Clinical use of analgesics in dogs and cats by Bangladeshi veterinarians

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List of Abbreviations

DVM : Doctor of Veterinary Medicine

NSAIDs : Nonsteroidal Anti-inflammatory Drugs

COX : Cyclooxygenase

CNS : Central Nervous System

LA : Local anesthetics

CVASU : Chattogram Veterinary and Animal Sciences University

HSTU : Hajee Mohammad Danesh Science & Technology University

BAU : Bangladesh Agricultural University

SAU : Sylhet Agricultural University

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Abstract

A clinical survey was conducted among 262 veterinarians practicing in the Bangladesh to assess views on pain evaluation and management in dogs and cats. Majority of the vets practice on pet dogs and cats were young male and freshly graduated who use their academic knowledge during practice. The majority of the vets suggest meloxicam in dogs 66.79% and cats 52.67% as NSAID. Ketoprofen was the second most choice in both orthopedic and muscular injuries. Among the steroids and opioids, dexamethasone and tramadol were recorded respectively as first choice. In most cases of worst pain, dexamethasone was the primary choice. Usual duration of analgesic therapy recorded was less than three-days. In most cases, vets suggest H2 blockers in association with meloxicam and ketoprofen to reduce adverse effects. Vomition and diarrhea were recorded as mostly occurring side effects following medication with analgesics. The current study reviewed the present scenario of pain management in dogs and cats in Bangladesh. Further studies are required involving more vets and detailed information on cases and response to analgesic therapy

Keyword: Analgesics, dogs, cats, pain management.

Introduction

Pain is a protective mechanism of body, and it occurs when any tissue is being damaged. It causes an individual to respond to remove the pain stimulus by medication of pain killer, called analgesics. Analgesics are a group of drugs used to relief pain (Booth and McDonald 1982). Analgesics are mainly four categories; non-steroidal anti-inflammatory drugs (NSAIDs), opioid, local anesthetics (LA), and centrally acting non-opioid. NSAIDs and LA produce analgesia by acting on CNS and others works on peripherally (Brander 1991).

The common NSAIDs used for post-surgical pain and different trauma managements include meloxicam, ketoprofen, flunixin, metamisole, aspirin, and paracetamol. The NSAIDs act by blocking the prostaglandin synthesis mediated by inhibition of cyclooxygenase (COX) enzyme (Allweiler 2019). Availability, relatively long duration of action, and low cost made the NSAIDs popular for the practitioners to pain management. However, they have a number of side effect, some are deadly. For example, gastrointestinal irritation induce vomiting, diarrhea, ulceration in the long-term use, and liver and kidney toxicity (Bostrom et al. 2006). Indiscriminate or ignorant use of NSAIDs in pet dogs and cats may sometimes cause life-threatening effect. For example, paracetamol is not recommended at any dose in cat and dog and can be fetal due to hepatotoxicity and methaemoglobin formation (Roy 2001, Murphy 2004). Meloxicam poisoning is typical of other NSAIDs with vomiting and diarrhea being the most common adverse reactions. Vomit and stool may contain signs of blood from gastrointestinal (GI) ulceration. GI symptoms are often combined with signs of kidney failure such as increased thirst and urination. Dogs will lose their appetite and seem generally weaker and depressed. Overdose can cause severe gastrointestinal bleeding, seizures, and fatal kidney failure. The most-common side effects of ketoprofen include ulceration of the GI tract and a drop in the red blood cell count due to GI bleeding (Walton et al. 2017). Ibuprofen also causes vomiting, nausea, diarrhea, intestinal upset and gastric ulcers. Reduced blood flow to the kidneys results in kidney

damage. Reduced platelet aggregation leads to an increased tendency to bleed abnormally (Davies and Avery 1971).

Local anesthetics like lidocaine, procaine etc. are applied locally to nerve tissue to relief from pain. Local anesthetics have some short-term side effects, such as: dizziness, headaches, blurred vision, twitching muscles (Murphy 2004). Opioids include morphine, meperidine, butorphanol, tramadol etc. are the most effective analgesics available for the systemic treatment of acute pain in many species although CNS effects like sedation, euphoria, excitement occurs and it releases histamine causes bronchoconstriction and hypotension in animals. Accidentally ingestion of opioids in oral or patch form, can result in severe poisoning as opioids are rapidly absorbed by all routes of administration. Signs of opioid poisoning include pinpoint pupils in dogs, dilated pupils in cats, sedation, walking drunk, decreased respiratory rate, respiratory depression which can lead to respiratory arrest or death (Gilman et al. 1986).

