A new modified myocardial infarction animal model

Esin Akbay*, Mehmet Ali Onur

Department of Biology, Hacettepe University, Faculty of Science, Ankara, Turkey
*Corresponding Author: Department of Biology, Faculty of Science, Hacettepe University, 06800, Beytepe, Ankara, Turkey Tel: +903122976440 Fax: +903122992028 e-mail: akbayesin@gmail.com

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Abstract

We aimed to develop a novel and fast surgical method to induce myocardial infarction that does not need ed ventilation. In the novel modified method, rats were anesthetized and myocardial infarction was induced without ventilated thoracotomy. Heart was exposed a small incision and myocardial infarction was induced by cauterization at the midpoint through the starting point and the cardiac apex, without taken outside of the thorax. This new modified myocardial infarction procedure is fast, with an average operation time of around 20 minutes. We believe that this novel model for rat myocardial infarction shows a more potent and less tissue damaging model of myocardial ischemic injury.

Introduction

Myocardial infarction (MI) is a leading cause of morbidity and mortality in western countries. Heart failure resulting from MI, is partly caused by the loss of cardiomyocytes and the limited capacity of spontaneous regeneration of the heart. Large cardiomyocyte loss provoked by ischemia leads to impairment of cardiac contractility, loss of pump force and subsequent risk of heart failure. In todays’ era, studies on cardiovascular diseases therapies are going on without limits. Application of animal models of MI play very important role in these stuides (1).

The animal models for MI (mice, rat and porcine etc.) include ligation, cauterization or cryoinjury of the left descending coronary artery (LAD) (2-4). The increased expenditure for animals and the need for special equipments for all types of models, such as an animal ventilation, limit the use of these models to extremely specialized laboratories. Inappropriate use of the ventilator and prolonged opening of the chest easily contribute to the death of the animal. Therefore, the most difficult problems facing the investigators are how to reduce the cost of the experiment, save operating time, and raise the success rates. In this model, our goal was to establish a practical, fast, safe and be reproducible rat model of MI.

Two of the most common models used by researchers are LAD ligation and coronary artery cauterization to cause MI. The MI model is usually used to investigate myocardial changes such as remodeling that occur over an extended period of time. Although a variety of surgical manipulations have been used during the past decade to induce the ischemic event, ligation of the LAD and cauterization methods are still the most commonly practiced methods (5,6). However, most investigators still use a method requiring ventilation and wide opening of the chest (referred to as the classic method), which can cause extensive tissue damage, high surgical-related death and be quite time consuming.

How To Do It

In this new method of MI induction, rats were anesthetized with ketamin (40 mg/kg) and xylazine (1 mg/kg) by intramuscular application, but not ventilated. After the petal reflex absence occured, animals were placed in the supine position by tying the legs. The left chest was shaved and disinfected before small skin cut (1.2 cm) was made over the left chest (Figure 1a), and a purse suture was made. After dissection and retraction of the pectoral major and minor
Akbay et al.

muscles (Figure 1b), somewhere between fourth and fifth intercostal space was exposed (Figure 1c). A small hole was made at the fourth intercostal space with a mosquito clamp to open the pleural membrane (Figure 1d). The pericardium was incised to expose the anterior surface of the heart and the heart was squeezed out by pressing the thorax lightly. LAD was cauterized at the midpoint through the starting point and the cardiac apex (Figure 1e). After cauterization, the air in the thorax were squeezed out by the forefinger and the thorax was closed with the suture that had been prepared before the thoracotomy. During the whole operation heart was not taken out of the thorax. The rats were then allowed to breathe room air and monitored during the recovery period. No artificial respiratory aid was required during the recovery time. Totally the operation takes place around 20 minutes.

Discussion

Left anterior descending artery is the major vessel that supplies blood to the left ventricle. If it is occluded, it results in MI of the anterior wall of the left ventricle and the anterior portion of the interventricular septum. Occlusion of LAD in small rodents has proved to be a good model for research in myocardial ischemia (7,8).

We developed a novel, modified and rapid surgical method for creating MI in rats that does not require animal ventilator. This procedure is significantly less time consuming than the classic way of rat MI models. It takes about 20 minutes in experienced hands. Practice is needed quickly cauterize the LAD. The major thing is that, this faster method results in less tissue damage and inflammation, and much faster postsurgery recovery. In this case, the most important key factor is the duration of anesthesia. Timing of anesthesia must be controlled severely; otherwise, the postoperative recovery of respiration will be affected. Also we have used this faster procedure in stem cell studies; we injected stem cells directly into the border zone of the ischemic heart five minutes after cauterization. We believe that this new and rapid method is extremely reproducible. The success ratio of method is high. We believe that this method is an advancement in studies of murine ischemic injury, compared with the classic methods of MI involving intubation and ligation.

This method also avoids bleeding. It is well known that hemorrhage is one of the factors contributing to the increased mortality of the “heart exteriorization” MI rat models.

Pneumothorax is another contributor to early postsurgical death and occurs when the operator forgets either to displace air before closing the suture or forgets to keep the hole open when manually evacuating air of the thoracic cavity. One of the advantages of this new procedure is that the pectoral muscles remain intact. This is very important because intact pectoral muscles are necessary to cover the opening once the heart has been returned to the thoracic space and eliminates the suturing of the muscle, which is one of the limitations of classic thoracotomy.

The procedure of murine model of MI without ventilation is technically demanding and challenging. Critical to the success of the novel model is its rapidness.

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Conflicts of Interest

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

References