Anesthesia of five captive amur tigers (*Panthera tigris altaica*) with a medetomidine-ketamine combination

Anesthesie van vijf amurtijgers (Panthera tigris altaica) met een combinatie van medetomidine en ketamine

[1]B. Alonso, [2]T. Bouts, [1]F. Gasthuys, [1]S. Schauvliege

[1]Department of Large Animal Surgery, Anesthesia and Orthopedics, Faculty of Veterinary Medicine, Ghent University, 9820 Merelbeke, Belgium
[2]Pairi Daiza SA, 7940 Domaine de Cambron Brugelette, Belgium

Bruna.alonso@ugent.be

ABSTRACT

Five adult healthy captive male amur tigers were anesthetized using a combination of medetomidine (0.03 mg/kg) and ketamine (2.5 mg/kg) target doses. After darting, the mean time to decubitus was 5 ± 1 minutes and to approach 13 ± 2.4 minutes. The time between approaching and the end of the procedure was 16.2 ± 3.3 minutes, and between darting and administering the antagonist 32.8 ± 4 minutes. After administration of atipamezole (0.08 mg/kg IV), the mean time to regain sternal recumbency was 9.4 ± 4.6 minutes and to stand 23 ± 11.4 minutes. Medetomidine in association with ketamine in single-dart injection produced fast and safe chemical restraint in the healthy tigers. Partial reversal with 15 mg of atipamezole IV resulted in a short recovery duration without obvious side effects.

SAMENVATTING

Vijf gezonde, mannelijke, in gevangenschap levende amurtijgers werden met een verdovingsgeweer onder anesthesie gebracht met medetomidine (0,03 mg/kg) en ketamine (2,5 mg/kg) gedoseerd op geschat lichaamsgewicht. De gemiddelde tijd tot decubitus was 5 ± 1 minuten en tot benaderen 13 ± 2,4 minuten. De tijd tussen het benaderen en het einde van de procedure was 16,2 ± 3,3 minuten en de tijd tussen de injectie van de anesthetica en de antagonist bedroeg 32,8 ± 4 minuten. Respectievelijk 9,4 ± 4,6 minuten en 23 ± 11,4 minuten na de injectie van atipamezole (0,08 mg/kg IV) lagen de dieren terug sternaal en stonden ze op. Medetomidine en ketamine gecombineerd in één pijltje resulteerden in een snelle en veilige immobilisatie van de gezonde tijgers. Partiële antagonisatie met 15 mg atipamezole IV resulteerde in een korte recoveryduur zonder duidelijke nevenwerkingen.

INTRODUCTION

Wild felids are often anesthetized for different reasons, such as microchipping, collection of blood samples, collaring, physical examination, administration of medication or surgical procedures. Large felids are dangerous animals, which makes an efficient anesthetic protocol essential to guarantee the safety of the personnel involved, as well as the safety of the patient. Many drug combinations have been used to anesthetize exotic felids, and the choice of the protocol depends on the personal experience, availability of drugs, costs, type of procedure and health status of the animal (Ramsay, 2014).

In tigers, the most often described combination is ketamine associated with an alpha$_2$ agonist such as xylazine (Allwin et al., 2018; Goodrich et al., 2001; Larsson et al., 2008; Sontakke et al., 2009), medetomidine (Forsyth et al., 1999; Miller et al., 2003; Zeiler et al., 2013) or dexmedetomidine (Cesare et al., 2018; Clark-Price et al., 2015). Combinations of ketamine with midazolam and an alpha$_2$ agonist have also been reported (Clark-Price et al., 2015; Curro et al., 2004; Reilly et al., 2014; Smith et al., 2018). Tiletamine,

another dissociative agent, in combination with zolazepam, has also been described in tigers, as sole agents (Seidensticker et al., 1974) or in combination with medetomidine (Lewis et al., 2014), detomidine (Laricchiuta et al., 2014) or xylazine (Mercado et al., 2020).

All these different protocols were considered efficient and safe for use in tigers by the authors, but some side effects have occasionally been observed, such as cyanosis and multifocal premature ventricular contractions with medetomidine and ketamine (Forsyth et al., 1999), seizures with ketamine and xylazine (Goodrich et al., 2001), or ketamine and dexmedetomidine (Clark-Price et al., 2015), and pronounced ataxia with detomidine in association with tiletamine and zolazepam (Laricchiuta et al., 2014). Tiletamine and zolazepam have traditionally been considered contraindicated in tigers due to anecdotal reports of ataxia and death within two days; however, in the literature, there are no original articles supporting these findings (Kreeger and Armstrong, 2010).

