

Administration of analgesia with the food: a step forward in refining surgery in embryo transfer

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INTRODUCTION

Embryo transfer (ET) is a widely used procedure in transgenic mice technology and it is also used to reestablish pathogen-free stocks of mice. The ideal analgesic regime for this technique would safely manage pain in the female without adversely affecting the quality or number of offspring from implanted embryos. Studies to date have found no effect on buprenorphine, AINEs or multimodal analgesia in number of embryos surviving after ET in a single postsurgical subcutaneous injection (Parker, 2011). However most of those drugs have effect just during 8-12 hours and repeated injections are needed to maintain effective therapeutic levels.

Surgery and subcutaneous injection of analgesia

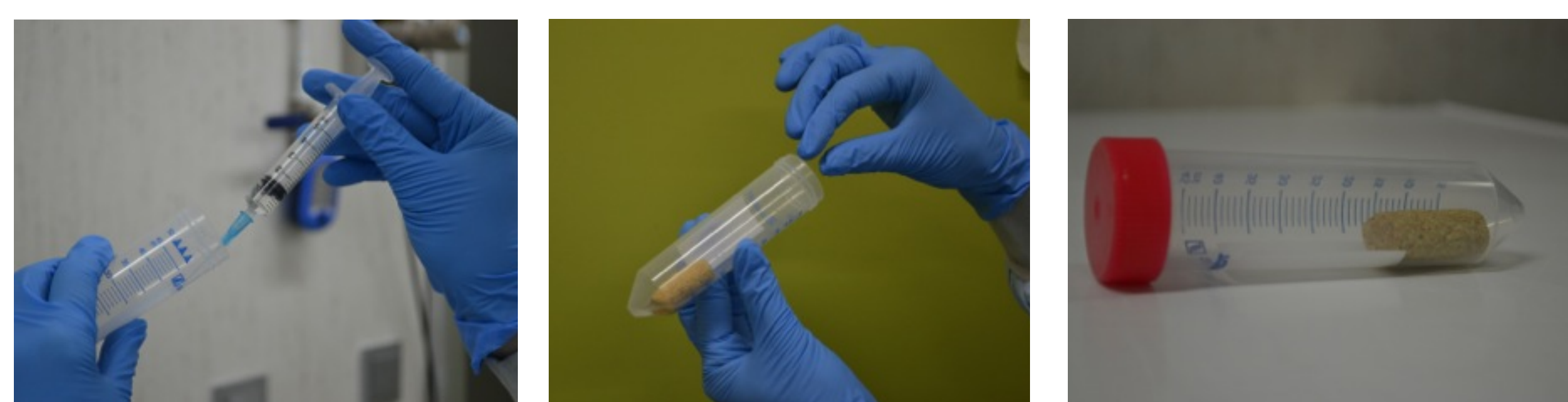


AIMS

The aim of this study was to explore if a recently described method of administering buprenorphine with the diet (Molina-Cimadevila, 2014), offers a potential treatment option in complementing the pain management of embryo-transferred females.

We also explored the embryo survival ratios comparing to common anesthetics used in ET: ketamine + xylazine and avertine

