The use of analgesic drugs by South African veterinarians

K E Joubert[a]

ABSTRACT

According to a survey, non-steroidal anti-inflammatory agents were the most popular analgesic used in South Africa for management of peri-operative pain, acute post-operative pain and chronic pain. The most popular non-steroidal anti-inflammatory agents are flunixin meglumine and phenylbutazone. The most popular opioid type drug is buprenorphine, followed by morphine. In the peri-operative setting, analgesic agents were not actively administered to 86.3 % of cats and 80.7 % of dogs. Analgesic premedications were frequently administered, *e.g.* xylazine or ketamine, but no specific drug was administered for post-operative pain. Veterinarians need to critically review their anaesthetic and analgesic practices in order to achieve balanced anaesthesia.

Key words: analgesia, non-steroidal anti-inflammatory agents, small animals, South Africa.

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INTRODUCTION

The use of analgesics by veterinarians worldwide has been inadequately addressed[6,7,14]. Only 40 % of dogs admitted to the North Carolina State University Hospital for major surgery received analgesics[14]. A more recent Canadian survey (1996) concluded that only 50 % of veterinary practitioners used analgesics perioperatively[7]. Pain is a subjective parameter and hence is difficult to quantify objectively. A number of pain rating scales and behavioural assessment scores are available for the evaluation of pain[10,13]. The use of analgesic drugs by South African veterinarians is unknown and anecdotal. This survey was undertaken to assess the use of analgesics for routine sterilisations, acute post-operative pain and general pain management. No information on the assessment of pain by veterinarians or the basis for administration of analgesic drugs was obtained.

MATERIALS AND METHODS

The sales representatives of a pharmaceutical company distributed 600 questionnaires to veterinary practices in South Africa between February and April 1999. The questionnaires were completed by the veterinarian in the practice and returned either *via* the company or by post to the author. Analgesic-type drugs available in South Africa were listed and the respondent was asked which of those drugs were administered routinely during sterilisation of dogs and cats. The list included non-steroidal anti-inflammatory agents, opioids and other drugs with analgesic properties. A similar question was asked as to which analgesic drugs were given for acute post-operative pain after any procedure. Lastly, drugs including non-steroidal anti-inflammatory agents, opioids, anaesthetic drugs, premedication and other analgesic drugs were listed, and the respondent was asked to identify the drugs with analgesic properties that they used for pain control. The survey is contained in Appendix 1. The list of drugs for each question was compiled from the South African Medicines Council list of registered drugs. The list of drugs has been omitted from certain questions where the drugs would be self-explanatory. Several phenylbutazone-containing drugs are available in South Africa and these drugs were grouped together.

The data were entered into a spreadsheet (Excel 97 SR-1, Microsoft Corporation). Tables and descriptive statistics were used to describe the data. Statistical analysis was performed with SigmaStat for Windows, Version 2.00 (Jandel Corporation).

RESULTS

In total, 162 questionnaires were completed. This represents a response rate of 27 %. One questionnaire was rejected, as it was incomplete. The remaining questionnaires (161) were used for analysis.

Use of analgesic drugs

The results indicate that 139 (86.3 %) respondents did not include any drugs specifically for their analgesic properties in the premedication and induction of cats undergoing routine sterilisation. However, when the author included premedication and induction agents with analgesic properties, this percentage was reduced to 34.2 % (55). This indicates that a large number of practitioners are unaware of the pharmacology of many drugs. A number of practitioners used more than one drug with analgesic properties in a case. The analgesic drugs used in cats are given in Table 1. A similar situation was reported for dogs. One hundred and thirty (80.75 %) respondents indicated that they did not intentionally give analgesic drugs to dogs undergoing sterilisation. Again, analysis of premedication and induction agents revealed that 111 (68.9 %) of the respondents did not administer any with analgesic properties. These results are presented in Table 2.

The 4 most commonly used drugs for acute post-operative pain were flunixin meglumine (87, 54.0 %), phenylbutazone (79, 49.1 %), pethidine, (41, 25.5 %) and buprenorphine (23, 14.3 %). Five practitioners indicated that they did not administer any drugs for acute post-operative pain. All the drugs used for acute post-operative pain are listed in Table 3.