There is little information regarding anesthesia induction and recovery times with the different described protocols, or the effect of alpha$_2$ antagonists such as yohimbine or atipamezole to reverse xylazine or medetomidine in tigers. The aim of this report is to describe a short anesthesia procedure with medetomidine and ketamine in five amur tigers, and the effect of partial reversion with atipamezole at the end of the procedure.

CASE DESCRIPTION

Five adult healthy captive male amur tigers (*Panthera tigris altaica*) were anesthetized for elective orchiectomy. They were housed alone in separate cages the day before, and food and water were withheld 12 hours before the procedure. The anesthetic protocol consisted of medetomidine (Domitor, Orion, Finland, manipulated by a local pharmacy to 30 mg/ml concentration) at a target dose of 0.03 mg/kg combined with ketamine (Nimatek 10%, Dechra, UK) at a target dose of 2.5 mg/kg, in a single intramuscular dart injection using a CO_2 rifle (Dan Inject JM St, Denmark). The weight of the tigers was estimated by an experienced zoo veterinarian, since a scale was not available to weigh the animals during the procedure.

The tigers were darted in the hindlimb region from an average distance of six meters using 3.5 bar pressure. The dart was prepared with a total dose of 5.4 mg of medetomidine, and 450 mg ketamine (total volume 4.68 ml in a 5 ml dart) coupled to a non-barbed metallic needle 25 x 2 mm size. After injection, the time from darting to the first effect of sedation, approach and start of surgery were recorded. Once the tigers were recumbent, the anesthesia level was assessed by stimulating the head and ears with a metal stick through the bars of the cage. If no response to the stimuli was observed, the cage was opened and the animals were approached.

The trachea of the tigers was intubated through the mouth with an endotracheal silicone tube (Kruuser, Denmark) with an internal diameter of 16 or 18 mm, which was connected to an anesthetic breathing circuit (Narcose Spiromat 656, Dräger, Germany). A 100% oxygen flow was delivered at 3 L/min, and the animals were allowed to breathe spontaneously. Isoflurane (Isoflo, Zoetis, Belgium) was added with an out-of-circuit vaporizer (Drägerwerk AG, Germany) if necessary. The monitoring during anesthesia consisted of a pulse oximetry sensor placed on the tongue, electrocardiography, non-invasive arterial pressure with a cuff (adult size, 25 to 35 cm circumference) placed around the metatarsus, and inspired and expired concentrations of carbon dioxide measured with a multiparameter monitor (D-LCC15-03; Datex Ohmeda, OR, USA).

At the end of the surgical procedure, meloxicam (Metacam 2%, Boehringer Ingelheim, Germany) at a target dose of 0.2 mg/kg IV, amoxicilline (Duphamox 15%, Zoetis, Germany) at a target dose of 6.6 mg/kg subcutaneously, and atipamezole (Antisedan 0.5%, Zoetis, Belgium) at a target dose of 0.08 mg/kg IV were administered. Extubation was performed immediately after the atipamezole administration, and the recovery was observed until the animals returned to a standing position. The times from atipamezole injection until sternal and standing position were recorded, as well as the times between darting and atipamezole administration.

RESULTS

The mean age was 2.3 ± 0.3 years, and the weight was estimated to be around 180 kg. After darting, the mean time to the first effect of sedation was 3.4 ± 1.8 minutes (range = 1-6 minutes), to decubitus 5 ± 1 minutes (range 4-6 minutes), and to approach 13 ± 2.4 minutes (range = 10-16 minutes).

For the first three tigers, isoflurane was administered during the procedure with the vaporizer opened at 1.5%, but since the mean duration of surgery was short, for the last two tigers it was decided that supplemental anesthesia with isoflurane was not necessary. The mean physiologic parameters heart rate (HR), systolic, mean and diastolic blood pressure (SAP, MAP and DAP), end tidal carbon dioxide tension ($EtCO_2$), peripheral saturation of oxygen (SpO_2) and temperature (T) are described in Table 1.