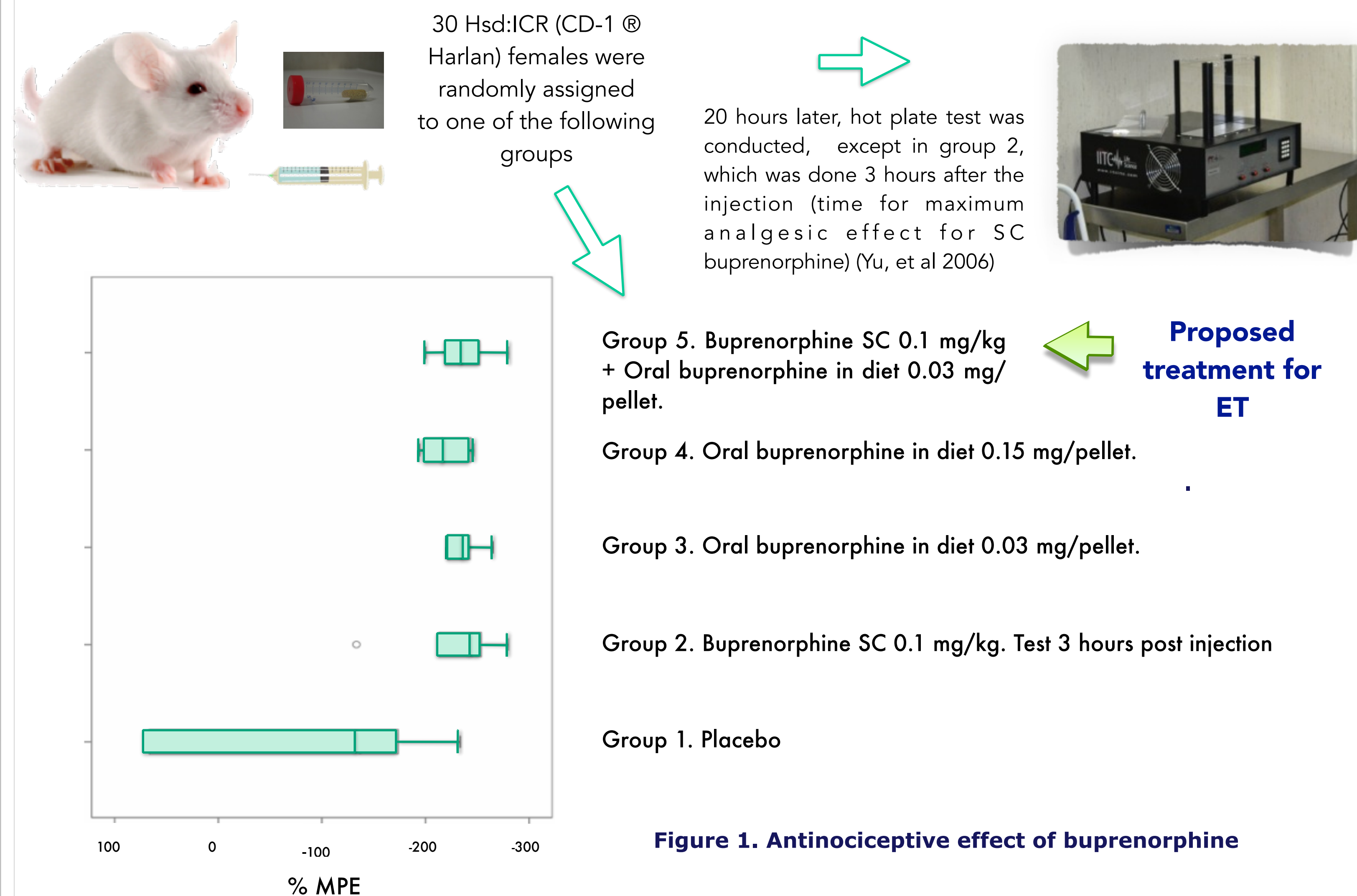
METHODS AND RESULTS



Medicated pellets were prepared with 2919 Teklad Global 19% Protein Extruded Rodent Diet (Harlan®) This diet is quite porous and may be easily mixed with liquids. 1ml of a 1:10 dilution of buprenorphine (Buprex®) in glucosaline (0.03 mg/ml) was mixed with each pellet of diet as shown in the pictures, so each pellet contained 0.03 mg of buprenorphine. Placebo pellets were prepared the same way using just 1 ml of glucosaline.

Mice were fed only with medicated pellets for two days after surgery (1 pellet/mice). The pellet was placed inside the cage, in order to facilitate the access to the food.

