UDC 616.831-009.86-02-091(027)

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STATINS AND PERIOPERATIVE MYOCARDIAL INFARCTION

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УДК 616.831-009.86-02-091(027)

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СТАТИНЫ И ИНФАРКТ МИОКАРДА В ПЕРИОПЕРАЦИОННОМ ПЕРИОДЕ

В настоящее время по-прежнему отсутствует единая точка зрения в вопросе периоперационного применения статинов и их роли в формировании кардиальных рисков. Анестезиологи-реаниматологи, настороженные риском инфаркта миокарда и различных негативных кардиальных событий в периоперационном периоде, преимущественно игнорируют роль статинов, как одного из основных компонентов фоновой терапии ИБС, тогда как обоснованием для применения препаратов группы статинов являются патофизиологические изменения при коронарных нарушениях в периоперационном периоде. Это указывает на актуальность решаемой проблемы и определяет цель настоящего исследования.

Цель исследования — решение вопроса о необходимости периоперационного применения статинов и их роли в формировании кардиальных рисков.

Материалы и методы. Использовались следующие статины — аторвастатин и флавостатин. В первом проспективном рандомизированном испытании были обследованы 100 пациентов. Одной группе перед сосудистой операцией было назначено 20 мг аторвастатина, другим — плацебо один раз в день в течение 45 дней независимо от концентрации холестерина сыворотки крови. Операция на сосудах была выполнена спустя 31 день после рандомизации пациентов. Послеоперационный контроль велся 6 мес.

Флавостатин в другом исследовании использовался у 497 пациентов сосудистого профиля по 80 мг однократно ежедневно. В группе сравнения применяли плацебо. Терапию начинали за 37 дней до операции.

Также выполнено ретроспективное исследование 981 пациента после выполнения сосудистой операции на фоне длительного приема статинов с целью регистрации осложнений: случаев острого канальцевого некроза, увеличения уровня креатинкиназы, проявлений миопатии.

Результаты. В случае с аторвастатином в послеоперационном периоде контроль велся 6 мес. В течение этого срока аторвастатин значительно уменьшил уровень кардиальных событий (8 % против 26 %).

Метаанализ 223 010 пациентов от 12 ретроспективных и 3 проспективных испытаний со статинами показал снижение летальности на 44 % в общей хирургии и на 59 % в сосудистой хирургии.

При применении флавостатина: миокардиальная ишемия была отмечена у 10,8 % (группа флавостатина) против 19 % (группа плацебо). Уровень кардиальной смерти или ОИМ в этих двух группах составлял соответственно 4,8 и 10,2 %. Как видно, различия в группах во всех перечисленных исследованиях достоверны. В ретроспективном исследовании 981 пациента после выполненной сосудистой операции не отмечено случаев острого канальцевого некроза, увеличения уровня креатинкиназы, проявлений миопатии.

Заключение. Таким образом, возникновению ОИМ в раннем послеоперационном периоде часто предшествуют эпизоды рецидивирующих ишемий миокарда. Помимо определенных стратегий сокращения риска, существует возможность контроля и оптимизации сердечно-сосудистых факторов риска с привлечением терапии статинами.

Различными зарубежными сообществами составлены рекомендации по применению статинов у рисковых больных. Основой этих рекомендаций является широкое применение препаратов у групп больных с высоким риском развития сердечно-сосудистых осложнений.

Ключевые слова: статины, инфаркт миокарда, периоперационный период.

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The aim of the research — to resolve the question about the necessity of perioperative application of statins and their roles for forming cardiovascular risks.

Material and methods. In our research we used the following statins — atorvastatin and flavostatin. In the first prospective, randomized test there were examined 100 patients. The 1st group was indicated atorvastatin 20 mg before the vascular operation, the 2nd — placebo once a day during 45 days, regardless of concentration of cholesterol in blood serum. Vascular procedure was executed 31 days after randomization of patients. Control was conducted within 6 months after the operation.

In another research flavostatin was used in 497 patients of vascular profile by 80 mg 1 time every day. In the group of comparison placebo was applied. Therapy began 37 days before the operation. Retrospective research was executed in 981 patients, after implementation of vascular operation, on a background the protracted intake of statins, with the purpose to registrate complications: cases of acute tubular necrosis, increase of creatine kinase level, signs of myopathy.

Results. In case with atorvastatin, control was conducted for 6 months after the operation. During this term atorvastatin considerably decreased the rate of cardiovascular events (8% against 26%). A meta-analysis of 223,010 patients from 12 retrospective and 3 prospective tests with statins showed the decline of lethality by 44% in general surgery and by 59% — in vascular surgery. With use of flavostatin: myocardial ischemia in this research was observed in 10.8% (group of flavostatin) against 19% (group of placebo). The level of cardiac death or acute miocardial infarction in these two groups made 4.8 and 10.2% correspondingly.

