Anesthesia with Intraperitoneal Propofol, Medetomidine, and Fentanyl in Rats

Heber Nuno Castro Alves,1,2,* Aura Luísa Maia da Silva,1,2 Ingrid Anna S Olsson,2 José Manuel Gonzalo Orden,3 and Luis Marques Antunes1

A safe and reliable method for anesthetizing rats has long been a leading concern of biomedical researchers. We recently found that the intraperitoneal administration of propofol combined with medetomidine and fentanyl is safe for mouse anesthesia. Here we studied whether the same combination could be used for general anesthesia in rats. We used male Wistar rats to test 10 combinations of propofol, medetomidine, and fentanyl administered intraperitoneally and reversed with intraperitoneal atipamezole 30 min after induction. The depth of anesthesia, induction time, loss of pedal withdrawal reflex, pulse rate, and respiratory rate were evaluated, along with the duration and quality of induction, surgical anesthesia, and recovery. The combination of propofol and medetomidine provided a predictable induction and sufficient hypnosis and muscle relaxation, but surgical anesthesia (loss of pedal withdrawal reflex) was difficult to achieve with this protocol. The addition of fentanyl increased analgesia, making it possible to achieve surgical anesthesia. In conclusion, combination of propofol (100 mg/kg), medetomidine (0.1 mg/kg), and fentanyl (0.1 mg/kg) is a safe and practical technique for intraperitoneal anesthesia in rats, providing a surgical window of 25 min and restraint for 30 min, with rapid recovery after administration of atipamezole.

Safe and reliable anesthesia of rats has long been a leading concern among biomedical researchers. Protocols with rapid recovery times can decrease the mortality associated with rodent anesthesia by minimizing hypothermia and hypoxia.1,3 Inhalant anesthesia tends to be the technique of choice for rapid recoveries. However, the necessary specific delivery equipment is not available in all facilities, and this technique is not recommended in some circumstances, such as neurosurgical and oropharyngeal procedures.1,9

Most injectable anesthetic protocols for rats are based on the combination of dissociative drugs or opiates with α2 agonists and tranquilizers or sedatives.13-15,17,21,23,33 Intraperitoneal barbiturates are another common technique.13 Unfortunately, most current injectable anesthetic protocols for rats typically lead to prolonged sedation, and full recovery of consciousness can take several hours.23 Anesthetic combinations such as medetomidine–ketamine18 and fentanyl–medetomidine23 have the advantage of providing faster recoveries through reversal of the medetomidine effect with a specific α2 antagonist such as atipamezole.32 Nevertheless, combinations including ketamine often are associated with low-quality recoveries,22,34 and subanesthetic treatment with ketamine can induce schizophrenic-like behavioral disturbances when applied for several consecutive days.7 Neuroleptanalgesic combinations of fast-acting opiates and medetomidine usually require high doses of both compounds to achieve anesthesia for surgical procedures, leading to side effects of respiratory depression and polypuria during the period of anesthesia.25

Recent studies in our laboratory showed that the combination of propofol and fast-acting opioids did not induce anesthesia in mice when administered by intraperitoneal route.2 However, the addition of medetomidine resulted in an easy and reliable way to anesthetize mice by the intraperitoneal route.3 In recent studies, a single intraperitoneal dose of propofol induced general anesthesia in a single rat.1,27 However, a large dose of propofol was necessary, which led to progressive bradypnea that persisted for more than 6 h and resulted in death from respiratory arrest. Similarly, previous studies from our group have revealed unpredictable effects from propofol and propofol–remifentanil intraperitoneal anesthesia in rats.4

In the current study, we hypothesized that the combination of propofol with a fentanyl–medetomidine protocol would reduce the doses of all drugs required and yield appropriate anesthesia, with good muscle relaxation and analgesia and minimal respiratory depression. In addition, reversal of the medetomidine effects with atipamezole would provide a rapid recovery, leading to a safe and practical anesthetic technique.