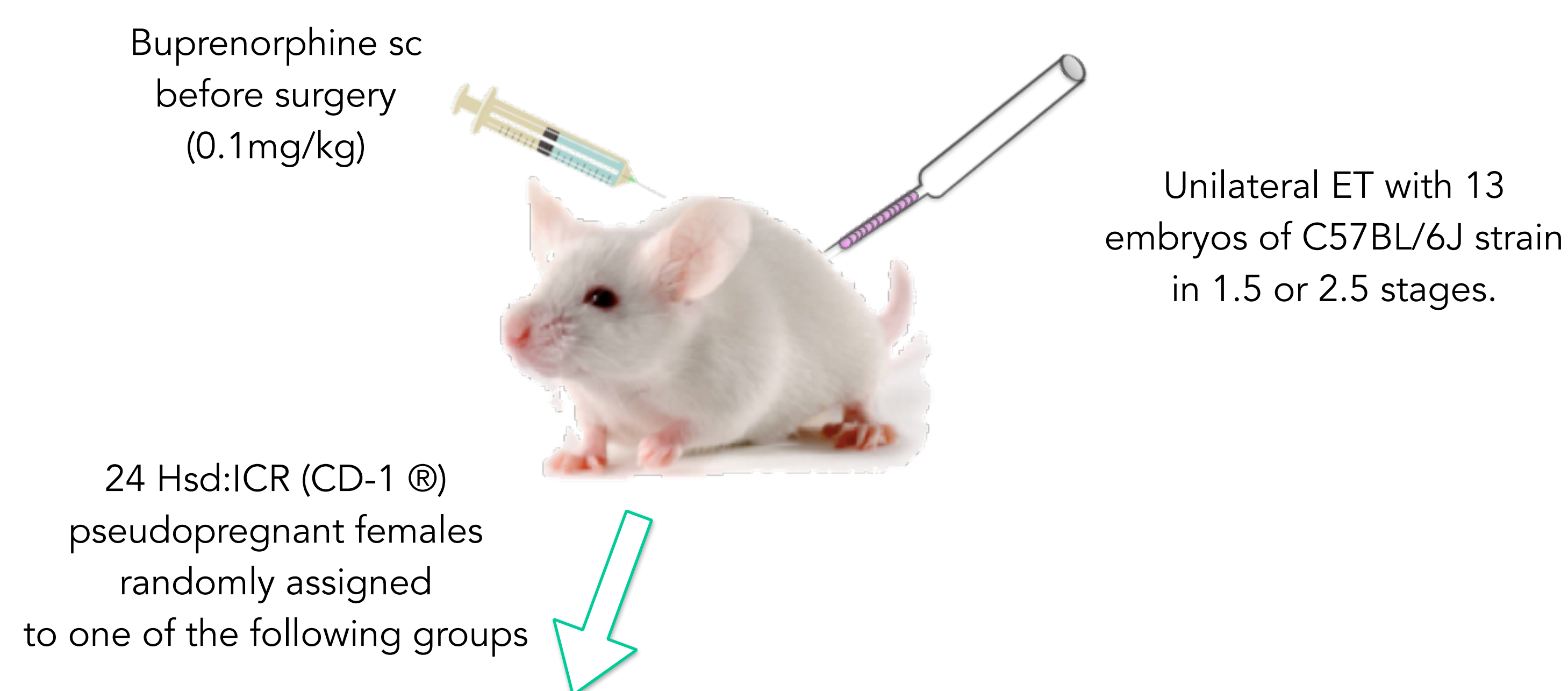
DOES IT PROVIDE POSTOPERATIVE ANALGESIA?



Percentage of maximal possible effect (%MPE) in hot-plate test for each treatment group is represented in the figure. The overall difference in relative paw withdrawal response between placebo and every of the other treatments was statistically significant (Mann-Whitney's U test, $P < 0.05$ for each one). No significant differences (Mann-Whitney's U test, $p = 0.8$, $p = 0.3$ and $p = 0.9$ for group 2 compared with groups 3, 4 and 5 respectively) were found between the group of buprenorphine sc at 3 hours (group 2) and the rest of the groups where oral buprenorphine was provided.

Buprenorphine administrated in the diet provides equivalent analgesia to subcutaneous injection at the point of maximum effect

DOES IT AFFECT EMBRYO SURVIVAL RATIOS?