Distinctions in groups in all enumerated researches are reliable.

The retrospective research of 981 patients didnot show the events of acute tubular necrosis, increase of creatine kinase level, myopathy signs after the vascular operation.

Conclusion. So, the occurrence of acute myocardial infarction in the early postoperative period is often preceded by episodes of recurrent myocardial ischemia. Besides of certain strategies of risk reduction, there is an ability to monitor and optimize cardiovascular risk factors involving statin therapy. Various foreign communities made recommendations for the use of statins for the risk patients. The basis for these recommendations is the widespread use of drugs in groups of high risk for cardiovascular complications.

Key words: statins, myocardial infarction, perioperative period.

Nowadays, a common ground in question of using perioperative statin and their role in the formation of cardiac risk have not reached yet. Anesthetists-resuscitators alert risk of myocardial infarction and various adverse cardiac events in the perioperative period, largely ignore the role of statins as a major component of the

background therapy of coronary artery disease. On the other side, internists, considering anesthesiologists' requirements to the prescription drugs (short, manageability, the intensity of the effect) do not use statins, even when they are indicated. Anyway, it is hard to understand the anesthesiologists' scepticism to statins as drugs affecting the operational risks.

The rationale for the using of statin drugs are the pathophysiological changes in the coronary disorders in the perioperative period.

All acute coronary syndromes (ACS) bear the following morphological changes: the functional instability of atherosclerotic plaque (AP) inflammation, coronary artery stenosis, coronary endothelial changes [9; 16; 17]. The biological activity of AP at the same time are provoked by such factors as mechanical stress, vasomotor tone, inflammation.

Unpredictable changes in AP associated with episodes of thrombosis, which, are caused by plaque rupture and/or erosion, endothelial dysfunction and inflammation [2; 6; 8]. Activation of platelets in the stress (perioperative) period is connected with the occurrence of histologic heterogeneity and provoked by hemodynamic activity, mental stress, infection, changes in hydration and blood pressure [17; 18].

The switch trigger gap in vulnerable AP, probably caused by changes willingness to thrombosis of blood and/or local release of pro-inflammatory cytokines that cause thrombosis, sometimes even in the absence of inflammatory infiltration of the cell and lipid core AP [2; 18].

Intimal plaque rupture — is the result of the combined effect of processes aimed at the distribution of the forces of surface tension on the plaque itself: the size of a blood clot that forms at the site of plaque rupture, release of biologically active substances (BAS) as the main factor of thrombogenesis at the site of coronary artery plaque composition, the value of stenosis platelet activation and a decrease in fibrinolytic activity [11]. The increase in platelet aggregation and a reduction of fibrinolytic activity provoke thrombosis [2; 18].

At rupture of AP the thrombus growth depends not only from the size of the expression of its bonds, but from the inflammatory response of endothelium [12]. The last causes disturbances of vasodilator and antiplatelet properties of blood. The situation worsens microthrombi distal embolization and coronary vasoconstriction caused by local mediators and activation of the sympathetic system [7].

As you can see from the summary of the mechanisms of coronary damage, all of them are parts of the cascade conjugate sanogenesis and pathological reactions, the activity of which is extremely difficult to predict and control. For the last need a whole range of drugs, making treatment cumbersome and have some negative effects. Partially task control of the injurious processes can be accomplished using relatively new group of preparations — statins [10].

Statins, introduced into clinical practice in the last decade of XX century have been initially considered as drugs that reduce the production of cholesterol by the liver and thus slows down the process of atherosclerosis. During the study, understanding of the effects caused by drugs of this group, stopped fit into the scheme exclusively blockade of cholesterol synthesis and activation of receptor uptake of low density lipoprotein liver. Later there were installed so called pleiotropic effects of statins, namely, the ability to remove endothelial dysfunction (due to conservation and restoration of its barrier function, increase the production of nitric oxide and, as a consequence, vasodilation), have anti-inflammatory, antioxidant, anti-arrhythmic, anti-thrombotic action, i.e. affect the basic pathogenesis of most the cardiovascular events [1; 3–5]. In this case, the pleiotropic effects are fast enough anyway before changing lipid metabolism.

It's important also the ability of an established fact at least two drugs in this group — atorvastatin and rosuvastatin — not only inhibit the formation of atherosclerotic plaque, but also cause its stabilization and even regression, which was confirmed in studies ASTEROID and REVERSAL [5].

As you can see, each of the pleiotropic effects aim to the pathogenetic link PIM.

The effectiveness of statins as a factor in reducing the risks of adverse cardiac events was proved in foreign studies [14].