Materials and Methods
All procedures were carried out under personal and project licenses approved by the national regulatory office (Direcção Geral de Veterinária, Ministério da Agricultura do Desenvolvimento Rural e das Pescas, Largo da Academia Nacional das Belas Artes, Lisboa, Portugal).

The experiments were divided into preliminary and main studies. In the preliminary study, the anesthetic effects of intraperitoneal propofol alone were evaluated to identify the most appropriate dose for subsequent experiments. The main study was divided in 2 parts. In the first part, we tested the anesthetic effects of propofol associated with medetomidine or fentanyl in separate combinations. In the second part, we tested the effects of propofol in simultaneous combination with medetomidine and fentanyl.

Animals. Outbred SPF male Wistar rats (n = 64; age, 8 to 9 wk; weight, 276 to 300 g; Crl:WI, Charles River Laboratories, Barcelona, Spain) were used. Excluded agents included Kilham

1Centro de Estudos de Ciências Animais e Veterinárias, Universidade de Trás-os-Montes e Alto Douro, Vila Real, Portugal; 2Laboratory Animal Science, Instituto de Biologia Molecular e Celular, Universidade do Porto, Porto, Portugal; 3Department of Medicine, Veterinary Surgery and Anatomy, Universidad de León Campus de Vegazana, León, Spain.
*Corresponding author. Email: heber.alves@unapo.pt
Propofol, medetomidine, and fentanyl in rat anesthesia

rat virus, pneumonia virus of mice, reovirus 3, Sendai virus, rat coronavirus, Théiler disease virus, Toolan H1 virus, rat parvovirus types 1 and 2, mouse adenovirus, Hantaan virus, lymphocytic choriomeningitis virus, Clostridium piliformis, Bordetella bronchiseptica, Corynebacterium kutscheri, Pasteurella pneumotropica, P. multocida, Salmonella spp., Streptobacillus monili- formis, β-hemolytic Streptococcus spp., S. pneumoniae, Helicobacter hepaticus, H. bilis, Helicobacter spp., cilia-associated respiratory bacillus, Mycoplasma pulmonis, E. cuniculi, helminths, pathogenic protozoa, and ectoparasites. The animals were kept in a room with controlled temperature (21 °C), humidity (55%), and photoperiod (12:12-h; lights off at 1700). Water and rodent pellets (4RF25-GLP, Mucedola, Milan, Italy) were provided ad libitum. The rats were divided in groups of 4 and housed in Makrolon type IV cages (Tecniplast, Dias de Sousa, Alcochete, Portugal) provided with corn-cob bedding material (Probiológica, Lisbon, Portugal), tissue nesting material, and a cardboard tube. Cages were changed once each week.

Drugs. Propofol (Diprivan 2%, AstraZeneca, Barcarena, Portugal), fentanyl (0.05 mg/mL; B Braun, Queluz de Baixo, Portugal), medetomidine (1 mg/mL; Domitor, Pfizer, Seixal, Portugal) and atipamezole (5 mg/mL; Antisedan, Pfizer) were administered in this study. Standard physiologic saline (0.9%; Soro Fisiológico, Paracelcia, Porto, Portugal) was used for dilution.

Support equipment. A homeothermic blanket (N-HB101-S-402, Panlab, Cornellà, Barcelona, Spain) with a rectal probe was used to monitor each rat’s body temperature and maintain it between 36 °C and 38 °C during the anesthetic period. A pulse oximeter (S&W 9040, Athens, Munich, Germany) placed on the upper right hind leg was used for monitoring oxygen saturation (SaO₂) and pulse rate during the main study. Oxygen (100%; 2 L/min) was delivered to each rat by using a face mask connected to a coaxial circuit.

General methodology. The rats were weighed by using an electronic scale (EMB 200-1, Kern and Sohn, Balingen, Germany). The drugs were freshly mixed in a multidose container and administered intraperitoneally as a mixture in a single injection.

