Propofol: a safe anaesthetic drug in experimental cardiac surgery in rabbits

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ACKGROUND: *Experimental surgery needs a pharmacological approach that can interfere with cardiac function.*
CASE REPORT: *In a animal model of regenerative medicine of myocardium we use an anaesthesiological protocol that included Propofol, a benzodiazepine (Midazolam) and an alpha-2 adrenergic agent.*
RESULTS: In *a group of 15 rabbits undergoing cardiac surgery we reported 1 arrhythmic complication during stem cell injection.*
DISCUSSION: *The functional cardio- respiratory depressor activity of Propofol was compensated by alpha-2 adrenergic drugs, avoiding serious complications. We hypothesize that the functional cardio-respiratory depressor of different anaesthesiological drugs can be reversed by the contemporary administration of with adrenergic agents.*

KEY WORDS: Arrhythmias, Cardiac ischemia, Cardiovascular toxicity, Propofol

Introduction

The choice of animals for cardiovascular experimental studies depends: first, on their physiological and anatomical characteristics; then, on the size of the animal, stabulation cost, human protective affection, and on anaesthesiological and monitoring facilities. In our experimental study on cardiac ischemia/reperfusion damage and subsequent treatment with homologous bone marrow mesenchymal stem cells (BMSC), we selected rabbits for their similarities with human coronary arteries and with patho-physiology of immunological system [1,2].
However, these animals have a particular pharmaco-anaesthesiology, in relation to their susceptibility to stressor agents and to particular sensibility to some anaesthetic agents.

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Case Report

The experimental protocol included 15 male adult "New Zealand white rabbits", with a mean weight of 4.1 kg.
The surgical procedure consisted in a left antero-lateral thoracotomy, pericardiotomy, and exposure of the anterior wall of the left ventricle. The anterior descending coronary artery, identified in its third proximal segment, was occluded for a time ranging from 4 to 5 minutes, until an area of myocardial tissue of 1-1.5 cm in diameter appeared ischemic. At the end of the surgical procedure, a complete re-expansion of the left lung was obtained with the simple aid of a temporary pleural aspiration [3].
The animals were subdivided in three groups of five rabbits each:
– Sham;
– Intravenous injection of BM stem cells;
– Intra-myocardial injection of BMSC.
The anesthesiological protocol included three drugs, a benzodiazepine (Midazolam), an alpha2-adrenergic agent, and an anaesthetic (2,6, -diisopropilfenol - Propofol), selected for their respective action of sedation, alpha-2 mimetic activity and analgesia. The first two drugs were

administered at the induction of anaesthesia, while the third was continued throughout the entire surgery.
Animals were sedated by an intra-muscolar injection of 1 mg/kg of Midazolan, associated with Medetomidyne 1 mg/kg. A marginal auricular vein was cannulated with a standard 22-Gauge intravenous catheter and an initial dose of 2.5 mg/kg Propofol solution was administrated 2 minutes before surgical positioning. The depth of anaesthesia was maintained with equivalent doses administered every 5 minutes throughout the entire surgery. The spontaneous respiratory activity was assured with a simple muzzle musk connected with a bag valve system of 0.5 litre using room air, enriched with a 50% O2, even during the one lung ventilation phase.
The intra-operative monitoring consisted of a continuous ECG recording and of a pulse oximetry. Hypotension and blood losses were compensated by saline infusion.
Evaluation of Side effects of anaesthesia was assessed during and early after surgery (within the first 12 hours). We monitored the following parameters:
– respiratory depression, requiring manual respiratory assistance and/or an increased oxygen supply;
– severe bradycardia or arrhythmia (recorded by ECG);
– death.
All animals received care in compliance with the European Convention on Animal (Directive 2010/63/EU of 22.09.2009).
The protocol was approved by Research Animal Care and Use Committee of the University of Modena and Reggio Emilia (Italy) (prot. # 25, 18/03/2008 and prot.# 83, 25/ 09/2009).

Results and Discussion

We reported 3 episodes of reversible ventricular tachycardia (VT) and one episode of ventricular fibrillation successfully cardioverted during induction of ischemia. We registered only one fatal complication (6.66%), represented by a ventricular arrhythmia developed during intra-myocardial BMSC injection. It is well known that the direct intramyocardial administration of BMSC can induce a transient pro-arrhythmic effect [4]
The anaesthesiological protocol we tested demonstrated a proper action of sedation and myo-relaxation, without hindering the spontaneous respiration [5]. The depth of analgesia was proved by suppression of any muscular reaction to surgical stimuli, which are potential stressors for rabbit. Neither administration of anti-arrhythmic drugs, such as lidocaine, nor invasive monitoring of the arterial pressure was necessary, considering the absence of cardio-circulatory adverse effects [6]. Interestingly, this venous anaesthesiological protocol avoided the use of neuromuscular blocking agent [7]. The correct oxygenation, recorded throughout the entire surgical time and obtained with enriched air, avoided oro-tracheal intubation, complex manoeuvre in rabbits. Moreover, the rapid effects of Propofol allowed a quick anaesthesiological recovery.
In conclusion, our experience in rabbit experimental cardiac surgery indicates Propofol as a suitable analgesic agent for the induction of anaesthesia and its maintenance. Propofol mild cardio-respiratory depressing action may be effectively balanced associating an alpha2–adrenergic agent[8].

Riassunto

PREMESSA.: La chirurgia sperimentale richiede un approccio farmacologico che può interferire con la funzione cardiaca.
METODI:In un modello animale di chirurgia rigenerativa del miocardio abbiamo utilizzato un protocollo anestesiologico che includeva Propofol, una benzodiazepina (Midazolam) e un alfa2-adrenergico.
RISULTATI:In un gruppo di 15 conigli sottoposti a chirurgia cardiaca abbiamo osservato 1 complicanza aritmica letale durante la somministrazione intramiocardica di cellule staminali.
DISCUSSIONE. L'azione di depressione della funzione cardio respiratoria del Propofol è stata compensate da farmaci con attività alfa2-adrenergica che hanno ridotto notevolmente le complicanze aritmiche.
Ipotizziamo che l'azione di depressione della funzionalità cardio respiratoria di farmaci anestesiologici utilizzati nella chirurgia sperimentale cardiaca nel coniglio possa essere controllata dalla somministrazione contemporanea di agenti adrenergici.

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