Table 1: **Drugs with analgesic properties given to cats undergoing routine sterilisation. Certain practitioners used more than one drug. The percentages are based on the 161 respondents that replied.**

Drug	*n*	%
Xylazine	76	47.20
Medetomidine	15	9.32
Ketamine	14	8.70
Phenylbutazone	9	5.59
Ketamine	8	4.97
Flunixin meglumine	4	2.48
Pethidine	3	1.86
Buprenorphine	1	0.62
Butorphanol	1	0.62
Carprofen	1	0.62
Cortisone	1	0.62

[a]Department of Companion Animal Surgery, Faculty of Veterinary Science, University of Pretoria, Private Bag X04, Onderstepoort, 0110 South Africa.

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Table 2: **Drugs with analgesic properties given to dogs under going routine sterilisation. Certain practitioners used more than one drug. The percentages are based on 161 respondents.**

Drug	*n*	%
Flunixin meglumine	16	9.94
Xylazine	15	9.32
Phenylbutazone	13	8.07
Medetomidine	5	3.11
Buprenorphine	2	1.24
Pethidine	2	1.24
Aspirin	1	0.62
Carprofen	1	0.62
Cortisone	1	0.62
Ibuprofen	1	0.62
Ketamine	1	0.62
Ketoprofen	1	0.62
Morphine	1	0.62

The drugs most commonly used for the treatment of pain in general practice in South Africa are flunixin meglumine (134, 83.2 %) followed by phenylbutazone (112, 69.6 %). Aspirin, pethidine, ibuprofen, xylazine and meloxicam were commonly used. The remaining drugs are listed in Table 4. A number of respondents identified drugs that have limited analgesic effect as having analgesic properties. Drugs included in this group are thiopentone, alphaxalone/alphadolone, diazepam, halothane, acetylpromazine, pentobarbitone, atropine, phenobarbitone, propofol and isoflurane. Details are given in Table 4.

Table 3: **Drugs given for acute post-operative pain in small animals. Some practitioners selected from more then one drug for the treatment of post-operative pain. The percentages are based on 161 respondents.**

Drugs	*n*	%
Flunixin meglumine	87	54.04
Phenylbutazone	79	49.07
Pethidine	41	25.47
Buprenorphine	23	14.29
Morphine	8	4.97
Aspirin	7	4.35
Butorphanol	5	3.11
No analgesic drug given	5	3.11
Ketoprofen	3	1.86
Medetomidine	3	1.86
Tilidine	3	1.86
Cortisone	2	1.24
Ibuprofen	2	1.24
Oxymorphone	2	1.24
Carprofen	1	0.62
Meloxicam	1	0.62
Methadone	1	0.62
Piroxicam	1	0.62
Xylazine	1	0.62

DISCUSSION

Most respondents in this study indicated that they did not actively administer analgesics to animals during routine sterilisation. In a British study, 53 % of ovariohysterectomies and 32 % of castrations received peri-operative analgesics[3]. The lower incidence of the use of analgesics in ovariohysterectomies compared to laparotomy (71 %) in the British study was attributed to the fact that an ovariohysterectomy is considered routine[3]. What is interesting about this study is that a laparotomy was considered to be as painful as an ovariohysterectomy[3]. A Canadian study showed dismal results for peri-operative use of analgesics in the sterilisation of cats and dogs (ovariohysterectomy cats 16.6 %, dogs 12.6 %, castrations cats 9.3 %, dogs 10.5 %)[7].

From our study it initially appeared that only 13.7 % of cats received peri-operative analgesics for routine sterilisation. When the premedications were considered, 43.5 % of cats received xylazine. Xylazine and medetomidine, both alpha2-adrenergic agonists, are known to have potent analgesic properties[22]. This had a dramatic impact on the number of cats receiving analgesics for sterilisation (65.8 %). The analgesic effect of alpha2-adrenergic agonists does not last as long as the sedative effect[22], therefore this drug is unlikely to have contributed much to post-operative analgesia. Dogs did not benefit as much from the inclusion of alpha2-adrenergic agonists.

The most commonly-used opioid for pain control during sterilisation in this study was pethidine. In Britain, buprenorphine was the most common, followed by butorphanol[3]. In Canada, butorphanol ranks above buprenorphine[7]. The most commonly used non-steroidal anti-inflammatory agent was flunixin meglumine followed by phenylbutazone. The most commonly used non-steroidal anti-inflammatory agent in Britain for sterilisation is carprofen[3]. Although use of butorphanol and carprofen was reported in this study, neither drug is currently registered by the South African Medicines and Drug Related Authority.