Intraperitoneal administration was performed lateral to the midline next to the umbilicus. A 1–25-gauge needle was inserted at a 45° angle to the abdominal wall in the lower left quadrant of the abdomen. The volume administered varied between 0.8 and 4 mL. Each rat was restrained and anesthetized by the same investigator. After administration, rats were observed in order to identify any clinical sign associated with potential pain or discomfort, including guarding, licking, or scratching the potential painful site and a hunched posture.

After drug administration, the rat was placed alone in a cage with bedding material until loss of the righting reflex (defined as lack of the ability to return to sternal recumbency) was achieved. This period of time was defined as the induction time (Figure 1). After induction, rats were moved to a homeothermic blanket. A facial mask was placed to provide oxygen (100%) throughout the procedure, and the pulse oximeter was placed on the right hindleg.

After induction, the pedal withdrawal reflex (assessed by pinching of the tail and the metacarpal region of the hind foot between the index finger and the thumb), was tested in periods of 5 min. This was the primary method for assessing depth of anesthesia. The responses were rated as described previously according to a scale from 1 to 5, with 1 indicating no response, which score is considered sufficient for performing surgical procedures, and 5 a marked response. Respiratory rate, rhythm, and pattern; eye blinking; and whisker movement also were included in the overall evaluation of depth of anesthesia. Animals were considered to have reached a surgical plane of anesthesia when they achieved a score of 1 on this scale (complete loss of the pedal withdrawal reflex). This reflex was tested every 5 min by the same investigator, alternating between the left and right limbs after induction time until the return of this reflex. The period of time between loss and return of the pedal withdrawal reflex was defined as duration of surgical anesthesia (Figure 1).

When the animals did not lose the righting reflex, for a period of 30 min after intraperitoneal injection, they were returned to their home cage and observed for the next 2 h for any occurrence of abnormal behavior by a researcher blinded to the doses administered. In combinations with medetomidine, animals received atipamezole 30 min after induction, in a dose 5 times that of the medetomidine administered by intraperitoneal route. After return of the righting reflex the rat was then returned to its home cage and observed continuously for another 2 h for abnormal behavior. The period of time between administration of atipamezole and return of the righting reflex, was defined as recovery (Figure 1). The period of time between loss and return of the righting reflex was defined as the duration of total anesthetic period (Figure 1). The animals were also observed during the following week to detect any postanesthetic complications.

Data recording and anesthetic monitoring. The essential anesthetic events recorded during the preliminary study and the main study are defined in Figure 1. These moments were recorded by a researcher blinded to the doses administered. In the main study, pulse rate, respiratory rate, and depth of anesthesia were recorded also.

Animal breathing was clinically assessed by monitoring thoracic movement including the type of movement observed (thoracic or abdominal) during anesthesia. Respiratory depression was defined as the absence of thoracic muscle movement or the respiratory movements that became shallower and more abdominal leading sometimes to apnea. If the animal stopped breathing for 10 s or longer, it was considered apneic.

Experimental procedures. In the preliminary study, 16 male rats were divided into 4 groups of 4 animals each. Four doses of propofol (50, 100, 150, and 200 mg/kg) were administered intraperitoneally, one dose to each group.

The first part of the main study involved 32 rats (4 groups of 8 rats). All rats received propofol at 100 mg/kg IP. In addition, each group received either fentanyl (0.1 or 0.3 mg/kg) or medetomidine (0.1 or 0.3 mg/kg) intraperitoneally.

The second part of the main study involved 16 rats (2 groups of 8 rats each). All rats in both groups received propofol (100 mg/kg) and medetomidine (0.1 mg/kg) intraperitoneally; groups also received fentanyl at either 0.1 or 0.3 mg/kg IP.

A researcher blinded to the doses administered recorded pulse rate, respiratory rate, and depth of anesthesia every 5 min for 30 min after induction. Pulse rates and respiratory frequencies were always recorded prior to evaluation of the pedal withdrawal reflex to avoid alteration of these values by noxious stimulation.

