

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



العلاجات الحديثة للملوية البوابية

إعداد د.لمى ياسين غنيمة

أخصائية بأمراض الجهاز الهضمي والكبد والطرق الصفراوية
طالبة دكتوراه في أمراض الجهاز الهضمي في جامعة دمشق
مشفى الأسد الجامعي

الندوة نصف السنوية للجمعية السورية لأمراض الهضم - حماه - ٥-٦ / ٩ / ٢٠١٩

الملوية البوابية كالعصية السلية تحتاج
لاستئصالها لأكثر من دواء ولمدة طويلة

العوامل التي تتدخل في نجاح العلاج الاستئصالي للملوية البوابية

الجراثيم

بقاء الجراثيم في مرحلة
اللاتكاثر

١ جرعة الميترونيدازول
٢ مدة العلاج
٣ الفواصل بين الجرعات

حمل جرثومي عالي

١ جرعة PPI
٢ الفواصل الزمنية بين الجرعات

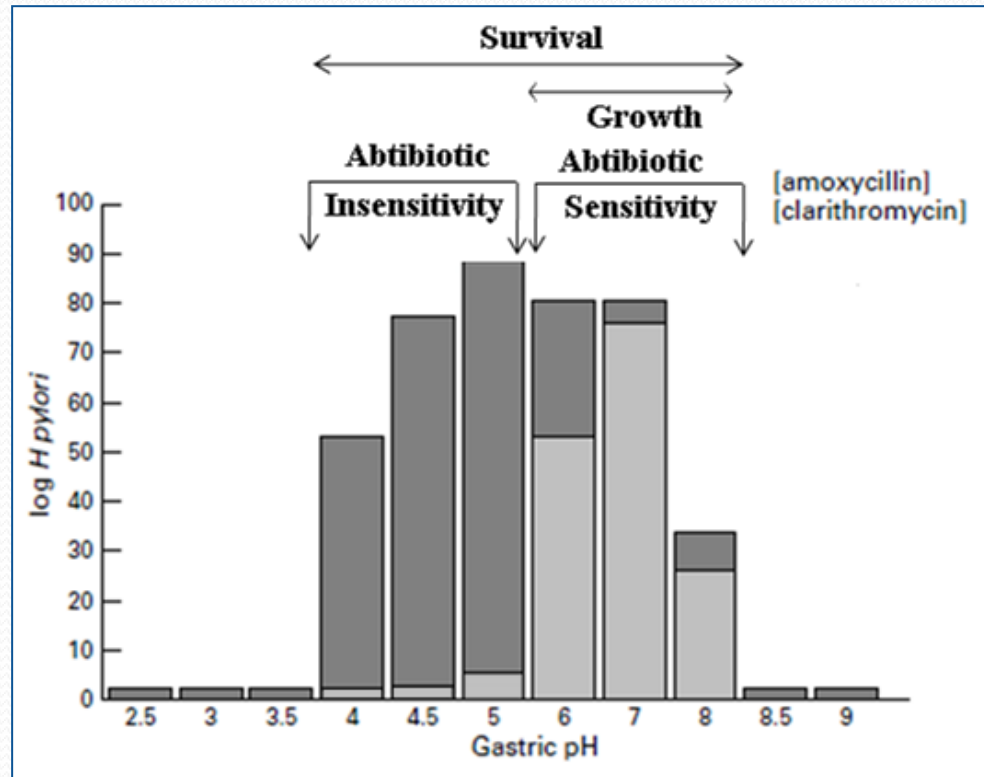
١ جرعة الصادات أو مدة المعالجة

مشاركة عدة صادات مع بعضها

معالجة سابقة بالـ PPI والبرموت



Phenotypical antibiotic resistance & HP



pH 4 – 8: *H. pylori* survives

pH 4 – 6: Non-dividing *H. pylori* – Phenotypical resistance

pH 6 – 8: Dividing *H. pylori* – Susceptible to AMO or CLA

Bigger JW. Lancet 1944 ; 247 : 497 – 500.

Scott D et al. Gut 1998 ; 43(Suppl 1): S56 – S60.

Graham et al. Gut 2010 ; 59 : 1143 – 1153.