To manage acute post-surgical pain, flunixin meglumine and phenylbutazone were the most popular choices. It is important to realise that non-steroidal anti-inflammatory agents seldom relieve pain immediately as they take 45–60 minutes to achieve their full effect after administration[20]. Opioids or other drugs with a rapid mechanism of action should be used initially for acute post-operative pain. Non-steroidal anti-inflammatory agents are synergistic with opioids and several benefits can be derived from using these drugs in combination[20].

Table 4: **Drugs recognised as having analgesic properties and used for this purpose in practice. Practitioners selected from a group of drugs and were asked to indicate which drugs they used for analgesia. These results are displayed. The drugs marked with an * are drugs with no analgesic properties. The percentages are based on 161 respondents.**

Drug	*n*	%
Flunixin meglumine	134	3.23
Phenylbutazone	112	69.57
Aspirin	79	49.07
Pethidine	71	44.10
Ibuprofen	55	34.16
Xylazine	39	24.22
Meloxicam	38	23.60
Morphine	33	20.50
Piroxicam	30	18.63
Buprenorphine	23	14.29
Thiopentone*	23	14.29
Ketamine	20	12.42
Medetomidine	18	11.18
Alphaxalone/Alphadolone	17	10.56
Diazepam*	16	9.94
Halothane*	15	9.32
Acetylpromazine*	14	8.70
Pentobarbitone*	11	6.83
Butorphanol	10	6.21
Dipyrone	9	5.59
Atropine*	8	4.97
Phenobarbitone*	7	4.35
Fentanyl	6	3.73
Ketoprofen	6	3.73
Tiletamine & Zolazepam	6	3.73
Etorphine	4	2.48
Propofol*	4	2.48
Isoflurane*	2	1.24
Metomidate*	2	1.24
Etomidate*	1	0.62
Mefenamic acid	1	0.62
Methadone	1	0.62

Non-steroidal anti-inflammatory agents pose several risks to patients, of which acute renal failure and gastric ulceration probably cause the most concern. Flunixin meglumine and phenylbutazone have been reported to cause peri-operative renal failure[5,9,16,20,21,26]. Older animals should be monitored for adverse renal side-effects[4]. Non-steroidal anti-inflammatory drugs should be used with caution when creatinine levels are raised[20]. The median value of creatinine is used as the upper limit when considering non-steroidal anti-inflammatory drugs. When creatinine is in the top normal range, up to two-thirds of renal function can already be lost.

Non-steroidal anti-inflammatory drugs should not be given to patients with known renal insufficiency, dehydration, hypotension, relative and absolute hypovolaemia, ascites, heart failure, thrombocytopenia, known coagulation

deficiencies, gastric ulceration or any other gastrointestinal disturbances, haemorrhage in non-compressible areas or with the concurrent use of corticosteroids[20]. Gastric ulceration can occur with all non-steroidal anti-inflammatory drugs and prophylaxis should be instituted[20]. Drugs that can be used are sucralfate (0.25 g p/o tid or bid), misoprostol (2–5 g/kg p/o tid) and ranitidine (3.5 mg/kg p/o bid, 2.5 mg/kg i/v bid)[20]. Non-steroidal anti-inflammatory drugs are safe in normovolaemic, normotensive patients.

The most commonly-used opioid-type drug for post-operative pain was pethidine, followed by buprenorphine. The most commonly-cited factors affecting the use of opioids are: analgesic potency, legal requirements, and side-effects[3,7]. Pethidine has been shown to be a useful analgesic in dogs and cats[1,17]. Pethidine has one third to half the potency of morphine[23]. The major problem associated with pethidine is its short duration of action, and it is in this respect an ineffective analgesic in small animal patients[7]. Buprenorphine is as effective as morphine for the relief of post-arthrotomy pain[2]. Buprenorphine is a mixed agonist-antagonist opioid and as such has a ceiling effect[2,7]. The major disadvantage of this is that once buprenorphine has been given, another more potent opioid cannot be given for anaesthesia or analgesia. As a result of this buprenorphine has been used to reverse opioid overdoses. Buprenorphine has a duration of action of up to 8 hours[2]. Mixed agonist-antagonist opioids are not considered adequate for moderate to severe post-operative pain[7]. A potent μ agonist, *e.g.* morphine, is more suitable for severe pain, as increasing the dose increases the analgesic effect[7]. Few practitioners in this survey used morphine or any of the other potent μ agonists. Major concerns exist about the use of μ agonists in cats, as they may cause excitement. This concern has been shown to be unfounded when they are used at clinically relevant doses[7]. Morphine has a duration of action of approximately 4 hours[2].