Data analysis. Data were recorded by using a macro we developed in Excel 2007 (Microsoft, Redmond, WA). For analysis, the essential anesthetic intervals (in minutes) were calculated (Figure 1) and are shown as mean and standard deviation. Kolmogorov-Smirnov and Levene tests were used to evaluate normality of distribution and homogeneity, respectively. ANOVA was used to compare induction time, time to achieve surgical anesthesia, duration of surgical anesthesia, and duration of...
Results

Preliminary study. In general, the propofol doses used were insufficient to achieve surgical anesthesia, and results were erratic with all doses. The most predictable dose was 200 mg/kg IP, for which 3 of the 4 rats in the group lost the righting reflex. The 50- and 150-mg/kg doses of propofol failed to induce anesthesia; anesthesia was induced with 100 mg/kg in a single rat. Limb shaking and head scratching were observed continuously after induction in some animals. Surgical anesthesia was not achieved in any animal in the preliminary study.

Main study. Induction of anesthesia was observed in all animals and with all combinations tested (Table 1). No signs of abdominal pain or discomfort were observed after intraperitoneal administration, and none of the animals died. Clinical effects varied markedly between anesthesia groups. No abnormal behavior was detected during the first 2 h after anesthesia, and none of the animals presented any sign of postanesthetic complications during a 7-d follow-up. Data for pulse rate (Figure 2), respiratory rate (Figure 3), and depth of anesthesia (Figure 4) are shown. A regular pulse rhythm was observed throughout anesthesia in all rats. Oxygen saturation exceeding 95% was maintained in all rats.

Propofol–medetomidine. A smooth anesthetic induction was observed in both groups, with an increasing reduction in motility until complete immobility. No signs of respiratory distress, muscle spasms, or ataxia were observed during this period. The rats’ breathing pattern was predominantly thoracic, and apnea was not observed with this drug combination. Surgical anesthesia was not observed in any rat receiving 100 mg/kg propofol IP with 0.1 mg/kg medetomidine IP; only 4 animals achieved surgical anesthesia when the medetomidine dose was increased to 0.3 mg/kg IP (Table 1). After atipamezole administration (Table 1), recovery time (Figure 1) was very fast in the rats that received 100 mg/kg propofol + 0.3 mg/kg medetomidine IP.

Propofol–fentanyl. Surgical anesthesia was achieved in only 4 rats, all of which received 100 mg/kg propofol + 0.3 mg/kg fentanyl IP (Table 1). Rats in both dose groups demonstrated muscle rigidity and spasms during anesthetic induction with propofol–fentanyl, but the signs were more prominent in those receiving the higher (0.3 mg/kg) dose of fentanyl. Muscle rigidity remained throughout the period of anesthesia in both groups. Pulse rate between minutes 0 and 10 and minutes 20 and 30 after induction of anesthesia was higher (P < 0.05) in rats that received 100 mg/kg propofol + 0.3 mg/kg fentanyl IP compared with other groups (Figure 2). In addition, 3 of the 8 rats that received 100 mg/kg propofol + 0.3 mg/kg fentanyl IP showed short periods of apnea (less than 10 s) during the first 5 min after induction, and the breathing pattern was mainly abdominal during the first 10 min after this period. The mean respiratory rate among rats given 100 mg/kg propofol + 0.3 mg/kg fentanyl IP increased (P < 0.05) by 167% between induction and 20 min afterward (Figure 3). When compared with those given 100 mg/kg propofol + 0.3 mg/kg medetomidine IP, rats treated with 100 mg/kg propofol + 0.3 mg/kg fentanyl IP had lower (P < 0.05) values for depth of anesthesia from 0 to 15 min after induction (Figure 4). Depth of anesthesia increased progressively throughout the procedure in rats given 100 mg/kg propofol + 0.3 mg/kg fentanyl IP (Figure 4).