The time between approaching and the end of the procedure was 16.2 ± 3.3 minutes (range = 13-20 minutes), and between darting and administering the antagonist 32.8 ± 4 minutes (range = 26-36 minutes). After administration of atipamezole, the mean time to regain sternal recumbency was 9.4 ± 4.6 minutes (range = 5-15 minutes), and to stand 23 ± 11.4 min-

Table 1. Mean physiological parameters of five adult amur tigers *(Panthera tigris altaica)* during anesthesia with medetomidine 0.03 mg/kg and ketamine 2.5 mg/kg. Mean values represented as mean ± standard deviation. Missing values were not recorded during the anesthesia.

	HR	SAP	MAP	DAP	$EtCO_2$	SpO_2	T
Tiger 1	75	197	146	139	71	98	36
Tiger 2	86	182	150	131	68	98	
Tiger 3	66	177	145	127	61		37
Tiger 4	87	200	152	133	53	98	
Tiger 5	64	200	169	159		90	36
Mean	76 ± 11	191 ± 11	152 ± 10	138 ± 13	63 ± 8	96 ± 4	36 ± 0,4

HR = heart rate (beats/min); SAP, MAP and DAP = systolic, mean and diastolic arterial pressure (mmHg); $EtCO_2$ = End tidal CO_2 (mmHg); SpO_2 = peripheral saturation of oxygen (%); T= temperature (°C).

utes (range = 11-40 minutes). No side effects such as excitation or seizures were observed, and all recoveries were considered smooth.

DISCUSSION

The administration of medetomidine in association with ketamine in a single intramuscular injection provided chemical restraint in adult tigers within maximum six minutes after darting. Similar induction times (ranging from 3 to 12 minutes) have been observed in other reports using the same combination (Forsyth et al., 1999; Miller et al., 2003; Zeiler et al., 2013). Ketamine (2.2 to 10 mg/kg) combined with xylazine (0.3 to 1.3 mg/kg) appears to provide a slightly longer induction time (ranging from 14 to 27 minutes) (Seal et al., 1987; Sontakke et al., 2009). Clinical doses of xylazine require a higher volume compared to medetomidine, making the administration with ketamine in single dose difficult. The need for more injections prolongs the process of inducing anesthesia and can be disadvantageous since it potentially increases stress for the animal.

Single injection of higher doses of medetomidine (0.05 mg/kg) in combination with midazolam (0.1 mg/kg) have also been reported to provide deep sedation and decubitus within eight minutes (Curro et al., 2004). In a report by Clark-Price (2015), dexmedetomidine 0.025 mg/kg or dexmedetomidine 0.0125 mg/kg in association with midazolam 0.1 mg/kg had similar sedative properties, with decubitus within 15 minutes after administration. After decubitus was obtained, ketamine was administered by hand or pole syringe injection in both reports.

Seizure-like behavior has been observed when combining higher doses of ketamine (10 mg/kg) with xylazine (0.8 mg/kg) (Goodrich et al., 2001) or with xylazine (0.5 mg/kg) and midazolam (0.1 mg/kg) (Curro et al., 2004). Seizures have also been reported after administration of ketamine (3 mg/kg) in combination with dexmedetomidine (0.025 mg/kg) (Clark-Price et al., 2015) or higher doses of tiletamine/zolazepam (7.7mg/kg) (Seidensticker et al., 1974). In the literature, there are no reports of seizures using the combination medetomidine-ketamine. This combination appears to be relatively safe in tigers, but electrocardiographic changes in T waves polarity, suggestive of myocardial hypoxia, have been detected in tigers and lions after the administration of a medetomidine-ketamine-midazolam protocol. An increased plasma potassium concentration (6.5 mmol/ml) has also been detected in one tiger (Reilly et al., 2014). Similar changes in T waves polarity during electrocardiography have also been detected in tigers during xylazine-ketamine anesthesia (Larsson et al., 2008).

Therefore, caution can be advised when administering medetomidine-ketamine to tigers suffering from previous illness. Harmful side effects such as severe cardiopulmonary depression after the administration of 0.03 mg/kg medetomidine and 2.35 mg/kg ketamine have been observed in a tiger with a history of a two-weeks' regurgitation (Forsyth et al., 1999), and persistent bradycardia and hypotension after 0.025 mg/kg medetomidine and 4 mg/kg ketamine in two cubs suffering from severe hyperparathyroidism (Zeiler et al., 2013).