	Avertine	Ketamine + Xylazine
Oral buprenorphine	n=6	n=6
Placebo	n=6	n=6

Table 1. Group distribution

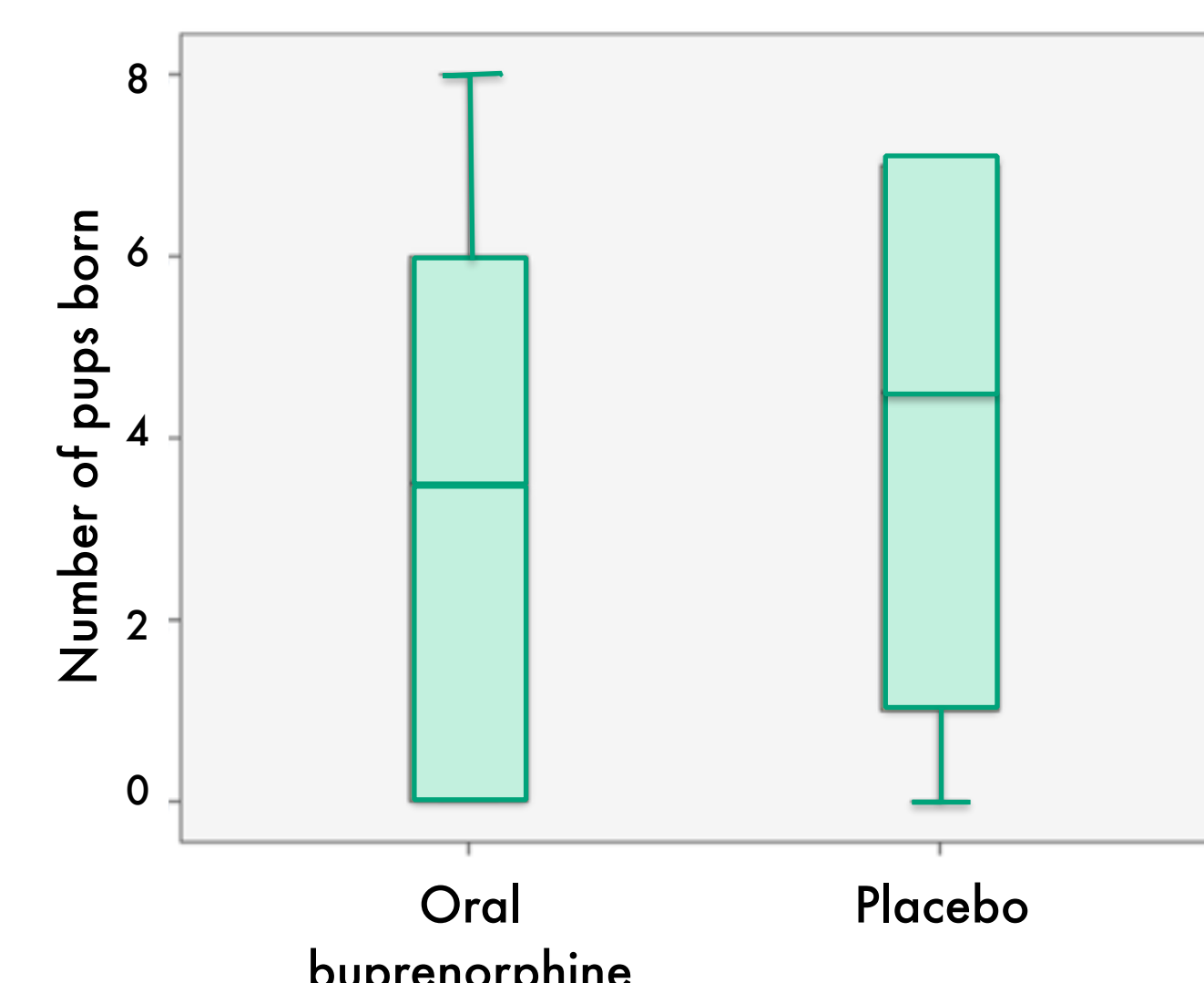


Figure 2. Number of pups born depending on analgesia

No significant differences (Mann-Whitney's U test) were found between the groups

