Anesthesia in experimental animal surgery

U. Windberger, DVM, BSc
Department Biomedical Research
MedUni Wien
Basically:

- Sedation
- Analgesia
- Relaxation
Basically:

- Volatile Anesthetics
- TIVA
- Combinations
What else?

- Artificial ventilation (O₂ vs. CO₂)
- Intravenous infusion regime
- Acid-base balance
- Temperature (not > Δ1°C)
- Hemodynamics
Ventilation

- **Supporting spontaneous breath:**
  - CPAP/PEEP (FRC increased)
  - SIMV (Seufzer)

- **Substituting spontaneous breath:**
  - Controlled ventilation
    - Volume controlled
    - Pressure controlled
  - High Frequency Ventilation, HFV (ARDS, at high CO₂)

- **Mixed forms of ventilation**
  - Biphasic positive airway pressure, BIPAP
## Fluid balance (1)

<table>
<thead>
<tr>
<th>Fluid input</th>
<th>Fluid output</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Ringer’s solution, saline</td>
<td>- Urine</td>
</tr>
<tr>
<td>- HES, Dextrane</td>
<td>- Bleeding</td>
</tr>
<tr>
<td>- Blood transfusion</td>
<td>- Drain</td>
</tr>
<tr>
<td>- Diverse short infusions</td>
<td>- Blood samples</td>
</tr>
</tbody>
</table>

- Breathing
- Saliva (ruminants)
Fluid balance (2)

Basis: 10 mL/kg/h Ringer’s lactate + potassium, starting with 15 mL/kg/h

Restoration of volume (slowly), Dextran, Hämaccel, HES

warmed
Blood

- Slowly, warmed blood, catheter with big lumen (not via venflon)
- (20 mval Ca\textsuperscript{++} per 500 mL blood!!)
  - Autologous whole blood, max 3 weeks, coll storage (post transfusion lung, hepatitis)
  - Autologous blood from Cell-Saver
  - Homologous blood (twins, sheep, rodents, rabbits)
  - Frozen autologous plasma
  - Humane albumine

- Transfusion reaction: treatment
  - Volume
  - Oxygen, controlled ventilation
  - Corticosteroids
  - Stabilize blood pressure
  - NaHCO\textsubscript{3}
  - Heparine
  - Diuretics

- Avoid bleeding during surgery
  - Training
  - Controlled hypotension
  - Acute normovolämic hemodilution
Acid-base balance

- BGA (0.7 ml blood / 0.2 ml blood in capillary)

- Metabolic acidosis: BE x kgBW/4 mval NaHCO₃

- Metabolic alkalosis: BE x kgKG/4 mval Lysin.HCl

- Respiratory acidosis: elevate tidal volume

- Respiratory alkalosis: decrease tidal volume
Necessary preparations

- Fasting depends on species and experiment
- Always water ad lib.
- Bedding for thermoregulation
- preOP und postOP individual housing with contact to other animals
- Shaving, cleaning of skin, fur, claws

- Conditioning on specific manipulations postOP (personal, measuring instruments, treadmill)
Premedication (1)

- Premedication is species specific
- Depends on animal type and temperament, feasibility of venous cannulation in the conscious animal
Premedication (2)

- Benzodiazepines
  - Midazolam
  - Diazepam

- Barbiturates
  - Thiopentone

- Neuroleptics
  - Promazin
  - Butyrophenone

- Dissociative anesthetics
  - Ketamine in combination with Xylazin

- Analgetics
  - Opiates not alone for premedication

- Anticholinergics
  - Atropine only for ruminants (saliva)
Start

- Measure body weight
- Premedication i.m. or s.c.
- Animal on the table
- Ear vein cannulation
- Application of pharmacon until loss of consciousness
- Orotracheal intubation
- Eye ointment
- Fixation
- Gastric tube, bladder catheter, rectal temperature probe
- ECG
- Thermoregulation
- Preparation of skin for surgery
Intubation rat
Intubation rat
Rat ventilated
Rat, tail vein
Rat preOP
Intravenous anesthesia

- TIVA: each species (except mice)
  - pro: good adjustment (Propofol), use of Ketamine to avoid hypotension
  - contra: in rodents cannulation of a vein might be problematical
or volatile anesthesia

- Useful for each species
- 1-2 Vol% (closed system)
  - pro: good adjustment
  - contra: decrease of blood pressure
- Problematic during electrophysiologic measurements
Anesthetics (1)

- Benzodiazepines: premedication and TIVA
- Opiates: always
- Ketamine, Xylazin: premedication and TIVA
- Propofol: TIVA
- Barbiturates: premedication
- Relaxants: if needed
- Volatile: Isoflurane
Anesthetics (2)

- **Benzodiazepines**
  - Not alone for surgery!
  - Anticonvulsant, anxiolytic, paradox reaction
  - Minor respiratory depression when given alone
  - Respiratory depression when given with opiates
  - No major influence on cardiovascular system

- **Opiate**
  - Respiratory depression
  - Brain perfusion decreases
  - Anti-stress
  - Hypotension, venous pooling
  - Histamine release
  - Take care of drug half-life in case of antagonisation
Anesthetics (3)

- **Ketamine**
  - Analgesia, amnestic (catalepsy)
  - Increase of brain pressure!
  - Emergency drug (limited respiratory depression)
  - Increase of blood pressure (systemic and pulmonal)
  - Pos. chronotropic – sympathomimetic
  - Pos. inotropic – cardiac output increases
  - Cardiac work load increases

- **Xylazine (α2-agonist)**
  - Sedating, hypnotic, relaxant
  - Potentiates Ketamine
Anesthetics (4)