Tiletamine-zolazepam is another combination reported in tigers. The mean time to induction of anesthesia with tiletamine-zolazepam (1.0 – 1.8 mg/kg) combined with detomidine (0.02 – 0.04 mg/kg) or xylazine (0.5 – 1 mg/kg) ranged on average from 3 to 20 minutes after darting, slightly longer than induction times reported with medetomidine-ketamine protocols. Some side effects have also been observed using tiletamine-zolazepam in tigers, such as pronounced ataxia during the recovery period after its administration in association with detomidine (Laricchiuta et al., 2014). A prolonged and difficult recovery over a 48-hour period has also been observed in one tiger after a higher dose of tiletamine-zolazepam (5.6 mg/kg) (Lewis et al., 2014). In the present study, ataxia was not observed and all tigers had a smooth recovery, similar to previous reports using the same drug combination (Miller et al., 2003) or a xylazine-ketamine combination (Sontakke et al., 2009).

Standardized ranges of physiological parameters

for tigers during anesthesia have not been established. However, the values for HR, SAP, MAP, DAP and SpO_2 observed in this study had a similar range to the range in previous reports in tigers anesthetized with a combination of $alpha_2$ agonists and ketamine (Curro et al., 2004; Miller et al., 2003; Sontakke et al., 2009). No harmful side effects were observed during anesthesia in the present study. High values were observed for arterial pressure, probably due to peripheral vasoconstriction mediated through the action of medetomidine on intravascular alpha receptors (Virtanen, 1989).

In the present study, all tigers maintained the values for SpO_2 (96 ± 4%) and $EtCO_2$ (63 ± 8 mmHg) within an acceptable range, without the need for mechanical ventilation. It is important to stress the fact that the tigers were intubated and a flow of 100% oxygen was provided. A great concern during immobilizations, especially in the wild, is the respiratory depression/arrest that can be caused by $alpha_2$ agonists. Mild hypoxemia was observed after administration of medetomidine or dexmedetomidine combined with ketamine and midazolam in tigers when oxygen suplementation was not available (Clark-Price et al., 2015; Curro et al., 2004).

In the literature, there are a few reports about the effects of $alpha_2$ antagonists in tigers. Administration of yohimbine (0.1 to 0.15 mg/kg IV) 20 to 40 minutes after induction of anesthesia with xylazine (0.4 – 1.3 mg/kg) and ketamine (2.6 - 4.5 mg/kg) shortened recovery duration to three to eight minutes compared to over 60 to 70 minutes of spontaneous recoveries (Seal et al., 1987; Sontakke et al., 2009). Atipamezole at a mean dose of 0.13 ± 0.014 mg/kg IM administered 59 to 232 minutes after a medetomidine (0.025 mg/kg)-ketamine (1.66 mg/kg) protocol in tigers provided sternal recumbency 14 ± 6 minutes after intramuscular administration (Miller et al., 2003). Excitation during recovery has been reported after administration of 10 mg atipamezole (5 mg IV and 5 mg IM) in an adult tiger thirty minutes after ketamine (2.9 mg/kg) and medetomidine (0.017 mg/kg) injection (Forsyth et al., 1999). In the present study, 15 mg of atipamezole (target dose 0.08 mg/kg) was administered intravenously 33 ± 4 minutes after darting, and sternal recumbency was observed five to fifteen minutes after administration. No side effects such as excitation or seizures were observed, and all recoveries were considered smooth.

CONCLUSION

Medetomidine 0.03 mg/kg in association with ketamine 2.5 mg/kg in single-dart injection produced fast and safe chemical restraint in healthy tigers. Reduced $alpha_2$ doses in association with other drugs such as midazolam may be considered for ill patients, in order to minimize the associated $alpha_2$ side effects. In the present study, reversal of medetomidine with 0.08 mg/kg of atipamezole intravenously at the end of the procedure resulted in a short recovery duration, without observation of side effects.