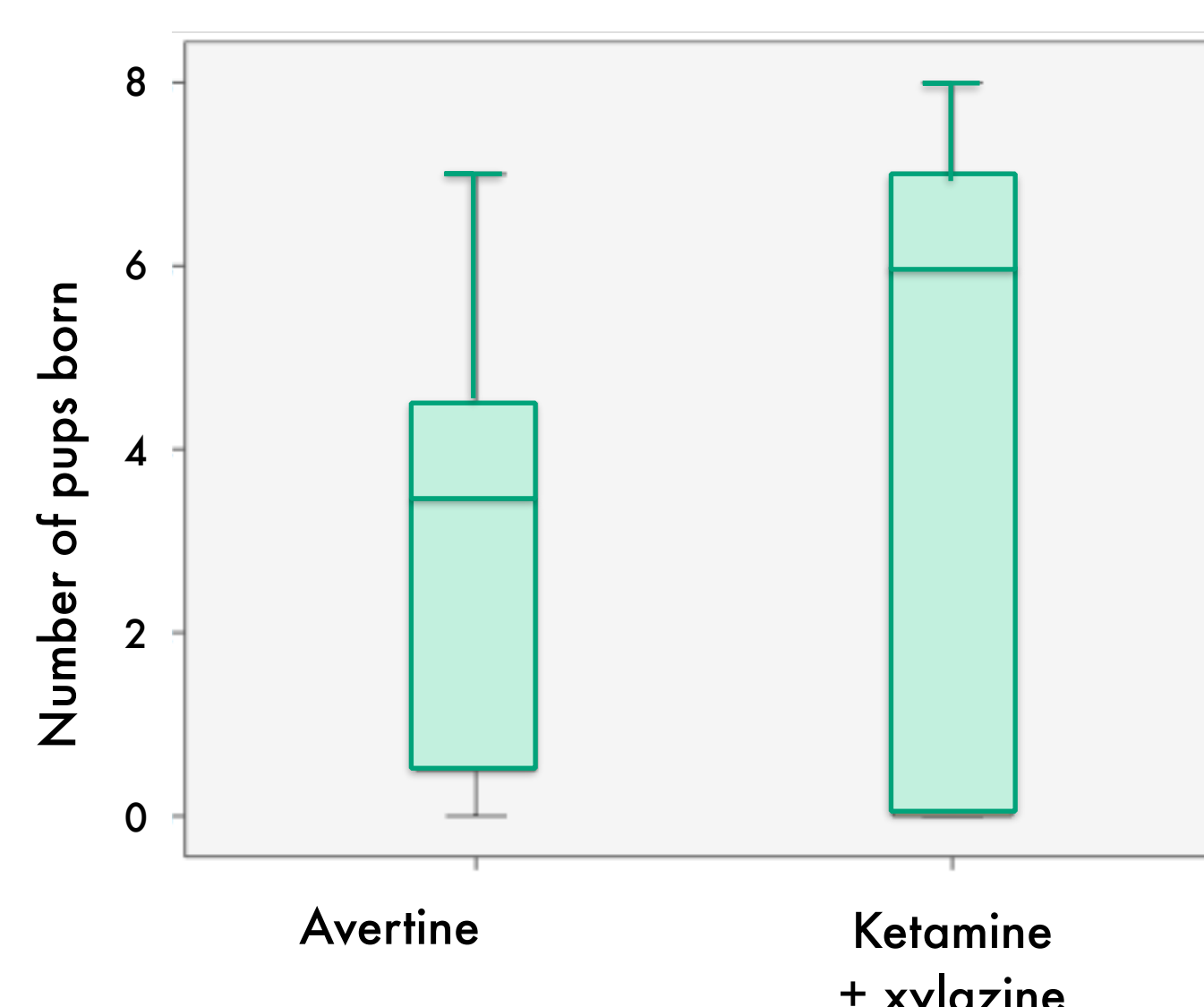


Figure 3. Number of pups born depending on anesthesia

No significant differences (Mann-Whitney's U test), were found between the groups

	Day 1	Day 2
Oral buprenorphine	2,42 +/- 1,17	4,32 +/- 0,37
Placebo	2,81 +/- 1,18	4,22 +/- 0,45