Propofol–medetomidine–fentanyl. Induction time did not differ between rats that received 100 mg/kg propofol + 0.1 mg/kg medetomidine + 0.1 mg/kg fentanyl and those given 100 mg/kg propofol + 0.1 mg/kg medetomidine + 0.3 mg/kg fentanyl. However, mean recovery time was 70% shorter (P < 0.05) in the 100 mg/kg propofol + 0.1 mg/kg medetomidine + 0.1 mg/kg fentanyl group. In addition, mean recovery time was 25.17 min longer in rats given 100 mg/kg propofol + 0.1 mg/kg medetomidine + 0.3 mg/kg fentanyl than in those treated with 100 mg/kg propofol + 0.3 mg/kg medetomidine (Table 1).

In both of the 3-drug dosage groups, anesthetic induction was smooth, with increasing reduction in motility until complete immobility. No signs of respiratory distress, muscle spasms, or ataxia were observed during induction. Surgical anesthesia was observed in all animals in both groups. Both propofol–fentanyl–medetomidine combinations required less (P < 0.05) time to achieve surgical anesthesia (Figure 1) and provided a longer duration of surgical anesthesia (Figure 1) than did 100 mg/kg propofol + 0.3 mg/kg medetomidine or 100 mg/kg propofol + 0.3 mg/kg fentanyl (Table 1). Neither time to achieve surgical anesthesia, its duration, nor pulse rate (Figure 2) differed significantly between rats that received 100 mg/kg propofol + 0.1 mg/kg medetomidine + 0.1 mg/kg fentanyl and those given 100 mg/kg propofol + 0.1 mg/kg medetomidine + 0.3 mg/kg fentanyl.

Breathing was predominantly thoracic without apnea among rats treated with 100 mg/kg propofol + 0.1 mg/kg medetomidine + 0.1 mg/kg fentanyl. In contrast, 4 of the 8 rats given 100 mg/kg propofol + 0.1 mg/kg medetomidine + 0.3 mg/kg fentanyl demonstrated short periods of apnea after loss of the righting reflex; these animals also had an abdominal breathing pattern. Compared with that in the group given the lower dose, the respiratory rate was significantly (P < 0.05) lower at beginning of anesthesia in the 100 mg/kg propofol + 0.1 mg/kg medetomidine + 0.3 mg/kg fentanyl group, which also showed the lowest (P < 0.05) mean respiratory rate when compared with all other groups in the main study (Figure 3).

Depth of anesthesia differed significantly (P < 0.05) only at minute 0 (Figure 4) between the group given 100 mg/kg propofol + 0.1 mg/kg medetomidine + 0.1 mg/kg fentanyl and that
treated with 100 mg/kg propofol + 0.1 mg/kg medetomidine + 0.3 mg/kg fentanyl. Surgical anesthesia was observed in all animals in both groups after the 10-min time point. Values for depth of anesthesia decreased ($P < 0.05$) between minute 0 and minute 5 in both 3-drug dosage groups (Figure 4). In addition, the mean depth of anesthesia values from minute 5 to minute 30 were lower ($P < 0.05$) for both 3-drug groups than for all other groups from the main study (Figure 4).

Gross postmortem results from rats treated with either of the 3-drug combinations included mild lymphangiectasis and findings compatible with chyloperitoneum; no other changes were present.

**Discussion**

A safe, effective, and practical method to achieve general anesthesia in rats is needed. Although volatile anesthetics might fill this need, their use requires specialized equipment that may not be available in all facilities. Furthermore, volatile anesthetics do not provide perioperative analgesia, which is mandatory for animals undergoing surgery, and issues of gas scavenging and operating room pollution should be considered when using these agents.26

The practical aspects of drug administration in rats limit the number of protocols suitable for anesthetizing these animals. The combination of fentanyl and medetomidine without propofol has been described to produce surgical anesthesia in rats.23 However, this combination requires large doses of both fentanyl and medetomidine (300 mg/kg each) to produce surgical anesthesia. Rats may need several hours to recover after fentanyl–medetomidine anesthesia, and the duration of anesthesia is influenced markedly by the dose of medetomidine used.23 Reversal of fentanyl–medetomidine anesthesia is obtained through administration of atipamezole and naloxone or butorphanol. However, this technique also reverses the analgesic action from the drugs used—a disadvantage for animals that have undergone surgery.

