Scholte broth agar) had been export from lobnane in cost (2.56 million I.D) (15). I m trained in the Al –KARAMMA teaching hospital about correct method for taken nasopharyngeal aspiration under supervision of ENT department for one month in 7/sept/2003 . In the clinic each specimen had been kept in transport medium in special container (temperature & humidity )at night in my house ,at morning transfer specimen to the lab and in order to overcome the technical lab error about halve specimen

culturing done in private lab &other halve done in central teaching lab. Each private lab result (slide) had been read by other microbiologist in central teaching lab &Vic versa ,later on each result had been read by myself (special training for 3 week) .time consumed for each result to be documented &become part of data was 5 days, 92 DFA test done in the lab by special reagent for all specimen (16). All cost pay for both labs was (1, 22 million Iraqi's).

## Statistical analysis

done using *SPSS* version 12.0 Computer software. Baseline individuality was compared one-sample test of (5-day group) and (10-day group) Paired Samples Test confidence intervals (CIs) (17). Binomial Test treatment group together & One-Sample Kolmogorov-Smirnov test estimated rates of bacteriologic cure it is duration. The clinical manifestation &its duration were compared one-sample test &mean compare test.

## Results

The Bacteriological culturing &its duration (180 culture/sensitivity) of 60 Child compares analysis of this study had proved the following: - Bacteriological cure rate of 5-day group (30 = 96.77%) more than in 10-day group (27 = 93.10%) &95% CI Paired Differences (-3.8531// 8.8531). Bacteriological failure rate of 5-day group (one =3.22%) less than in 10-day group (two =7.40 %) & 95% CI Paired Differences (-18.5593// 19.5593) other result as shown in table 1A, B, C, E&figure1.the Bacteriological persistence rate of 5-day group(nil=0%) less than in 10-day group(one =3.44 %) &95% CI Paired Differences(-5.8537//6.8531). ,further more the Bacteriological relapse rate of 5-day

group( one=3.22% ) less than in 10-day group( one =3.44% )&95% CI Paired Differences(-11.7062//13.7062). other result As shown in table 1A,B,C,E&figure1 .The average time was needed for Bacteriological cure rate of 5-day group (16.48 days) less than in 10-day group(24.2625 days)& One-Sample Kolmogorov-Smirnov test for5-day group(0.774) less than in 10-day group(0.820) in addition to other result As shown in table 1D.The clinical manifestation &it's duration of 60 Child compares analysis of this study had proved the following:-the average Mean percent of 5-day group for cough(89.2 ), a paroxysm cough (79.4 ), Whoop(32) less than the average Mean percent of in 10-day group for cough(95.2), a

paroxysm cough (84.9), Whoop(41) & it were about equal in both group for Posttussive vomiting( 18/ 19), other result as shown in table 2A,2B& GRAPH 2,3 . the Mean duration of 5-day group for cough(16), a paroxysm cough (6), Whoop(5) less than the Mean duration in 10-day group for cough(20), a paroxysm cough (9), Whoop(10) & it were equal in both group for Posttussive vomiting(3 / 3). The overall Variance in clinical manifestation duration for 5-day group(36.666) less than in 10-day group( 47.58333) in addition to other result As shown in table 2C & GRAPH 4

One-Sample Test-TABLE-1A

| | Test Value = 0.5 | |
|---|---|---|
| | t | Sig. (2-tailed) |
| Fpersistant | .000 | .001 |
| Tpersistant | 1.036 | .227 |
| Frelaps | 1.033 | .190 |
| Trelaps | 1.036 | .227 |
| Ffalure | 1.033 | .190 |
| Tfalure | 1.111 | .357 |
| Fcure | 30.000 | .011 |
| Tcure | 27.500 | .023 |

Paired Samples Statistics-TABLE-1B

| | | Mean | Std. Deviation |
|---|---|---|---|
| Pair 1 | Fpersistant | 15.500 | 21.9203 |
| | Tpersistant | 15.000 | 19.7990 |
| Pair 2 | Frelaps | 16.000 | 21.2132 |
| | Trelaps | 15.000 | 19.7990 |
| Pair 3 | Fcure | 30.500 | 7.0711 |
| | Tcure | 28.000 | 1.41421 |
| Pair 4 | Ffalure | 16.000 | 21.2132 |
| | Tfalure | 15.500 | 19.0919 |

(4-9)

Paired Samples Test-1C

| | Paired Differences | | |
|---|---|---|---|
| | | 95% Confidence Interval of the Difference | |
| | Std Deviation | Lower | Upper |
| Fpersistant - Tpersistant | 2.12132 | -5.853 | 6.853 |
| Frelaps - Trelaps | 1.41421 | -11.71 | 13.71 |
| Fcure - Tcure | .78711 | -3.853 | 8.853 |
| Ffalure - Tfalure | 2.12132 | -18.56 | 19.56 |

