The 1998 national Belgian consensus meeting on HP-related diseases : an extensive summary

Deltenre M., Geboes K., Ectors N., Burete A., Debongnie J. C., Lamy V., Cadranel S., Colemont L., De Koster E., De Prez C., Deprez P., Dumonceau J. L., Glupczunski Y., Mélange M., Peeters M., Ramdani B., Scaillon M.

Abstract

"HP testing must be regarded as ONE of the important elements of the proper diagnostic work-up of a DISEASE, managed in close cooperation between GP's and specialists": that's the key message of the national consensus meeting held in CHU Brugmann on February 6th and 7th 1998. HP testing (usually by 2 direct methods : RUT-histology) and eradication treatment (ER), in infected patients, are *strongly recommended* in : 1. Past or current GDU (absolute indication), regardless of activity, complication(s), NSAID intake ; 2. Low-grade MALT Lymphomas (Stage IE1) unequivocally diagnosed, managed and followed-up in specialised centers ; 3. Post endoscopic resection of EGC. ER is *advisable* in HP carriers with a family history of gastric cancer. Chronic atrophic-, lymphocytic-, giant folds gastritis and hyperplastic polyps are *acceptable* indications for ER as well as scheduled long-term NSAID treatment in individuals with *known* HP status. Systematic ER in HP+ patients with fully investigated NUD is not indicated but could be considered in individual patients. Extra alimentary disorders and auto immune gastritis are no indication and there was no consensus for a "test and treat" policy in patients under 45 yrs old without alarm symptoms. Systematic screening of asymptomatic individuals is not recommended. A correct monitoring of eradication after treatment is recommended, mainly by UBT. In severe or refractory PUD, symptom recurrence and follow-up of EGC and Maltomas, endoscopic follow-up with HP testing is mandatory. The recommended first line treatment course (except known allergy or intolerance) is PPI full dose bid, Clarithromycin 500 mg bid Amoxycillin 1000 mg bid (7 days minimal 10 days maximal). RBC-based schemes must be locally validated and quadruple therapy is proposed when re-treatment is needed. Culture, optional after the first treatment failure, is strongly recommended after a second failure. Overall, ER therapies are safe and neither the decreased efficacy of acid-lowering drugs, nor the possible increased risk of peptic oesophagitis are considered as contra-indications to eradicate. ER is cost-effective and cost-beneficial in PUD and adjusted number of pills delivered would cut costs. No clear economic data are currently available for a potential benefit of ER in GC prevention or NUD management. A national monitoring of HP resistance (Macrolides and Imidazoles) must be organized by specialised centers. (Acta gastroenterol. belg., **1998**, 61, **299-302**).

Key words : Helicobacter pylori, treatment, review

These guidelines are applicable to routine clinical practice. They do not concern clinical research, therapeutic trials or assessment of new therapies. Separate guidelines for HP-related diseases in children will be released by members of Belgian Society for Paediatrics.

Belgian consensus/guidelines for the management of *Helicobacter pylori*-related upper gastrointestinal diseases

Brussels, 6-7 feb. 1998

Reviewers & referees

— Profs. S. Cadranel, M. Deltenre, N. Ectors, K. Geboes, Y. Glupczynski, M. Mélange

— Drs. A. Burette, L. Colemont, J.C. Debongnie, E. De Koster, C. De Prez, P. Deprez, J.M. Dumonceau, V. Lamy, M. Peeters, B. Ramdani, M. Scaillon

Participants

— Professors of Gastroenterology : M. Adler (ULB), J. Belaïche (ULg), P. Pelckmans (UIA), D. Urbain (VUB). Excused : A. Elewaut (UG), A. Geubel (UCL), J. Janssen (KUL)

— Representatives from the Scientific Associations :
  — SBED-BVES : Drs. Dr. M. Buset, Dr. V. Gillard, P. Laukens, Dr. H. Vanvlierberghe.
  — SRBGE : Prof. R. Fiasse, Dr. E. Louis.
  — VVGE : Drs. M. Cabooter, Dr. Ph. Van Hooteghem.
  — SRB Pédiatrie/KV Kindergeneeskunde : Dr. X. Pletincx, Dr. M. Van Winkel.

— Representatives from GP : SSMG : Dr. M. Vanhalewyn ; WVVH : excused.

— Representatives APB (Pharmacists) : Dhrs. H. Robays (UZ Gent) & F. Van Beek (Voorzitter BVZA) ; excused : Prof J.P. Delport (UL).

— Members of HPBCG : P. Bontems, A. Burette, S. Cadranel, M. Castelain, B. Caucheteur, L. Colemont, J.C. Debongnie, E. De Koster, M. Deltenre, C. De Prez, P. Deprez, J.M. Devaster, J.M. Dumonceau, A. Driessen, N. Ectors, K. Geboes, Y. Glupczynski, M. Hiele, C. Jonas, A. Jouret, P. Lammens, V. Lamy, B. Maillet, M. Mélange, M. Peeters, B. Ramdani,

Prof. M. Deltenre, CHU Brugmann, Place Van Gehuchten 4, B-1020 Bruxelles.

M. Scaillon, N. Struyf, Y. Vandenplas, E. Van Cutsem, M. Witterwulghe.

— Observer representatives-M.D. from the Mutual Insurance companies : Drs. Vandenbremt (U.N. Mut. Libres), J. Voisey (U.N. Mut. Libérales).

Who ? When to treat ?

Reports

GD Ulcer. L. COLEMONT (AZ UIA)
Gastric Malignancies. M. MELANGE (Mont Godinne UCL)
Gastritis, particular histological lesions, NSAID, Extra alimentary diseases. P. DEPREZ (St. Luc UCL)
Non Ulcer Dyspepsia. J.C. DEBONGNIE (Ottignies UCL) Gord/long-term PPI treatment. E. DE KOSTER (CHU Brugmann VUB)
Children. S. CADRANEL (HUDERF ULB)

Referee

N. ECTORS (St. Rafael, KUL)

Preliminary remark

Indications for HP eradication are based on a proper diagnosis of a *disease*.

Ten recommendations were unanimously adopted :

1. All HP positive gastric or duodenal ulcer diseases, active or not, regardless of NSAID intake, of first presentation or relapse, of present or past complication(s) are an absolute indication for HP eradication.
2. HP eradication is strongly recommended after local endoscopic resection of early gastric carcinoma in an infected patient.
3. HP eradication is recommended in infected patients with low-grade MALT lymphoma provided :
   — The diagnosis of low-grade MALT lymphoma is based on unequivocal evidence ;
   — The extent of the disease is limited (stage IE1) ;
   — A long-term follow-up can be achieved ;
   — The patient is managed in specialised centres.
4. HP eradication is advisable for infected patients with a family history of gastric carcinoma.
5. Although there is no convincing evidence that HP eradication may interrupt or reverse mucosal atrophy and intestinal metaplasia (potentially precancerous lesions), HP positive chronic atrophic gastritis is an acceptable indication to eradicate HP, especially in young individuals.
6. Although there is little supportive evidence for a causal relationship between HP and lymphocytic gastritis, giant folds gastritis and hyperplastic polyps, it is an acceptable indication to eradicate HP in infected patients presenting these special forms of gastritis.
7. Despite the uncertainty on the interaction of HP and NSAID in the genesis of peptic ulcer disease, it is acceptable to prescribe eradication treatment in known HP carriers before a long-term treatment with NSAID.
8. Extra-alimentary diseases and autoimmune gastritis are no indication for HP eradication.
9. Systematic eradication of HP in HP positive patients with fully investigated (endoscopy, ultrasonography) non-ulcer dyspepsia is NOT recommended but could be considered in individual patient.
10. Although it is neither certain that atrophic gastritis will develop faster during longterm acid suppression therapy in HP positive patients, nor HP eradication may interrupt or reverse this process, the possibility of an accelerated development of atrophic gastritis during long-term acid suppression therapy is an acceptable indication for HP eradication in infected patients with reflux oesophagitis.

One recommendation did not reach a consensus (roughly 50% pro and 50% contra) : "It is not recommended to eradicate HP in infected patients with upper abdominal complaints without further investigations : however, it could be acceptable in young patients (under 45 y old) without alarm symptom(s)".

When ? How to search for HP ?

Reports

Serology and Culture. Y. GLUPCZYNSKI (Mont Godinne UCL)
Histology. C. DE PREZ (CHU Brugmann ULB)
Biopsy Urease Test. B. RAMDANI (CHU Jumet ULB)
Urea Breath Test. M. PEETERS (AZ KUL)
Who, When, How to test and/or retest for HP ? A. BURETTE (IM E Cavell/Basilique ULB)

Referee

K. GEBOES (St Rafael, KUL)

Preliminary remark

HP testing is ONE element of the diagnostic work-up and the purpose is to treat a DISEASE.

When ? (Primary diagnosis)

1. Search for HP is strongly recommended in past or present GD Ulcer with or without complication, Gastric Maltoma, macroscopic or microscopic gastritis, including special forms.
2. Search for HP is advisable in individuals with a family history of gastric carcinoma.
3. Search for HP is acceptable in NUD when full investigations are planned or performed in patients above 45 y old and patients with "ulcer-like" dys-

pepsia and in younger patients with recurrent or chronic dyspepsia.
4. In GORD the search for HP, before long-term PPI treatment, remains, so far, optional.
5. Search for HP is not indicated for screening symptomatic-free individuals or before starting long-term NSAID therapy.

How ? (Primary diagnosis)

1. In patients eligible for treatment, HP status will be preferentially determined by two tests, Rapid Urease Test (RUT) and Histology, in order to improve sensitivity.
2. In DU, one RUT might be sufficient, provided standby biopsies for histology are performed.
3. Culture is not recommended in patients who are tested for the first time and have never been treated for the infection (except in reference centres, for primary resistance survey).
4. The "test and scope" policy using a non-invasive test (Urea Breath Test or serology) in order to select young dyspeptic patients for endoscopy cannot be recommended so far and needs validation.

When ? And How ? (Follow-up)

1. Monitoring of eradication efficacy by UBT is recommended after treatment.
2. It is strongly recommended to follow-up by endoscopy and HP testing patients with severe or refractory GDU, with gastric ulcer, with previous local resection of EGC and, on case by case basis, patients with recurrent symptoms.
3. Maltoma requires early testing of eradication and endoscopic follow-up of the underlying disease at 4-6 months, and eventually later.
4. HP status re-assessment must be done at least 4 weeks after the end of treatment : after one month without antibiotics, PPI or Bismuth salts.
5. Culture is optional after a first treatment failure (depending of the treatment already prescribed) but is strongly recommended after a second failure of eradication.

How to treat ?

Reports

First choice, second choice, in case of failure : M. DELTENRE (CHU Brugmann ULB)

Referee

V. LAMY (CHU Jumet ULB)

Preliminary remarks

Mono- and bitherapies are obsolete and the first attempt of eradication will use a polytherapy that do not need culture with sensitivity testing. Low-dose, one-week triple therapies (PPI uid, Clarithromycin 250 bid, plus Imidazole or Amoxycillin) are NOT effective in Belgian experience.

1. The first choice, recommended for a 7-days course minimum to a 10-days course maximum, is PPI one dose before meal morning and evening, Clarithromycin 500 mg and Amoxycillin 1000 mg after meal morning and evening.
2. A possible future alternative that needs validation in Belgium is RBC bid, Clarithromycin S00 bid, and Amoxycillin 1000 mg bid.
3. The second choices, recommended in case of allergy or known intolerance to first choice's compounds are : 1) PPI (Ome or Lanso) bid, Colloidal Bismuth Subcitrate qid, Tetracycline 500 qid or Amoxycillin 1000 bid, Metronidazole 500 tid, for 7 days ; or 2) PPI bid, Clarithromycin 500 bid, Metronidazole 500 bid, for 7-10 days (if primary Imidazole-resistance is below 20% in the local community).
4. In case of previous failure, re-treatment schemes will be based on a detailed inquiry about previous treatment(s) to determine the need for culture and sensitivity testing according to previous and planned therapies.
5. Since patient's compliance is a key factor of success, it is strongly recommended to inform the patient about the difficulties of treatment, the precise daily dosage, the potential side effects and the advantage of preparing pills every day.
6. In DU, despite some supportive data suggesting the one-week triple therapy is sufficient both to eradicate and to heal ulcer, it is currently recommended to achieve treatment with 2 or 3 weeks of PPI uid.
7. Symptomatic relief in PUD must be assessed by double blind, randomised studies comparing different proposed schemes.

Adverse events and complications

Adverse events and complications : short-term. J.M. DUMONCEAU (Erasme ULB)
Adverse events and complications : long-term. E. DE KOSTER (CHU Brugmann VUB)

Referee

A. BURETTE (IM E. Cavell/Basilique ULB)

Preliminary remark

Overall, therapies aimed at eradicating HP are safe and well tolerated.

1. The incidence of *short-term* adverse events with the first line triple therapy PPI (RBC)-based triple ranges from 20-30% with 1-3% of patients stopping therapy because of side effect(s).
2. Quadruple therapy has up to 40% *short-term* side effects (around 4% of patients stopping therapy).

3. HP eradication seems to potentially hamper acid suppressive treatments. However, it remains currently unknown to what extent this is clinically relevant : therefore, it should not preclude HP eradication.
4. Patients successfully treated with anti-HP therapy may be at risk to develop GORD during the first year after treatment. However, these observations need to be confirmed and the strength of a possible causal relationship between the two events remains equivocal. Consequently, this possible increased risk must not be considered as a contra-indication for HP eradication therapy.

Public health issues

Reports

Pharmacoeconomics. M. DELTENRE (CHU Brugmann ULB)
Bacterial Resistance. Y. GLUPCZYNSKI (Mont Godinne UCL)
Screening Prospects. M. SCAILLON (HUDERF ULB)

Referee

J.C. DEBONGNIE (Ottignies UCL)

1. Systematic eradication of HP in infected patients with peptic ulcer disease is cost effective and cost beneficial.
2. Cost effectiveness of gastric cancer prevention is not proven.
3. Systematic eradication of HP in NUD is not cost effective.
4. The most effective treatment is the most cost effective and adjusted-number of pills delivery is necessary to cut costs.
5. Primary imidazole resistance (5-50% in Europe, around 30% in Belgium, primary macrolide resistance (8-14% in Europe, 3-14% in Belgium) and multiresistance (3.7% of strains) raise an important ecological question.
6. Reference centres must be developed to assess and follow primary resistance rates, help routine labs where adequate culture is difficult and collect data on secondary resistance.
7. So far, screening of asymptomatic population is not indicated, except in gastric cancer families.