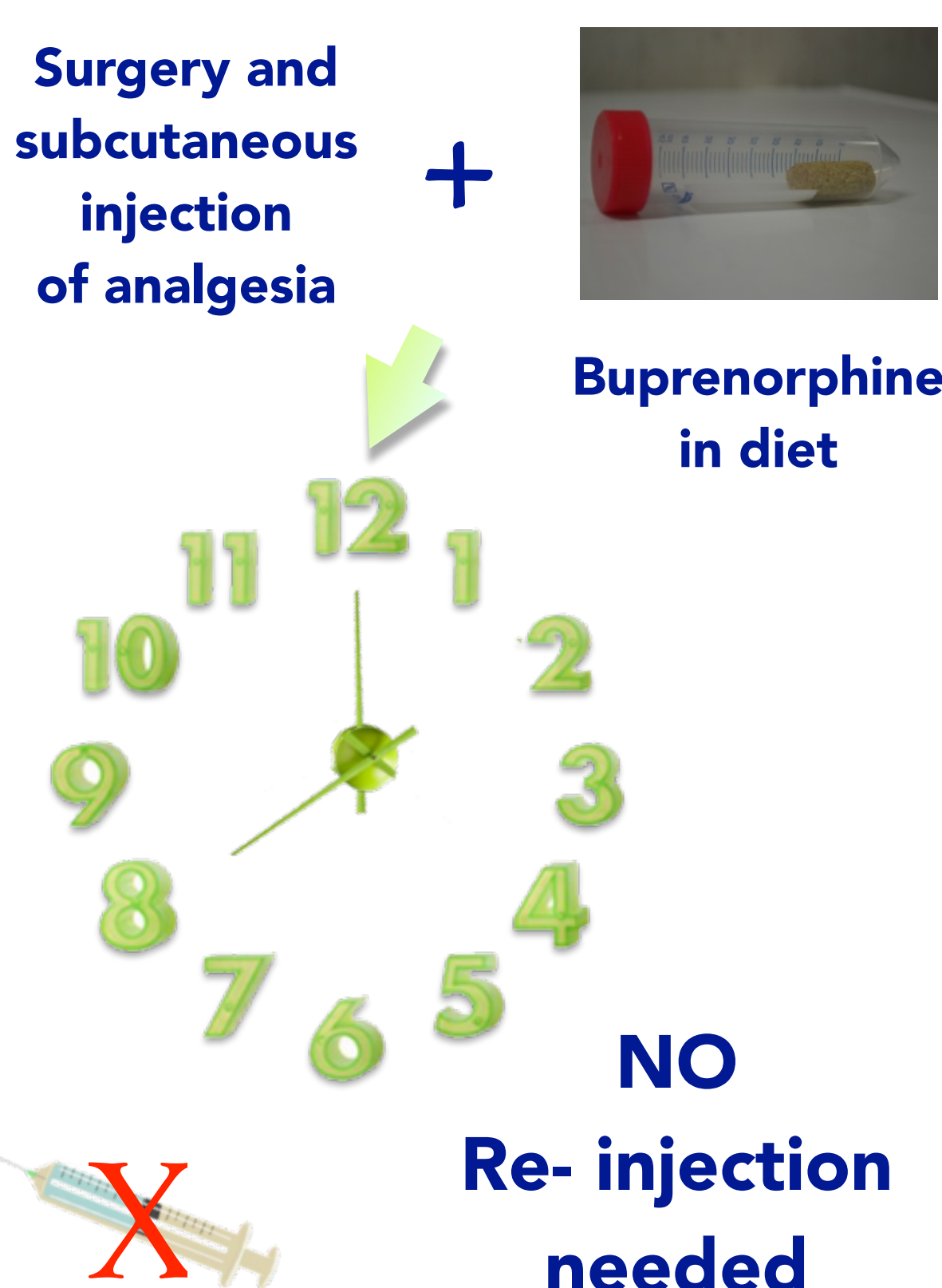
Table 2. Food consumption after surgery (g)

The average dose of buprenorphine that mice ate in voluntary ingestion was 0,55 +/- 0,28 mg/kg for day 1 and 1,03 +/- 0,1 mg/kg for day 2. Media +/- standard deviation

CONCLUSION

Diet with buprenorphine can be easily added after a standard anesthetic and analgesic procedures in embryo transfer, does not affect birth rates and improves analgesia of embryo-transferred females and thus wellbeing.

NO PAIN



Neither the analgesic regime nor the anesthesia significantly affected the number of pups born.