One-Sample Kolmogorov-Smirnov Test-TABLE-1D

| | | 5 day cure duration | 10 day cure duration |
|---|---|---|---|
| Bacteriological cure time | Mean days | 16.480 | 24.26 |
| | Std Deviation | 2.2465 | 5.768 |
| Kolmogorov-Smirnov Z | | .774 | .821 |



GRAPH -1-Case Number
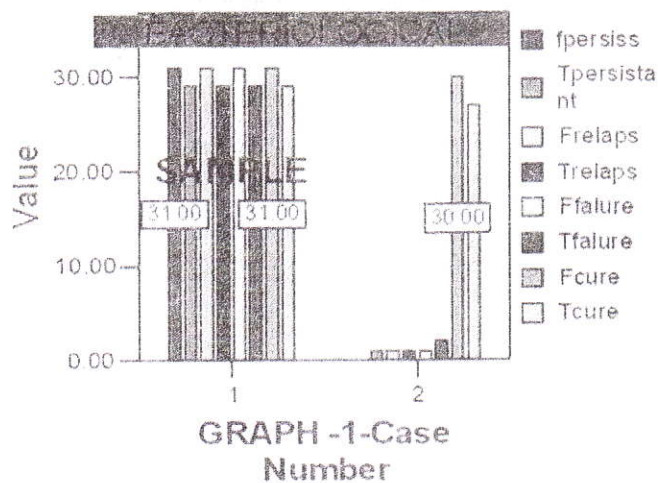
(5-9)

Binomial Test-TABLE-1 E

| | | Categ ory | frequ ncye | percet% |
|---|---|---|---|---|
| Tpersista nt | Sample | 31 00 | | |
| | cases | 00 | nil | ( 0% ) |
| Tpersista nt | Sample | 29 00 | | |
| | cases | 1 00 | one | 3 44 % |
| Frelaps | Sample | 31 00 | | |
| | cases | 1 00 | one | 3 22 % |
| Trelaps | Sample | 29 00 | | |
| | cases | 1 00 | one | 3 44 % |
| Ffalure | Sample | 31 00 | | |
| | cases | 1 00 | one | 3 22 % |
| Tfalure | Sample | 29 00 | | |
| | cases | 2 00 | two | 7 40 % |
| Fcure | Sample | 31 00 | | |
| | cases | 30 00 | 30 | 96 77 % |
| Tcure | Sample | 29 00 | | |
| | cases | 27 00 | 27 00 | 93 10% |

One-Sample Test TABLE-2A

| | Test Value = 0 5 | |
|---|---|---|
| | Sig (2-tai led) | Std Devia tion |
| Cough | 0 21 | 4 243 |
| Pnxrcgh | 0 19 | 3 394 |
| Whoop | 0 42 | 5 798 |
| Postfuss ive vomiting | 0 31 | 3 748 |

MEANS COMPARE TEST-TABLE-2B

| clinical | | | 5Day | 10Day |
|---|---|---|---|---|
| | Cough | MEAN% | 99 20 | 96 20 |
| | Duratcog | MEAN DAY | 16 00 | 20 00 |
| | Duratpos | MEAN DAY | 3 00 | 3 00 |
| | Duratprx | MEAN DAY | 6 00 | 9 00 |
| | Duratwho | MEAN DAY | 5 00 | 10 00 |
| | Posttussiv | MEAN% | 18 00 | 19 00 |
| | Prxrcgh | MEAN% | 79 40 | 84 90 |
| | Whoop | MEAN% | 32 00 | 41 00 |
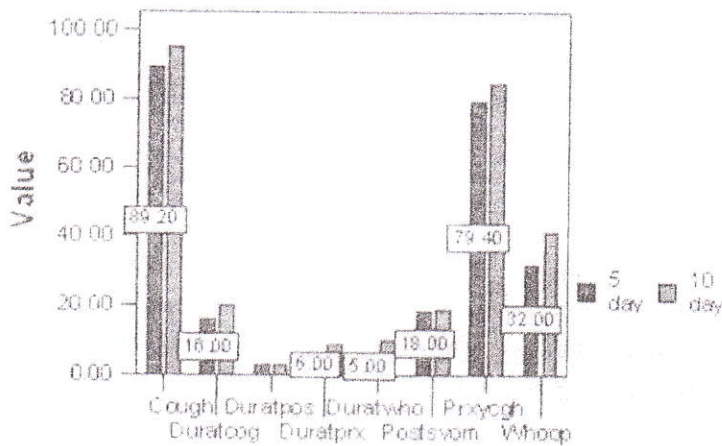


GRAPH -2-CLINICAL PRESENTION &DURATION

(6-9)