REFERENCES

Allwin, B., Jayathangaraj, M. G., Latha, B. R., Vijayarani, K., Vairamuthu, S. (2018). Clinical evaluation of xylazine and ketamine for immobilization of the captive bengal tigers (Panthera tigris tigris). *Indian Journal of Animal Research 52*, 1236–1239. https://doi.org/10.18805/ijar.B-3325

Cesare, F. Di, Cagnardi, P., Ravasio, G., Capasso, M., Magnone, W., Villa, R. (2018). Pharmacokinetics of ketamine and norketamine following intramuscular administration combined with dexmedetomidine in tigers (Panthera tigris). *International Journal of Health, Animal Science and Food Safety 5*(1s). https://doi.org/10.13130/2283-3927/10062

Clark-Price, S. C., Lascola, K. M., Schaeffer, D. J. (2015). Physiological and biochemical variables in captive tigers (Panthera tigris) immobilized with dexmedetomidine and ketamine or dexmedetomidine, midazolam and ketamine. *Veterinary Record 177*, 570. https://doi.org/10.1136/vr.103526

Curro, T. G., Okeson, D., Zimmerman, D., Armstrong, D. L., Simmons, L. G. (2004). Xylazine–midazolam–ketamine versus medetomidine– midazolam–ketamine anesthesia in captive siberian tigers (Panthera tigris altaica). *Journal of Zoo and Wildlife Medicine 35*, 320–327. https://doi.org/10.1638/03-049

Forsyth, S. F., Machon, R. G., Walsh, V. P. (1999). Anaesthesia of a sumatran tiger on eight occasions with ketamine, medetomidine and isoflurane. *New Zealand Veterinary Journal 47*, 105–108. https://doi.org/10.1080/00480169.1999.36123

Goodrich, J. M., Kerley, L. L., Schleyer, B. O., Miquelle, D. G., Quigley, K. S., Smirnov, Y. N., Nikolaev, I. G., Quigley, H. B., Hornocker, M. G. (2001). Capture and chemical anesthesia of amur (Siberian) tigers. *Wildlife Society Bulletin 29*, 553–542.

Kreeger, T. J., Armstrong, D. L. (2010). Tigers and Telazol®: The unintended evolution of caution to contraindication. *The Journal of Wildlife Management 74*, 1183–1185. https://doi.org/10.1111/j.1937-2817.2010.tb01238.

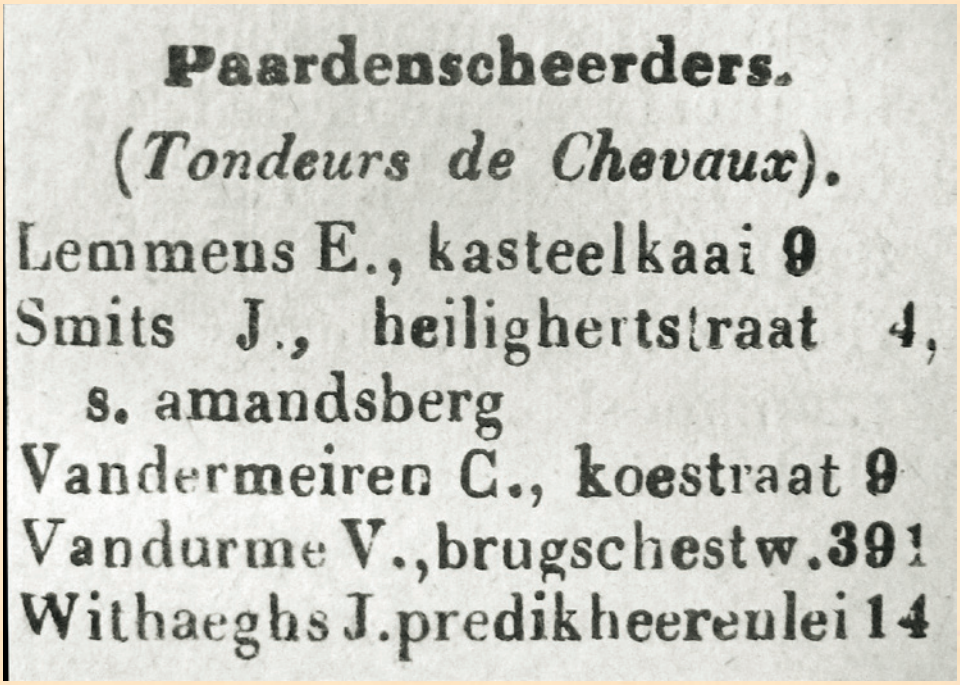
Laricchiuta, P., De Monte, V., Campolo, M., Grano, F., Crovace, A., Staffieri, F. (2014). Immobilization of captive tigers (Panthera tigris) with a combination of tiletamine, zolazepam, and detomidine. *Zoo Biology 34*, 40–45. https://doi.org/10.1002/zoo.21157