Steroids are for emergency rather than chronic treatment of painful conditions. Dexamethasone, prednisolone, triamcinolone are commonly used steroids. Steroids are powerful healing drugs although they are not solely free from harmful effects. Stomach ulcers, delayed wound healing, thyroid hormone suppression, immune suppression so that the body does not fight infection well are common adverse effects of long-term steroid medication. Moreover, increased appetite, high blood sugar, polydipsia, edema, polyuria, and hepatomegaly may also occur during long-term medication with steroids (Donovan 2017, Hunter 2018, Morassi et al. 2018).

Although none of the analgesics is free from adverse effects, their use is beyond debate due to unbearable sensation of pain. However, proper selection of specific analgesics considering types of tissue injury, species of animals, severity of pain, dosage and duration of analgesic use can minimize adverse effects. A number of studies have been performed towards veterinary pain assessment and management (Mathews 2000, Pascoe 2000). Moreover, the attitudes of veterinarians towards postoperative pain in dogs and cats have been studied in Canada (Dohoo and Dohoo 1996, Dohoo and Dohoo 1998), the United States (Hansen and Hardie 1993, Hellyer et al. 1999, Wagner and

Hellyer 2000), the United Kingdom (Capner et al. 1999), Finland (Raekallio et al. 2003), France (Hugonnard et al. 2004), and Australia (Watson et al. 1996), However, most of the studies reported that the usage of analgesics was mainly during perioperative periods, and there was lower tendency of analgesic use in non-surgical cases (Hansen and Hardie 1993, Watson et al. 1996, Capner et al. 1999, Hellyer et al. 1999, Pascoe 2000, Wagner and Hellyer 2000, Raekallio et al. 2003, Hugonnard et al. 2004). One of the chief reasons cited for limited use was the veterinarian's perception of the amount of pain felt and their concerns about the risk of adverse reactions of analgesics (Dohoo and Dohoo 1996).

Companionship with a pet dog or cat is trending to be popular in Bangladesh. A lot of people are now rearing pets as a household companion, source of enjoyment, and a safeguard as well. The owners often come to the veterinary hospitals with their pets when they got injured or suffer from any medical condition, and most importantly for surgical procedure such as spaying and castration. During the case management the owners often demand for minimization of pain by using appropriate analgesics although there is very limited report on the types of analgesics suggested by the pet practitioners of this region. Therefore, the current study was designed to investigate the selection of analgesics and their uses, doses, side-effects in dogs and cats in Bangladesh.

The overall aim of the present study was to study the analgesics commonly used in dogs and cats for pain management by veterinarians in Bangladesh. The specifics objectives are:

i. To study the veterinarians practicing on pet animals.
ii. To get knowledge on the types of analgesics commonly used in pain management of dogs and cats.
iii. To understand the current trend of analgesic use in different tissue injuries.
iv. To know the status of using H2 blocker with analgesics.
v. To identify the uses of analgesics in medical and surgical cases.
vi. To be aware of analgesic use to minimize potential adverse effects

Materials and Methods

Study population: A total of 262 registered veterinarians were interviewed who had a minimum bachelor degree on veterinary medicine.

Study period: The survey was conducted for a total of 4 month period starting from January to April 2019.

Data collection: Extensive information on the use of analgesics was collected using a formulated questionnaire (Appendix 1). Most of the questions in the format were close ended for the veterinarian's convenience with a few open questions. The questionnaire was solicited information about 2 major topics; (i) information of veterinarian, and (ii) information on use of analgesics.

Data of veterinarian: In the veterinarian's information, name of the practitioner and their working organization was added to correlate the type of organization with pet patients handled. The veterinarian's school of graduation was added to correlate graduates with their trends of types of analgesics use. Moreover, year of graduation will determine the type of analgesic use with experiences or age of a vet. Working area or district was added investigate the pet patient load as well as the analgesics use at different areas. Source of knowledge about analgesics were included to study the source of information from where a vet got informed about the types of analgesic use.

Data on analgesics use: In the questionnaire, we have taken information on nine non-steroidal anti-inflammatory drugs (NSAIDs): flunixin, meloxicam, ketoprofen, metamisole, salicylic acid, aspirin, paracetamol, ibuprofen, and diclofenac sodium; two steroids: dexamethasone and prednisolone together or alone; and three opioids: butorphanol, meperidine, and tramadol. In addition, an open option was given to take information on any other analgesic not listed above. Options were provided to investigate which analgesic is used the most in dogs and cats, against the nature of the cases, for example medical or surgical, and types of tissues affected, such as skeletal,

muscular or soft tissues. The veterinarian's perception of the pain felt by dogs and cats undergone the above procedures, rated on a scale of 0 for 'no pain' to 10 for 'worst pain' will help to determine the veterinarian choice of analgesics in different scale of pain.