مقاومة الملوية البوابية على الصادات

- لا يمكن التغلب على المقاومة بزيادة الجرعة أو زيادة المدة
- يجب عدم استخدامه في حال كانت المقاومة $< 15\%$

Clarithromycin
'all or none'

- لا يمكن التغلب على المقاومة بزيادة الجرعة أو زيادة المدة
- يجب عدم استخدامه في حال كانت المقاومة $< 13\%$
- تزداد المقاومة عليه بشكل سريع

Levofloxacin
'all or none'

- لا يمكن التغلب على المقاومة بزيادة الجرعة أو زيادة المدة
- يجب عدم استخدامه في حال كانت المقاومة $< 40\%$

Metronidazole
'not all or none'

- نادرا ما تحدث المقاومة في معظم البروتوكولات العلاجية

Amoxicillin

- نادرا ما تحدث المقاومة في معظم البروتوكولات العلاجية

Tetracycline

- لم تحدث مقاومة عليه

Bismuth

يتحسن نتائج العلاج الثلاثي

● زيادة جرعة PPI

- تزداد نسبة نجاح الاستئصال باستخدام Esomeprazole 40 mg bid ٨-١٢ %

● زيادة مدة المعالجة

- مدة العلاج ١٠ يوم تزيد نسبة الاستئصال ٤ %
- مدة العلاج ١٤ يوم تزيد نسبة الاستئصال ٥-٦ %

البرتوكولات العلاجية المستخدمة في العلاج الاستئصالي للملوية البوابية

البرتوكولات العلاجية المستخدمة في العلاج الاستئصالي للملوية البوابية

Regimen	Dosage	Duration	Recommendation
•Concomitant non-bismuth quadruple (PAMC)	•PPI bid •Amoxicillin 1000 mg bid •Metronidazole 500 mg bid •Clarithromycin 500 mg bid	•TOR: 14 d •MAA: 14 d unless 10 d proven •locally •ACG: 10–14 d	•First line: recommended by all •Rescue: MAA and ACG only
•Bismuth quadruple (PBMT)	•PPI bid •Bismuth qid •Metronidazole 400 mg qid or 500 mg tid–qid •Tetracycline 500 mg qid	•TOR: 14 d •MAA: 14 d unless 10 d proven locally •ACG: 10–14 d	•First line: recommended by all •Rescue: recommended by all
•PPI triple (PAC, PMC)	•PPI bid •Amoxicillin 1000 mg or metronidazole 500 mg bid •Clarithromycin 500 mg bid	•TOR: 14 d •MAA: 14 d •ACG: 14 d	•First line: restricted by all •Rescue: MAA only (restricted)
•Levofloxacin triple (usually PAL)	•PPI bid •Amoxicillin 1000 mg bid •Levofloxacin 500 mg once daily or 250 mg bid	•TOR: 14 d •MAA: 14 d •ACG: 10–14 d	•First line: suggested by ACG only •Rescue: recommended by all

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•Sequential non-bismuth quadruple	•PPI bid •Amoxicillin 1000 mg bid for first half only •Metronidazole 500 mg •clarithromycin 500 mg bid for second half only	•TOR: Not recommended •MAA: Not recommended •ACG: 10–14 d	•First line: non-ideal ACG optione •Rescue: not recommended by any
•Hybrid non-bismuth Quadruple	•PPI bid •Amoxicillin 1000 mg bid •Metronidazole 500 mg •clarithromycin 500 mg bid for second half only	•TOR: Not recommended •MAA: Not recommended •ACG: 14 d	•First line: non-ideal ACG optione •Rescue: not recommended by any
•High-dose dual therapy	•Rabeprazole 20 mg qid •Amoxicillin 750 mg qid	•TOR: 14 d •MAA: not stated •ACG: 14 d	•Rescue: considered an option by all
•Rifabutin-containing therapy (PAR)	•PPI bid •Amoxicillin 1000 mg bid •Rifabutin 150 mg bid or 300 mg qd	•TOR: 10 d •MAA: not stated •ACG: 10 d	•Rescue: considered an option by all as third or fourth line

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اجماع على استخدام أفضل
برتوكول ناجح محلياً ك معالجة
أولى

أدوية الخط الأول

اجماع على اختيار العلاج بناء على معطيات
محلية لدراسة الفعالية الدوائية والحساسية
أو المقاومة المحلية على الأدوية المستخدمة

First-Line Treatment Recommendations by the Toronto Consensus, Maastricht V/Florence Consensus, and the American College of Gastroenterology Guidelines

Therapy	Toronto	Maastricht V/Florence	ACG
Bismuth quadruple therapy	Recommended choice	Recommended (only choice if high dual resistance)	Recommended choice
Concomitant therapy	Recommended choice	Recommended if high C-Res or if bismuth unavailable	Recommended choice
PPI triple therapy	Restricted to areas of <15% C-Res or proven eradication success >85%	Recommended only in areas of low C-Res	Recommended if area of C-Res <15% and no previous macrolide exposure
Sequential and hybrid therapies	Recommended against its use	Not recommended	Suggested
Levofloxacin regimens	Not recommended	No statement	Suggested