Larsson, M. H. M. A., Coelho, F. M., Oliveira, V. M. C., Yamaki, F. L., Pereira, G. G., Soares, E. C., Fedullo, J. D. L., Pereira, R. C., Ito, F. H. (2008). Electrocardiographic parameters of captive lions (Panthera leo) and tigers (Panthera tigris) immobilized with ketamine plus xylazine. *Journal of Zoo and Wildlife Medicine 39*, 314–319. https://doi.org/10.1638/2007-0028.1

Lewis, J. C. M., Teale, P., Webber, G., Sear, J. W., Taylor, P. M. (2014). Comparison of tiletamine and zolazepam pharmacokinetics in tigers (Panthera tigris) and leopards (Panthera pardus): Do species differences account for ad-

verse effects in tigers? *Veterinary Journal 201*, 302–306. https://doi.org/10.1016/j.tvjl.2014.05.041
Mercado, J. A., Romano, J., Cueva, H. D. la, Haro, P. (2020). Multiple successful tiletamine-zolazepam-xylazine immobilizations in an Amur tiger cub. *Veterinary Record Case Reports 8*, e001081. https://doi.org/10.1136/VETRECCR-2020-001081
Miller, M., Weber, M., Neiffer, D., Mangold, B., Fontenot, D., Stetter, M. (2003). Anesthetic induction of captive tigers (panthera tigris) using a medetomidine–ketamine combination. *Journal of Zoo and Wildlife Medicine 34*, 307–308. https://doi.org/10.1638/02-036
Ramsay, E. C. (2014). Felids. In: West, G., Heard, D., Caulkett, N. (editors). *Zoo Animal and Wildlife Immobilization and Anesthesia*. Second. Edition, John Wiley & Sons Inc, Hoboken, p. 635–646. https://doi.org/10.1002/9781118792919.ch45
Reilly, S., Seddighi, M. R., Steeil, J. C., Sura, P., Whittemore, J. C., Gompf, R. E., Elliott, S. B., Ramsay, E. C. (2014). Selected clinical, biochemical, and electrolyte alterations in anesthetized captive tigers (Panthera tigris) and lions (Panthera leo). *Journal of Zoo and Wildlife Medicine 45*, 328–334. https://doi.org/10.1638/2013-0202r.1
Seal, U. S., Armstrong, D. L., Simmons, L. G. (1987). Yohimbine hydrochloride reversal of ketamine hydrochloride and xylazine hydrochloride immobilization of bengal tigers and effects on hematology and serum chemistries. *Journal of Wildlife Diseases 23*, 296–300. https://doi.org/10.7589/0090-3558-23.2.296
Seidensticker, J., Tamang, K. M., Gray, C. W. (1974). The use of CI-744 to immobilize free-ranging tigers and leopards. *The Journal of Zoo Animal Medicine 5*, 25. https://doi.org/10.2307/20094266
Smith, C. K., Seddighi, R., Zhu, X., Tepe, A. J., Ramsay, E. C., Cushing, A. C. (2018). Use of plethysmographic variability index and perfusion index to evaluate changes in arterial blood pressure in anesthetized tigers (Panthera tigris). *American Journal of Veterinary Research 79*, 845–851. https://doi.org/10.2460/ajvr.79.8.845
Sontakke, S. D., Umapathy, G., Shivaji, S. (2009). Yohimbine antagonizes the anaesthetic effects of ketamine-xylazine in captive Indian wild felids. *Veterinary Anaesthesia and Analgesia 36*, 34–41. https://doi.org/10.1111/j.1467-2995.2008.00427.x
Virtanen, R. (1989). Pharmacological profiles of medetomidine and its antagonist, atipamezole. *Acta Veterinaria Scandinavica. Supplementum 85*, 29–37.
Zeiler, G. E., Rioja, E., Boucher, C., Tordiffe, A. S. W. (2013). Anaesthetic management of two bengal tiger (panthera tigris tigris) cubs for fracture repair. *Journal of the South African Veterinary Association 84*, 5. https://doi.org/10.4102/jsava.v84i1.995

uit het verleden


Paardenscheerders.
(Tondeurs de Chevaux).
Lemmens E., kasteelkaai 9
Smits J., heilighertstraat 4,
s. amandsberg
Vandermeiren C., koestraat 9
Vandurme V., brugschestw. 391
Withaeghs J. predikheereulei 14

Paardenscheerders, een verdwenen beroep ... (Uit: Wegwijzer van Gent en Oost-Vlaanderen, Gent, 1910).