GRAPH -3-CLINICAL PRESENTION MEAN



-GRAPH-4-CLINICAL DURATION MEAN
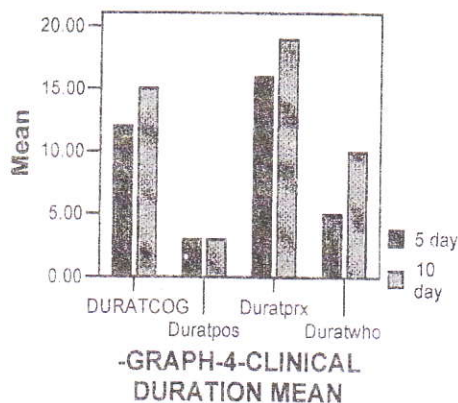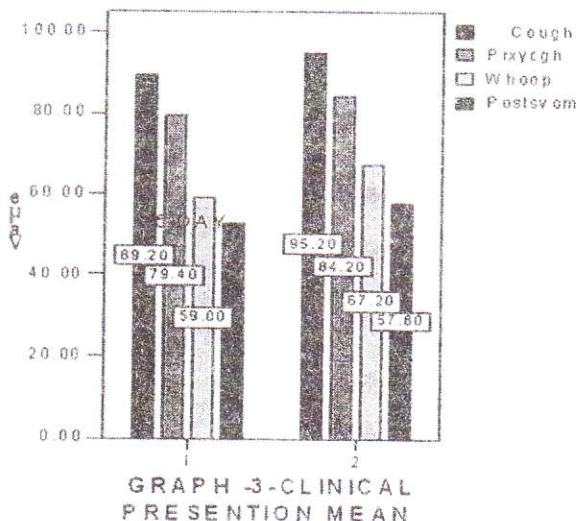
## Discussion

This study is the first eventual, randomized, clinical experiment in Iraq assessing the more efficiency of a 5-day course azithromycin in compares to a 10-day course erythromycin therapy for pertussis. Bacteriological persistence did not happened for azithromycin (0%) but for erythromycin (one =3.44 %) and relapse occurred in one case for both group. Azithromycin bacteriological failures ( one =3.22%) may be owing to poorer conformity of patient's family with dose of drug and timing of culture &further may be include differences in intestinal absorption of the drug (18). The estimates of bacterial cure were elevated (96.77%for azithromycin and 93.10% for erythromycin) this may be due to fact that once daily dose of azithromycin has longer halve life &better pharmacodynamic/kinetic properties than for erythromycin (19). The bacterial cure rate time was 16.48 days for azithromycin less than for erythromycin 24.2625 days this may be due to shorter (5-day) course of

azithromycin and/or more sensitivity of Bordetella pertussis to azithromycin. The Variance in duration of clinical manifestation for azithromycin 36.6 days less than for erythromycin 47.5 days. This is strong evidence that azithromycin is more efficient than erythromycin for the treatment of pertussis in children. It was preferably to did this study in pediatric teaching hospital (bigger sample make result more precise &dependable) but due to uncooperative health office, incompetent laboratory services and resources &security threat to patient's families enforced me to executed in private clinic . Many practical problems markedly affect the sensitivity and specificity of the laboratory diagnosis of pertussis that include delay in specimen collection, poor specimen collection technique, specimen transport problems, laboratory medium, laboratory contamination, equipment expense, enforced me to select these two lab (lab list). there is no similar study in medical journal and /or web site in Iraq, Iran, Kuwait, Jordan,

turkey and Syria but  In compares to other(developed country ) study we notice erythromycin failures are reported to occur in 10% ($n = 1$ of 10) (20) to 11% ($n = 2$ of 18) (21)  of patients. We have previously shown that Relapse did not occur in patients who were treat with azithromycin in one case series (22) but had reported in one case report (23).

## Conclusions

This study recommended that 5-days azithromycin is more efficient than 10-day erythromycin in the treatment of pertussis in children. In spite that a course of azithromycin is more expensive than erythromycin it must be consider when an antimicrobial choice made. Precise and early identification by rapid diagnostic tests and early treatment of pertussis with 5-day azithromycin will reduce transmission and disrupt progress of illness. We need more study about effect of 5-day azithromycin on different pediatric age group in relation type of vaccination coverage and/or chronic debilitating                    disease ACKNOWLEDGMENTS        I   do appreciation the patient's families for their compliance and the staff of the Microbiology central health laboratory & private laboratories in Baghdad ABBREVIATIONS              NPA, nasopharyngeal aspirate culture. CI, confidence interval. Fpersistant, 5-persistant. Tpersistant, 10-persistant, Frelaps, 5-relaps. Trelaps, 10-relaps. Fcure, 5-cure. Tcure 10-cure  Ffalure, 5-falure. Tfalure, 10falure. DURATCOG, cough Duration  Duratpos, post tussive vomiting        Duration.        Duratprx, paroxysmal Duration. Duratwho, whoop coughs Duration.

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