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سيرة على
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في حال عدم وجود دراسات
محلية لدراسة المقاومة
اختيار العلاج الأفضل كما لو
كانت المقاومة عالية

رباعي - بزموت

رباعي تشاركي

رباعي - بزموت

الاجماع على عدم استخدام صاد
استخدم سابقاً ضمن برتوكول سابق
Clarithro+ Levo
Metro يمكن استخدامه له تأثير تأزري

الخط الثاني للعلاج

اجماع على استخدام رباعي -بزموت أو
ثلاثي -ليفو فلوكساسين
بناء على المستخدم سابقاً

Treatment of Patients With Prior Failed Attempts

Regimen	Toronto	Maastricht V/Florence	ACG
Bismuth quadruple therapy	Recommended choice	Recommended choice	Recommended choice
Levofloxacin therapy	Recommended choice	Recommended choice	Recommended choice
Clarithromycin-based PPI triple therapy	Not recommended	Recommended if failed bismuth quadruple and levofloxacin and from a low Clarithromycin resistance area	Not recommended
Concomitant Non-bismuth quadruple therapy	Not enough evidence to comment	Recommended if failed bismuth quadruple and levofloxacin and from a low clarithromycin-resistance area	Recommended if previous bismuth quadruple treatment failed
High-dose dual therapy	Promising but insufficient evidence to recommend	Consider if high rate of dual clarithromycin/ metronidazole resistance	Suggested
Rifabutin therapy	Restricted to those who failed 3 times	Consider if failed clarithromycin based and bismuth quadruple therapies and is from high fluoroquinolone resistance area (ie, failed 2 times)	Suggested

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توصيات مؤتمر Maastricht V ٢٠١٦

في حال فشل الخط الأول

رباعي تشاركي

ثلاثي -
ليفو

رباعي -
بزموت

ثلاثي -كلاريثرو

ثلاثي أو
رباعي
ليفو

رباعي -
بزموت

رباعي -بزموت

ثلاثي -
ليفو

رباعي
تشاركي
ليفو

في حال مقاومة عالية
على الليفوفلوكساسين

ثلاثي
ريفابيوتين

بزموت مع
صادين
آخرين

علاج ثنائي
HDDT

الاعتماد على الزرع
والتحسس

الخط العلاجي الثالث

ثلاثي ريفابيوطين
PAR
خيار أخير

رباعي - بزموت
أو
ثلاثي ليفو
في حال لم يستخدم
سابقا

Culture-guided therapy

Recommended third line therapy

- **PPI** Standard dose, bid
- **Bismuth** 2 tablets, qid
- **1st antibiotic** Selected by antimicrobial sensitivity tests
- **2nd antibiotic** Selected by antimicrobial sensitivity tests

For 14 days

توصيات مؤتمر Maastricht V ٢٠١٦

الخط الأول

معتمد على الكلاريثرومايسين



الخط الثاني

ثلاثي - ليفوفلوكساسين



الخط الثالث

رباعي - بزموت

الخط الأول

مقاومة العالية
للفلوروكينولونات == البزموت مع
صادين آخرين
أو
العلاج الحاوي على البيفابوتين

البزموت مع صادين آخرين

البرتوكول الحاوي على الريفامبيوتين

- يعتبر خيار أخير
- يستخدم الريفامبيوتين كأحد أدوية التدرن
- إمكانية حدوث التثبيط النقوي
- فقط ٢% من كل المرضى الموضوعين على الريفامبيوتين
- قابل للعكس كلياً
- لا يترافق مع زيادة الانتانات

هل يجب التأكد من استئصال الملوية البوابية بعد كل علاج لها

• الاستطابات :

