

ISSN 1312-1723 (print) ISSN 1313-3551 (online)

Case Report

# PREVENTION OF ISCHEMIC INSULTS WITH CLOPIDOGREL (PLAVIX)

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### ABSTRACT

The authors investigate atherosclerosis and atherothrombosis as some of the major risk factors for development of cerebrovascular, cardiovascular and chronic arterial insufficiency of the extremities (CAIE). Emphasis is given to the great social significance of the development of methods for primary and secondary prevention. Considering the various comparative and clinical methods of the action of various thrombocyte antiaggregants, the authors highlight the better effect of Clopidogrel (Plavix) for atherothrombosis prevention.

Key Words: Atherosclerosis, atherothrombosis, primary prevention, secondary prevention.

### **INTRODUCTION**

The main reason for development of ischemic insults is atherosclerosis of extra- and intracranial arteries The atherosclerotic process affects predominantly the carotid arteries in the carotid bifurcation and in the artery siphon, more rarely can it impair the vertebral arteries. The atherosclerosis leads to stenosis of impaired arteries and appearance of atheromatous plates, which ulcerate and cause atherothrombosis. The atherothrombosis on the other hand represents a chronic progressive disease, characterized by sudden rupture or erosion of an atheromatous plate, formation of a thrombus and development of a cerebral or myocardial infarction.

A series of studies shows that an atherothrombotic disease increases the risk of ischemic insult up to three times (1) and increases the probable appearance of a chronic arterial insufficiency of the lower extremities (CAILE) up to four times, (2). Even higher (five to seven times) is the risk of appearance of acute myocardial infarction.

Due to the great social significance it is necessary to develop methods for primary and secondary prevention of cerebral insults, which are basically oriented at influencing the cerebrovascular disease risk factors, which are more or less well documented.

These methods could be represented as follows:

### **1. Primary prevention**

- 1.1. Non-medicamentous prevention:
- Rational feeding with limited reception of salty, sweet and fatty foods, without alcohol and smoking;
- Moderate physical activity.
- 1.2. Medicamentous prevention:
- Antihypertensive agents (ACE inhibitors and calcium antagonists);
- Antiaggregants;
- Treatment of sugar diabetes;
- Antihyperlipidemic agents.

### *1.3. Surgical prevention:*

• carotid endarterectomy with patients having asymptomatic carotid stenosis (from 60 to 99%).

#### 2. Secondary prevention

- 2.1. Non-medicamentous prevention:
- Oriented at favourable influencing of the same risk factors as in primary prevention.

### 2.2. Medicamentous prevention:

- 2.2.1. Thrombocyte antiaggregants:
- Acetysal irreversibly inhibits the thrombocyte and endothelial

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cyclooxigenase and impedes the biosynthesis of Tx A2 and prostacyclin. This way the thrombocyte aggregation is suppressed;

- Dipyridamol a thrombocyte antiaggregant with weaker effect that is normally combined with Acetysal;
- Clopidrogel (Plavix). This is an ADPreceptor antagonist. It irreversibly changes the thrombocyte functions by affecting the final phase of thrombocyte aggregation, which is specifically dependent on ADP-activation of IIb/IIIa glycoprotein. It is more effective than the ticlodipine and stronger than the thrombocyte antiaggregant.

## 2.2.2. Anticoagulants

It is most often applied in patients with chronic non-rheumatic atrial fibrillation.

## 3. Surgical prevention:

It is applied with recurrent transient ischemic disturbances of brain blood circulation (transient ischemic attacks – TIA) when the carotid stenoses exceed 70%.

The Acetysal has proved its efficiency in long-term prevention of the ischemic disturbances of the cerebral blood circulation where both its high and low doses are equally efficient (3). The effect of this medicament has been studied by our authors as well (4).

The results of twenty-six double-blind randomised trials dedicated to secondary prevention of brain insults, other vascular events and vascular death, by research of the efficiency of Dipiridamol among 19 842 patients, have been analysed. The data show that Dipyridamol is no more efficient than Acetysal and does not reduce the risk of vascular death. (5).

Over the last years the particularly efficient inhibitor of thrombocyte aggregation Clopidogrel (Plavix) was introduced in clinical practice.

The CAPRIE trial was carried out among 19 185 patients with acute ischemic insult, fresh myocardial infarction and peripheral arterial insufficiency that appeared during atherothrombosis. For a period of one to three years the therapeutic efficiency of 75 mg of Clopidogrel and 325 mg of Acetysal were compared. The trial is designed as a multinational, multi-centre, stratified, randomised, double-blind and parallel-group trial. The analysis of the results shows a significant reduction in the relative risk in favour of Plavix of 5,2(95%CI, 7, 9-16,7) with ischemic insult outcomes; 19,2(95% CI 5,3 -31,0) with myocardial infarction outcomes and 7,6(95% CI 6,9 – 20,1) with vascular death outcome (6).

During the CURE study 12 562 patients with unstable stenocardia or myocardial infarction were followed. The patients in one of the groups were treated with an initial dose of 300 mg of Clopidogrel and a subsequent dose of 75 mg/day together with Acetysal 75-325 mg/day, and the patients in the other group were treated with placebo and the same dose of Acetysal (7).

In the group of patients treated with Clopidogrel, 582 (9,3%) suffered myocardial infarction, ischemic insult or vascular death, while in the control group vascular events were observed with 719 patients. From a statistical point of view a significant reduction in the frequency of vascular events was observed with patients treated with Clopidogrel compared to the control group - 20%(95% CI 10,0-28,0) (CURE 2000).

New clinical trials among more than 100 000 patients with ischemic insult, myocardial infarction with or without stenting and CAIE (chronic arterial insufficiency of the extremities) confirm the high efficiency of Clopidogrel in the prevention of atherothrombosis. These Clopidogrel features and the low percentage of complications make it especially suitable for long-term use in clinical practice.

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