The hypnotic effect of intraperitoneal propofol in rats has been reported.27 However, similar to results obtained in mice,2 the effects of administration of propofol alone by the intraperitoneal route were unpredictable in the present study. Increases in the propofol dose were associated with increasing numbers of animals losing the righting reflex, in agreement with the reported hypnotic effect of propofol.24 However, intraperitoneal propofol alone did not induce unconsciousness with immobility, and some rats continuously showed limb shaking and head scratching after induction. The inconsistency observed between and within groups that received propofol as the sole agent may reflect the variability associated with the intraperitoneal route. Although the large surface area provided by the omentum and abdominal organs facilitates the absorption of hydrophobic compounds, the rate of absorption may be insufficient to achieve the minimal propofol effect site concentration to induce

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**Table 1. Results of intraperitoneal anesthesia in groups (n = 8 rats per group) in which loss of the pedal withdrawal reflex occurred**

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>No. of rats with loss of PWR</th>
<th>Induction time (min)</th>
<th>Time to achieve surgical anesthesia (min)</th>
<th>Duration of surgical anesthesia (min)</th>
<th>Recovery time (min)</th>
<th>Total duration of anesthesia (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propofol + medetomidine</td>
<td>100 + 0.3</td>
<td>4</td>
<td>5.4 ± 1.5</td>
<td>11.25 ± 2.5</td>
<td>18.75 ± 9.47</td>
<td>5.53 ± 1.47</td>
</tr>
<tr>
<td>Propofol + fentanyl</td>
<td>100 + 0.3</td>
<td>4</td>
<td>5.5 ± 1.0</td>
<td>10.0 ± 4.08</td>
<td>13.75 ± 6.29</td>
<td>not evaluated</td>
</tr>
<tr>
<td>Propofol + medetomidine + fentanyl</td>
<td>100 + 0.1 + 0.1</td>
<td>8</td>
<td>6.9 ± 2.8</td>
<td>4.38 ± 3.2a</td>
<td>30 ± 3.8a</td>
<td>9.4 ± 4.0</td>
</tr>
<tr>
<td>Propofol + medetomidine + fentanyl</td>
<td>100 + 0.1 + 0.3</td>
<td>8</td>
<td>5.2 ± 0.9</td>
<td>2.5 ± 2.7a</td>
<td>31.88 ± 3.7a</td>
<td>30.7 ± 18.4a</td>
</tr>
</tbody>
</table>

PWR, pedal withdrawal reflex

All rats in all groups lost the righting reflex, regardless of the drug combination used.

*Significantly ($P < 0.05$) different from groups without superscript symbol.
adequate anesthesia. Because these agents are absorbed into the portal system, drugs administered intraperitoneally undergo considerable first-pass hepatic metabolism. Another possible explanation for the variability is extraperitoneal or gastrointestinal drug loss.\(^8,20,25\)

The synergistic effect of \(\alpha\)2-agonists such as medetomidine or dexmedetomidine is known to reduce the dose requirements of propofol to achieve loss of consciousness in several species.\(^1,9,10,29\) In the first part of the main study, 100 mg/kg propofol was combined with either medetomidine (0.1 mg/kg and 0.3 mg/kg) or fentanyl (0.1 mg/kg and 0.3 mg/kg). The combination of propofol with the higher dose of medetomidine provided smooth induction with rapid recovery after administration of atipamezole. Both propofol–medetomidine combinations yielded adequate muscle relaxation and hypnosis. The increase in the medetomidine dose from 0.1 mg/kg to 0.3 mg/kg decreased the induction time without increasing the recovery period. However, surgical anesthesia was difficult to accomplish with both propofol–medetomidine combinations and was achieved only briefly (less than 5 min) in the groups receiving the higher medetomidine dose (0.3 mg/kg).

Similar to effects previously reported in mice\(^2\) and rats,\(^4\) the additive or synergistic effect of propofol and opioids (such as fentanyl) used in the present study was insufficient to achieve acceptable surgical anesthesia. This combination failed to consistently eliminate the pedal withdrawal reflex, and the quality of surgical anesthesia was unsatisfactory due to excessive muscle tone and movement. In some animals, depth of anesthesia was very difficult to evaluate due to the severe muscle rigidity and spasms. Tail rigidity, limb shaking, and head scratching with the forefeet were observed in various animals from both propofol–fentanyl dose groups, thereby raising concerns regarding the rats’ wellbeing. The increase in the fentanyl dose from 0.1 to 0.3 mg/kg dramatically reduced the respiratory rate, with the occurrence of apnea after induction in some animals. In addition, abdominal movement during breathing was variably present and considered as respiratory depression.

In the second part of the main study, we tested the combination of propofol (100 mg/kg), medetomidine (0.1 mg/kg) associated with 2 different doses of fentanyl (0.1 mg/kg and 0.3 mg/kg). Combination of medetomidine and opioid drugs has been demonstrated to produce excellent sedation and anesthesia in dogs and rats.\(^31,23\) However, the large doses required can induce severe side effects like respiratory depression, marked polyuria, and long recoveries in rats.\(^23\) Previous studies in our laboratory showed that a combination of propofol, medetomidine, and fentanyl is an effective technique to anesthetize mice.\(^3\)

Fentanyl is a potent micro-opioid agonist that produces a rapid onset of analgesia and sedation with a brief (approximately 30 min) duration of action.\(^15\) Medetomidine is an \(\alpha\)2-agonist drug; some of its pharmacodynamic effects include hypothermia, hypertension, and cardiovascular depression.\(^32\) Transient hypertension usually occurs during the initial phase of medetomidine combination anesthesia due to the agents effect on peripheral \(\alpha\)2 adrenoceptors and is followed by hypotension and bradycardia.\(^30,31\) These effects may explain the lower pulse rates we saw associated with medetomidine when compared with propofol–fentanyl combinations. In addition, fentanyl can cause decreases in blood pressure and heart rate.\(^26\) Therefore, we chose the medetomidine dose of 0.1 mg/kg in combination with fentanyl, to avoid severe cardiovascular depression.

Both propofol–medetomidine–fentanyl combinations provided smooth induction of anesthesia with rapid recovery after administration of atipamezole. All animals in both dose groups achieved surgical anesthesia after 10 min, and the pedal withdrawal reflex remained absent in all rats until administration of atipamezole. The rapid recovery, adequate analgesia, and predictability of effects are major benefits of the propofol–medetomidine–fentanyl anesthetic protocol. Improvements in the quality of anesthesia are essential for animal wellbeing, experimental standardization, and limiting postanaesthetic morbidity associated with hypothermia, pain, and cardiorespiratory depression.

In conclusion, here we found that a freshly prepared combination of propofol–medetomidine (100 mg/kg + 0.3 mg/kg) administered intraperitoneally provided suitable restraint for nonpainful procedures for at least 30 min. To provide surgical anesthesia, intraperitoneal administration of a combination of propofol, fentanyl, and medetomidine (100 mg/kg + 0.1 mg/kg + 0.1 mg/kg) is a safe, easy, and reversible technique for anesthetizing rats. This dosage combination provides 25 to 30 min of surgical anesthesia and more than 30 min for restraint, with rapid recovery from anesthesia. The durations of restraint and surgical anesthesia in the current study potentially were shortened by use of the reversal agent.

References