• لكل المرضى الذين كشفت لديهم الملوية البوابية وعولجت

• الطرائق

• المستضد الملوية البوابية في البراز أو اختبار اليورياز في النفس

• بالطرائق التنظيرية فقط إذا كان مستطاباً إعادة التنظير لسبب

آخر

قبل التأكد من شفاء الملوية البوابية

- إيقاف الصادات قبل ٤ أسابيع من الاختبار

- إيقاف PPI قبل اسبوعين من الاختبار

توصيات عامة للعلاج

● الخط العلاجي الأول

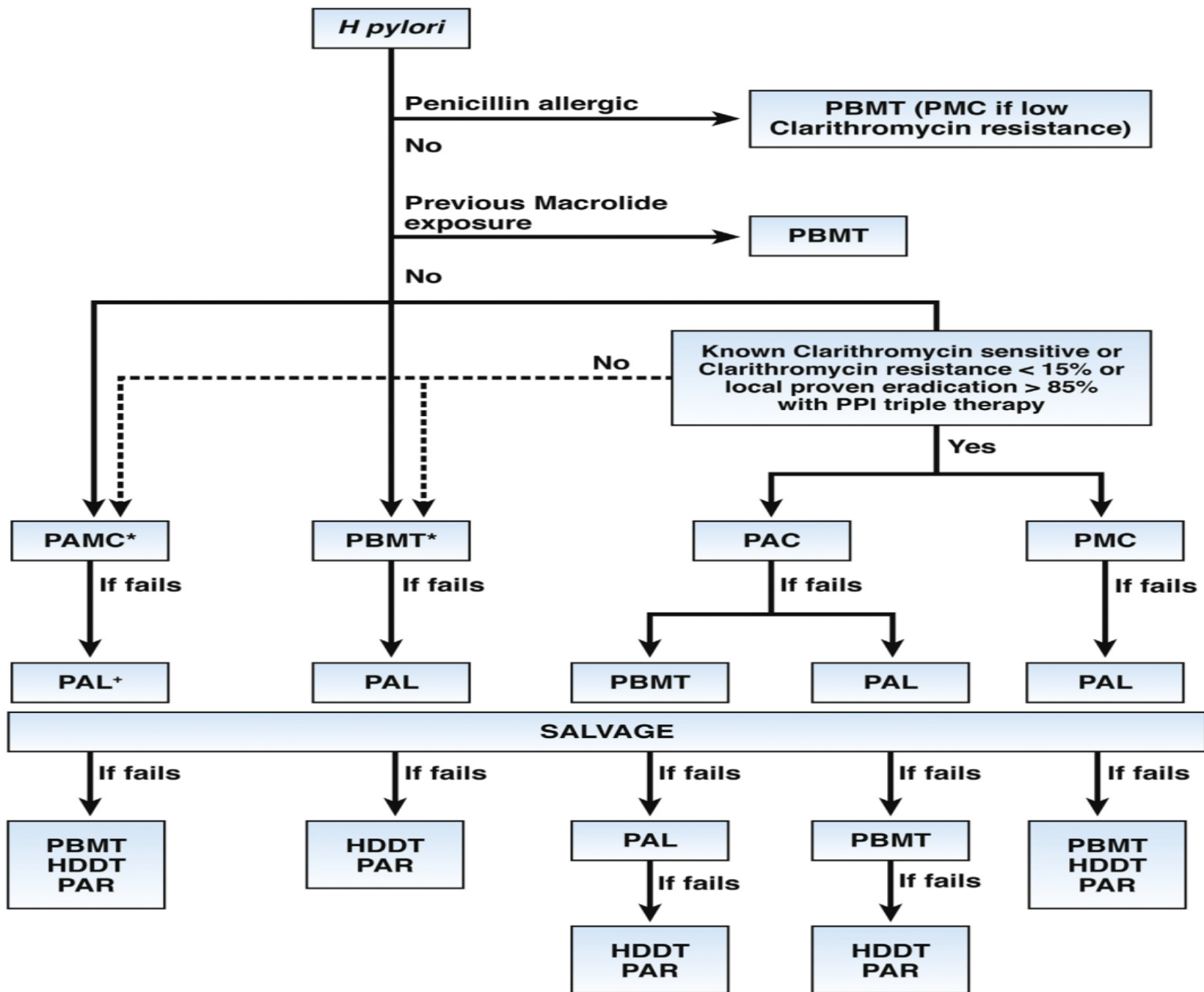
- تجنب الكلاريثرو في حال تم استخدامه سابقاً لأي سبب ، أو مقاومة محلية عالية
- استخدم ٤ أدوية : Concomitant,bismuth,
- استخدم الجرعات الأعلى من الأدوية لاسيما PPI
- مدة العلاج ١٤ يوم

● الخط العلاجي الثاني

- لا تستخدم نفس الدواء
- تجنب الليفو في حال تم استخدامه سابقاً لأي سبب ، أو مقاومة محلية عالية

● الخط العلاجي الثالث

- المعالجة معتمدة على نتائج الزرع والتحسس
- احتفظ بعلاجات الريفامبيوتين كخط علاجي أخير



شكراً لاصفائكم