The need of the use of statins for secondary prevention of adverse cardiac events was proved in the group of patients with non-coronary atherosclerosis (aortic arch branches, peripheral and renal vessels, the aorta), regardless of the accomplishments extracardiac operations [13].

In the study of the pleiotropic effects of statins significantly proved the possibility of preventing the development of acute myocardial infarction in the postoperative period. At destabilization AP with statins reaches a reduction of oxidative processes in the lipid core itself plaque inflammation arresting, reducing apoptosis and matrix metalloproteinases, metalloproteinase inhibitor, an increased level of collagen in the tissue [19].

Multiple clinical trials and studies have demonstrated the beneficial effect of using postoperative statin [15; 23]. In the first prospective, randomized trial there were examined 100 patients. The first group, was prescribed 20 mg of atorvastatin before vascular surgery, the second — placebo once daily for 45 days, regardless of the serum cholesterol concentration [20]. Vascular surgery was performed 31 days after randomization of patients. The control was conducted 6 months after the operation.

During these six months, atorvastatin significantly reduced the level of cardiac events (8% vs. 26%).

Meta-analysis of 223,010 patients from 12 retrospective and 3 prospective trials — with statins showed a reduction in mortality — 44% in general surgery and 59% — in vascular surgery [23].

Flavostatin, in another study, was used in 497 patients of the vascular profile, 80 mg once daily. The comparison group used placebo. Therapy started 37 days before the operation. Myocardial ischemia in this study was observed in 10.8% (flavostatin group) versus 19% (placebo group). The level of cardiac death or MI in the two groups were respectively 4.8% and 10.2% [20].

As you can see, the differences in these groups all studies are proved.

When used statins can cause anxiety and during preoperative preparation their numerous side effects are myopathy, rhabdomyolysis with acute tubular necrosis and acute renal failure. However, by now there has been no large-scale studies that would confirm the occurrence of these side effects. For example, in a retrospective study of 981 patients performed after vascular surgery, there occurred no cases of acute tubular necrosis, increased levels of creatinekinase, symptoms of myopathy [21].

As for the withdrawal of statins in the perioperative period, it suggests an adverse impact of the cancellation for a coronary heart disease and other cardiac risk factors [22].

So, the occurrence of acute myocardial infarction in the early postoperative period is often preceded by episodes of recurrent myocardial ischemia. In addition to certain risk reduction strategies, there is an ability to monitor and optimize cardiovascular risk factors involving statin therapy.

Various foreign communities made recommendations for the use of statins for the risk patients. The basis for these recommendations is the widespread use of drugs in the risk group for cardiovascular complications [14].

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Submitted 29.01.2014

УДК 616-036.882-08

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ПРОГНОЗИРОВАНИЕ ОТВЕТА НА ИНФУЗИОННУЮ НАГРУЗКУ: ОТ ТЕОРИИ К ПРАКТИКЕ

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Точное прогнозирование ответа на инфузионную нагрузку у пациентов отделения интенсивной терапии — повседневная задача реаниматологов. При шоке инфузионная терапия направлена на повышение ударного объема или сердечного выброса (на 10–15 %) и улучшение доставки кислорода, а также, в конечном итоге, функции органов. Примечательно, что инфузионная терапия улучшает состояние гемодинамики лишь у 50 % пациентов отделения интенсивной терапии, при этом спустя несколько суток после поступления этот процент может быть значительно ниже. Важность корректного прогнозирования ответа гемодинамики обусловлена также тем, что неоправданная инфузионная терапия, проводимая «наугад», ведет к снижению доставки кислорода, усилению капиллярной утечки и нарастанию тканевых отеков, а также повышению риска развития острого респираторного дистресс-синдрома и полиорганной недостаточности.

На сегодняшний день мы располагаем так называемыми функциональными, или динамическими, показателями кровообращения и набором тестовых процедур, позволяющих прогнозировать ответ гемодинамики на усиление преднагрузки. У релаксированных пациентов, находящихся на искусственной вентиляции легких и не имеющих значимых нарушений ритма сердца, могут применяться вариабельность пульсового и систолического давления, а также ударного объема. При восстановлении спонтанного дыхания или наличии прочих ограничений могут использоваться тест с подъемом ног, повышением положительного давления в конце вдоха и недавно предложенный мини-тест с нагрузкой жидкостью. Широко применяемый стандартный тест с нагрузкой жидкостью подразумевает введение 5–10 мл/кг инфузионной среды за 5–30 мин, однако основной его недостаток — риск неоправданной гипергидратации.

В этом кратком обзоре обсуждается физиология кардиореспираторных взаимодействий, представлены наиболее важные функциональные показатели кровообращения и тесты, позволяющие прогнозировать чувствительность к