Veterinarians identified several anaesthetic drugs as having analgesic properties. The drugs included thiopentone, alphaxalone/alphadolone, diazepam, halothane, acetylpromazine, pentobarbitone, atropine, phenobarbitone, propofol and isoflurane. In fact, thiopentone and halothane have been shown to potentiate painful stimuli or have limited analgesic properties[11,24,28]. Propofol may have moderate analgesic properties and does not increase sensitivity to pain[24]. Anaesthesia is defined as a state of reversible unconsciousness, amnesia, muscle relaxation and analgesia. Acepromazine, thiopentone and halothane constitute the most commonly-used anaesthetic protocol for sterilisation in dogs and alphaxalone/alphadolone in cats. None of these anaesthetic protocols meet all the requirements for anaesthesia. Veterinarians should critically review their anaesthetic practices in order to achieve a more balanced anaesthetic protocol.

Ketamine is an anaesthetic agent with potent analgesic properties, and has most commonly been used as an analgesic in burn wound patients[12,15,19,29]. Sub-anaesthetic doses of ketamine given pre-operatively have been shown to be effective in reducing post-operative pain[25].

A few practitioners indicated that they used corticosteroids for acute post-operative pain and during sterilisation. Corticosteroids have a limited role to play in peri-operative analgesia. They affect the inflammatory pathways and may exert effects similar to non-steroidal anti-inflammatory agents[27]. Corticosteroids produce multiple effects in various organ systems and are thus associated with numerous side-effects[27]. Their use is indicated in cases of immune-mediated and rheumatoid arthritis, but is seldom indicated as the primary choice in other types of chronic pain. The routine use of corticosteroids as an analgesic cannot be justified.

It has been demonstrated that sex is one of the important factors dictating the prescription of analgesic drugs[6]. Female members of staff are far more likely to give analgesic drugs than male counterparts[3,6]. Nurses in general increase the use of analgesic drugs[6,8]. Even in teaching hospitals, the knowledge and use of analgesic drugs has been shown to be poor, ineffectual and inappropriate in many cases[14]. In order to relieve pain effectively, a multimodal approach is frequently required[17,18]. This includes the use of non-steroidal anti-inflammatory agents, opioids and other adjuncts.

The analgesic care of patients can be dramatically improved through continuing education, creating more awareness amongst veterinarians about pain and increasing their knowledge about analgesic drugs.

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APPENDIX 1: Anaesthetic Survey

Anaesthesia for Cat Ovariohysterectomy:
What drugs are given for routine Induction of Anaesthesia?
What drugs are given for routine Maintenance of Anaesthesia?
Are any of the following drugs given peri-operatively to cats for ovariohysterectomies?

Aspirin:	Buprenorphine:	Butorphanol:
Dipyrone:	Finadyne:	Ibuprofen:
Ketamine:	Ketoprofen:	Ketorolac:
Meloxicam:	Morphine:	Pethidine:
Phenylbutazone:	Piroxicam:	
Other:		

Anaesthesia for Dog Ovariohysterectomy & Orchidectomy:
What drugs are given for routine Induction of Anaesthesia?
What drugs are given for routine Maintenance of Anaesthesia?
Are any of the following drugs given peri-operatively to dogs for ovariohysterectomies or orchidectomies?

Aspirin:	Buprenorphine:	Butorphanol:
Dipyrone:	Finadyne:	Ibuprofen:
Ketamine:	Ketoprofen:	Ketorolac:
Meloxicam:	Morphine:	Pethidine:
Phenylbutazone:	Piroxicam:	
Other:		

General Questions on Pain management:
What analgesic do you give for acute post-operative pain?
Which of the following drugs have analgesic properties?

Acetylpromazine:	Aspirin:	Atropine:
Azaperone:	Buprenorphine:	Butorphanol:
Dipyrone:	Etomidate:	Etorphine:
Fentanyl:	Finadyne:	Halothane:
Ibuprofen:	Isoflurane:	Ketamine:
Ketoprofen:	Ketorolac:	Medetomidine:
Meloxicam:	Metomidate:	Morphine:
Pentobarbitone:	Pethidine:	Phenobarbitone:
Phenylbutazone:	Piroxicam:	Proprionyl promazine:
Propofol:	Saffan:	Thiopentone:
Valium:	Xylazine:	Zoletil: