

Is this section, the reader can find comments on POEMs published in several magazines. The term POEM stands for "Patient-Oriented Evidence that Matters". POEMs are based on studies with a robust methodology, especially randomised controlled trials, meta-analyses, systematic reviews and validated guidelines whose outcomes are patient-oriented. Additional information may be found in Rev Port Clinica Geral, Nov/Dec 2005.¹ RPCG also published a glossary of terms and levels of evidence in its issue of May/June of 2006 for a better understanding of the taxonomy of evidence, including the Level Of Evidence (LOE), which is provided at the conclusion of each POEM.²

Contributions to this section may be sent to poems.rpcg@gmail.com.

1. Sanchez JP. Simplesmente POEMs (Simply POEMs). Rev Port Clin Geral 2005;21:631-4.

2. Mateus A, Sanchez JP. POEMs: glossário e níveis de evidência (POEMs: glossary and levels of evidence). Rev Port Clin Geral 2006; 22: 400-4.

DIET, EXERCISE, AND DRUGS MAY PREVENT DIABETES IN HIGH-RISK PATIENTS

Commentary on the POEM 'Can the onset of diabetes be delayed or prevented in people with impaired glucose tolerance?' Available in <http://www.infoPOEMs.com> [accessed on 03/06/2007].

Reference: Gillies CL, Abrams KR, Lambert PC, et al. Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. BMJ 2007;334:299.

Clinical question

Can the onset of diabetes be delayed or prevented in people with impaired glucose tolerance?

Study design

To answer this question, the authors completed a systematic review and meta-analysis, financed by governmental funds in the United Kingdom, with the objective of quantifying the efficacy of pharmacological interventions and lifestyle changes to prevent or delay the onset of type 2 diabetes in patients with impaired glucose tolerance.

The researchers completed a thorough search of 4 databases, contacted experts on the relevant studies, and checked the references of identified studies.

They included only randomized controlled trials (most were not blind)

that evaluated medicine or lifestyle changes to prevent the onset of type 2 diabetes in patients with impaired glucose tolerance. They included research in all languages. Two authors independently assessed the validity of studies (Jadad score) and abstracted data from them. They excluded 6 studies considered not appropriately randomized, or in which prevention of type 2 diabetes was not the primary goal of intervention. From the 21 studies included in the systematic review, 17 (8,084 patients) had sufficient data and were adequate for meta-analysis. The 17 studies included 2 studies done in Japan and 3 in China, and most of the studies were of several years in duration. Since data were not reported in the same way in all of the studies, the authors had to estimate some data. They used the more conservative random effect model when combining the data.

In the studies, the baseline risk of diabetes was 37,1% in 5 years. Overall, the interventions decreased the onset of frank diabetes by approximately half (Hazard ratio [HR] = 0.51; 95% CI, 0.44 - 0.60). There was a similar reduction in risk (HR=~0.50) with diet changes, exercise or in combination. The oral antidiabetic drugs (acarbase, glipizide,

metformin and the biguanide flumamine) decreased the onset of diabetes by 30% (HR = 0.7; 0.62 - 0.79). The Number Needed to Treat to prevent one patient for developing diabetes was 6,4 for lifestyle changes (IC 5,0-8,4), 10,8 for oral antidiabetics (IC 8,1-15,0) and 5,4 for orlistat (IC 4,1-7,6). Although less well studied, it seems that the rate of diabetes returns to baseline once drug therapy is stopped.

Conclusions

The authors concluded that pharmacological intervention and lifestyle changes will slow the progression of diabetes by approximately 50% in patients with impaired glucose tolerance. However, research has not been conducted for long enough to determine whether diabetes onset is prevented or just delayed. Lifestyle changes are at least as efficient as drug therapy. **(Level of Evidence = 1a)**

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CLOPIDOGREL COMBINED WITH ACETYLSALICYLIC ACID IS NOT MORE EFFICIENT THAN USING ACETYLSALICYLIC ACID ALONE IN THE PREVENTION OF CARDIOVASCULAR EVENTS IN HIGH RISK CARDIOVASCULAR PATIENTS WITH STABLE DISEASE

Comment to the POEM "Clopidogrel + ASA no better than ASA alone for high risk patients. Available at URL: <http://www.infoPOEMs.com> and at www.aafp.org/aafp/20061001/tips/7.html [accessed on 07/10/2006].

Reference: Bhatt DL, Fox KA, Hacke W, Berger PB, Black HR, Boden WE, et al. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. N Engl J Med 2006 April 20; 354 (16):1706-17.

Clinical question:

Is treatment with Acetylsalicylic Acid (ASA) combined with Clopidogrel efficient in the prevention of cardiovascular events in high risk cardiovascular patients with stable disease?

The CHARISMA Study (*Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance*) was a prospective, randomised, double-blinded study, controlled against placebo that included 15,603 patients aged 45 or over, with symptoms of stable cardiovascular disease (symptomatic coronary, cerebrovascular or arterial disease) or with multiple risk factors (Table I – for inclusion the patient should have two *major* risk factors or three *minor* or one *major* and two *minor*). Patients with recent myocardial infarction (MI) or acute coronary syndrome were excluded. Patients were divided in two groups. One group was treated with ASA (75 to 162 mg/day) and clopidogrel (75 mg/day) and the other treated with ASA (75 to 162 mg/day) and placebo.

The mean follow-up time was 28 months. The primary endpoint was

a combination of events that included the number of acute MIs, strokes or number of cardiovascular deaths. The secondary endpoints included events like hospital admission for ischemic events, coronary revascularisation, transient ischemic accident and mortality for all causes, among others. The mean age of patients was 64 years, 80% were Caucasian, 70% were males. Approximately 75 % of patients were excluded for having symptoms of stable cardiovascular disease and the remainder because they had multiple risk factors.

Regarding the primary endpoint, the occurrence was 6.8% in the ASA + clopidogrel group and 7.3% in the ASA + placebo group (RR (relative risk) – 0.93; CI 95% 0.83 to 1.05; p=0.22).

Regarding the main secondary endpoint that included hospital admissions for ischemic events, the incidence was 16.7% and 17.9% respectively (RR – 0.92; CI 95% 0.86 to 0.995; p=0.04).

The occurrence of severe hemorrhagic events was 1.7% and 1.3% for the experimental and control groups respectively (RR – 1.25; CI 95% 0.97 to 1.61; p=0.09). The occurrence of death for cardiovascular causes was higher in the ASA + clopidogrel group, 3.9% vs 2.2%, p=0.01.

The occurrence of death for all causes was also higher in the ASA + clopidogrel group, 5.4% vs 3.8%, p=0.04.

The authors concluded that, over all, clopidogrel combined with ASA was not significantly more efficient in the prevention of MI, stroke or in the prevention of deaths from cardiovascular causes when compared with ASA alone in patients with stable cardiovascular disease or with multiple risk factors. **(LOE=1b)**

Comment

Evidence already exists that ASA is efficient in the prevention of cardiovascular events in patients with a high risk of cardiovascular disease and that clopidogrel increases the preventive efficacy when combined with ASA in patients with acute MI, unstable angina or after stent placement. Nevertheless it was not known if clopidogrel also had increased preventive efficacy when combined with ASA in stable patients with high risk of cardiovascular disease. This study by Bhatt *et al* answers that question and hence its relevance.

According to these results, double treatment with platelet anti-aggregates should be avoided, because its risks seem to outweigh possible benefits. An additional point for consideration by Portuguese family physicians, even though the article did not address financial issues is that clopidogrel is one of the medicines that weighs heavily in the drug budget of the Portuguese National Health Service.

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TABLE I

ATHEROTHROMBOTIC RISK FACTORS CONSIDERED IN CHARISMA

Major risk factors

- Type I or II Diabetes mellitus
- Diabetic nephropathy
- Ankle brachial index < 0.9
- Asymptomatic carotid stenosis
- One or more carotid plaques

Minor risk factors

- Systolic blood pressure ≥ 150 mm Hg, after three months under treatment
- Primary hypercholesterolemia