- **Barbiturates**
  - Take care of respiratory depression
  - Decreases brain pressure
  - Neg. inotropic
  - Decreases blood pressure and preload
  - Reflectory tachycardia, VPCs

- **Propofol**
  - No analgesia
  - Decreases brain perfusion and $O_2$-consumption in brain
  - Neg. inotropic
  - Decreases blood pressure
  - Brady- or tachycardia
Volatile anesthetics

- Isoflurane
  - brain
    - Spasms (ton.-clon.), O$_2$-consumption decreased, dilates brain vessels (metabol. coupling deranged, ischemic regions?), brain pressure relatively stable
  - Cardiovascular system
    - VPCs, neg. inotropic, cardiac filling pressures increase, coronary dilatation (shunt, steal)
    - Direct action on vascular wall + autonomic NS, hypotension,
  - Lung
    - FRC decreases, death space increases, HPV diminished (shunt)
  - Kidney
    - GFR decreases, nephrotoxicity (fluoride),
  - Splanchnic compartment
    - Liver perfusion decreases, hepatotoxicity of Halothane
Typical combinations

- **Ruminants**
  - Atropine (1mg i.m.)
  - Thiopentone 15 mg/kg i.v. bolus
  - Fentanyl 0.1 mg/kg i.v. bolus
  - Fentanyl bypass: 0.01 mg/kg/h
  - Propofol bypass: 10 mg/kg/h
Typical combinations

- Pig
  - No atropine!!!
  - 20 mg/kg Ketamine + 1.76 mg/kg Acepromazin i.m.
  - Thiopentone 15 mg/kg i.v. bolus
  - Fentanyl 0.1 mg/kg i.v. bolus
  - Fentanyl bypass: 0.016 mg/kg/h
  - Propofol bypass: 10 mg/kg/h
Pig intubated
Pig: ear artery for pressure monitoring and blood gas
Typical combinations

- **Rabbit**
  - 25 mg/kg Ketamine + 2 mg/kg Xylazin i.m.
  - 50 mg Ketamine + 2 mg Xylazin ad 5 ml NaCl
  - Ketaminebypass: 60 mg/kg/h
  - Fentanylbypass: 0.15 mg/kg/h; Fentanylbolus: 0.025 mg
  - Or: Xylazinbypass: 2 mg/kg/h
  - If necessary Isoflurane
Rabbit: ear vein and ear artery
Rabbit intubation
Typical combinations

- Rat
  - 100 mg/kg Ketamine + 5 mg/kg Xylazin i.p.
  - 0.6-1 Vol% Isoflurane
  - 50 mg/kg Thiopentone i.p.
Typical combinations

- **Mouse**
  - 100 mg/kg Ketamine + 10 mg/kg Xylazin i.p.
    - 1 ml Ketamin® + 0.1 ml Rompun® ad 10 ml saline: give 0.1 ml per 10 g mouse.
    - Re-dosing is done using a forth of the dose to effect
Monitoring during anesthesia

- Minimum requirement (except mouse)
  - ECG
  - ETCO\(_2\)
  - Inspiratory pressure
  - Body temperature
  - Clinical examination!

- Long-term surgery
  - Arterial blood pressure (invasive)

- If necessary
  - CVP, PAP, PCWP, CO
Monitoring during anesthesia

- Blood gas
  - arterial: \(\text{paCO}_2\), pH, \(\text{HCO}_3\), \(\text{O}_2\)-sat, \(\text{paO}_2\)
  - venous: \(\text{O}_2\)-sat, pH, BE
- Electrolytes
  - K, Na, Ca,
- Substrates
  - glucose, lactate
Anticoagulation

- Heparin i.v. (low MW)
  - Total anticoagulation (HLM): 300 IE/kgBW i.v.
  - postOP anticoagulation: 30 IE/kgBW i.v. every 8-12 hrs.

- Lovenox s.c. (large animals)
  - 40 mg twice daily

- Protamin: to antagonize heparin
  - Take care of blood pressure decrease! Same amounts of units as heparin. Start with half of dosis
End of anesthesia

- Stop bypasses and volatile anesthetics
- Criteria for extubation
  - Spontaneous breaths against 10 mmHg
  - $\text{SaO}_2 > 95\%$ at $\text{FiO}_2 0.3$; $\text{paO}_2 > 70$ mmHg
  - $\text{paCO}_2 < 45$ mmHg
- Warm up (Bair-Hugger)
- Suction from intratracheal tube
- Silence
- Eyelid reflex positive
- Start postoperative therapy against pain
- Start postoperative management against stress in pigs to prevent overheating
Postoperative therapy

- i.v.-infusions
- Oxygen via mask
- Warm up or cool down (pigs)
- Antibiotics (start preOP, follow 3 days)
- Smooth bed made of bedding material
- **Personal care!!!**
Postoperative analgesia

- Cave: respiratory depression
  - Sufficient spontaneous breaths
  - Start as early as possible
  - Control the animal
    - Animals does not eat
    - Animal has buckled back
    - Respiration is accelerated
    - Pulse/heart frequency is accelerated
    - movements
    - Loss of body weight (chronic pain/distress)
Postoperative analgesia

■ Opiates
  ■ Bolus s.c. oder i.m. (during the night!)
    • Buprenorphin each 4-8 hrs.
    • Piritramid each 6-8 hrs.
  ■ Via drinking water (rodents)
    • Piritramid ad lib.

■ Ketamine
  ■ i.v. bypass

■ Nonsteroid antiphlogistics
  • Metamizol each 8 hrs.
THANK YOU!