Options for analgesic doses, frequencies, routes and durations were added in questionnaire to compare the recommended signalment versus suggested one recommended by the veterinarians in the field condition. Moreover, the most effective route that is whether the intravenous, intramuscular or subcutaneous route is the best for analgesic therapy will be determined by the 'route' option. However, how long the dogs and cats are giving analgesics will be determined by the option 'duration of drugs'. H2 blockers are used in treating and preventing NSAID induced mucosal damage (Tuskey and Peura 2013). In this study, information on use of H2 blocker was taken to correlate whether they are used beforehand the uses of analgesics. Efficacy of drugs, rated on a scale '0' for 'not effective' and '5' for 'excellent' and the side effects of post medication were considered to explore the safest and best effective analgesic for pain management in dogs and cats. All the data have been collected by physical interviewing of the veterinarian or by telephone call.

Statistical analysis**:** Confirmation of normal distribution of data sets was established using D'Agostino & Pearson normality test in GraphPad Prism & statistical software (Appendix 2). The data sets from different groups that passed D'Agostino & Pearson normality test was compared and tested using one-way analysis of variance (ANOVA) or t-test. Non-parametric Kruskal-Wallis tests and Mann-Whitney tests were performed to compare data that weren't normally distributed. A p value of ≤ 0.05 was considered significant (Appendix 2).

Results

We interviewed a total of 262 registered veterinarians all over the country. The respondents had different views of using analgesics in dogs and cats as pain relief.

Demographic characteristic of veterinarians

To report the current situation of veterinary sector in Bangladesh we have noted information of veterinarians and observed that the sector is still dominated by the young male doctors with age less than 40 years (Table 1). In this study, most of the respondents were graduated from Chattogram Veterinary and Animal Sciences University (CVASU) followed by Bangladesh Agricultural University (BAU). Moreover, the veterinarians also informed that their main source of knowledge update is veterinary books followed by drug literature rather than internet.

Table 1 Statistic features of veterinarians

Characteristics	Distributions (%)
Gender	
Male	71
Female	29
Age	
<40y	69
>40y	31
Year since graduation: <10y	60
School of graduation	
CVASU	61
BAU	22
HSTU	9
SAU	8
Source of knowledge	
Books	70
Drug literature	19
Internet	11

CVASU: Chattogram Veterinary and Animal Sciences University, BAU: Bangladesh Agricultural University, HSTU: Hajee Mohammad Danesh Science & Technology University, SAU: Sylhet Agricultural University

Analgesic uses against medical and surgical cases

We investigated the overall uses of analgesics in dogs and cats irrespective of the medical or surgical conditions (Figure 1a). We found meloxicam was the most used pain relief for both dogs ($p>0.05$) and cats ($p<0.0001$) when compared to the second most ketoprofen. Meloxicam ($p<0.01$), ketoprofen ($p<0.0001$) and dexamethasone ($p<0.01$) were used significantly in dogs compared to cat patients. Moreover, these three were the most used drugs in both medical and surgical cases of dogs (Figure 1b) and cat (Figure 1c). Furthermore, meloxicam is the drug of choice for most of the vets followed by ketoprofen and dexamethasone (Figure 1b). However in cats, ketoprofen was the choice followed by meloxicam and dexamethasone (Figure 1c). The least used pain reliefs reported were flunixin, metamisole, salicylic acid, paracetamol, diclofenac sodium, prednisolone and tramadol.

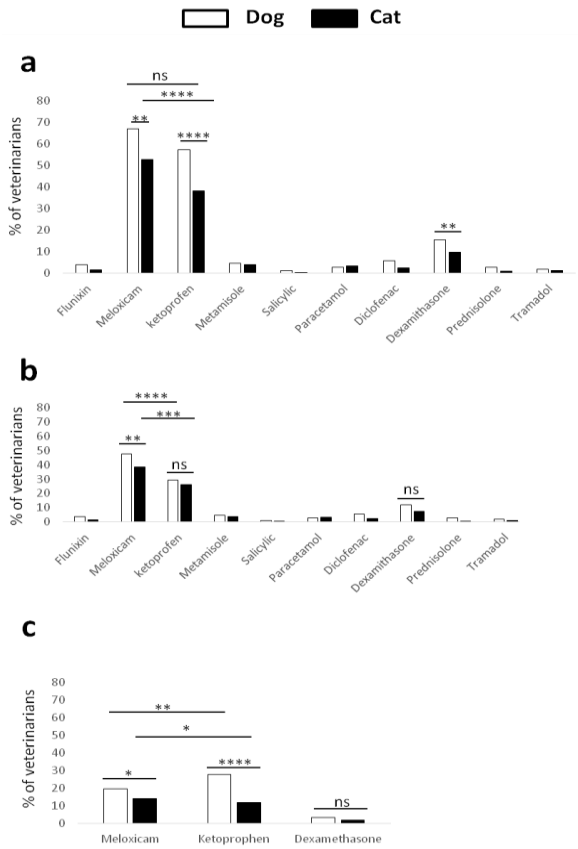

Figure 1 Overall use of analgesics in dogs and cats. In both dogs and cats, meloxicam is the mostly prescribed analgesic followed by ketoprofen and dexamethasone whereas flunixin, salicylic acid and tramadol are the least used (a). The situation is similar in medicinal (b) and surgical (c) cases. Statistical analysis by Mann Whitney test except dexamethasone (c) which was analysed by unpaired t test. p*<0.05, **<0.01, ***<0.001, ****<0.0001, ns: not significant.

Analgesic uses against tissues affected

The results of the current study reported that meloxicam and ketoprofen were the mostly prescribed analgesics in skeletal, muscular and soft tissue injuries irrespective of the patient species (Figure 2). In dogs, ketoprofen ($p<0.01$) was the drug of choice during treatment of skeletal tissue injuries followed by meloxicam ($p<0.5$) and flunixin (Figure 2a). However, some vets use diclofenac sodium in addition to meloxicam and ketoprofen in muscular injuries. Pain originated from soft tissue injuries were treated with ketoprofen, meloxicam and dexamethasone in dogs though the difference was not significant. In cats, ketoprofen was mostly used for skeletal injuries compared to muscular and soft tissues ($p<0.001$) (Figure 2b). However, meloxicam ($p<0.05$) was the drug of choice for muscular injuries by most of the vets. Flunixin and dexamethasone were used in skeletal and soft tissue injuries alone respectively in both dogs and cats.

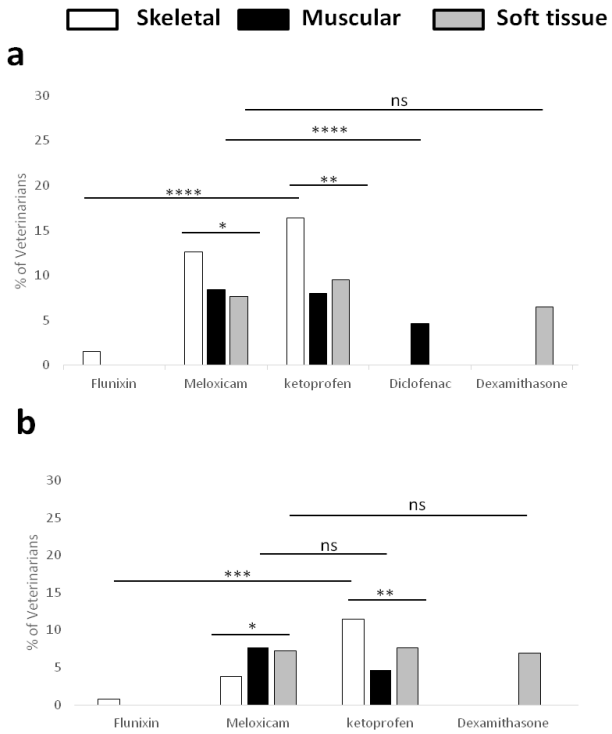

Figure 2 Use of analgesics in different tissues affected. Different analgesics used in skeletal, muscular and soft tissues injuries are presented in dogs (a) and cats (b). In dogs, ketoprofen was used the most skeletal tissue injuries followed by meloxicam (a). Both the drugs were used equally for muscular and soft tissue injuries. However, in cats, meloxicam was used in most cases of muscular injuries although ketoprofen was used for skeletal tissue conditions (b). Statistical analysis by Kruskal-Wallis test except muscular (b) which was analysed by Mann Whitney test. p*<0.05, **<0.01, ***<0.001, ****<0.0001, ns: not significant.

Analgesic use against different degrees of pain

The results of the current study revealed that ketoprofen ($p<0.0001$) was the only analgesic used for pain relief irrespective of the severity. Dexamethasone was frequently used ($p<0.0001$) in both dogs and cats when the pain is severe (Figure 3). The moderate pain symptoms were treated with ketoprofen followed by meloxicam though the difference was not statistically significant. Few practitioners suggest ketoprofen even in the absence of pain signs.

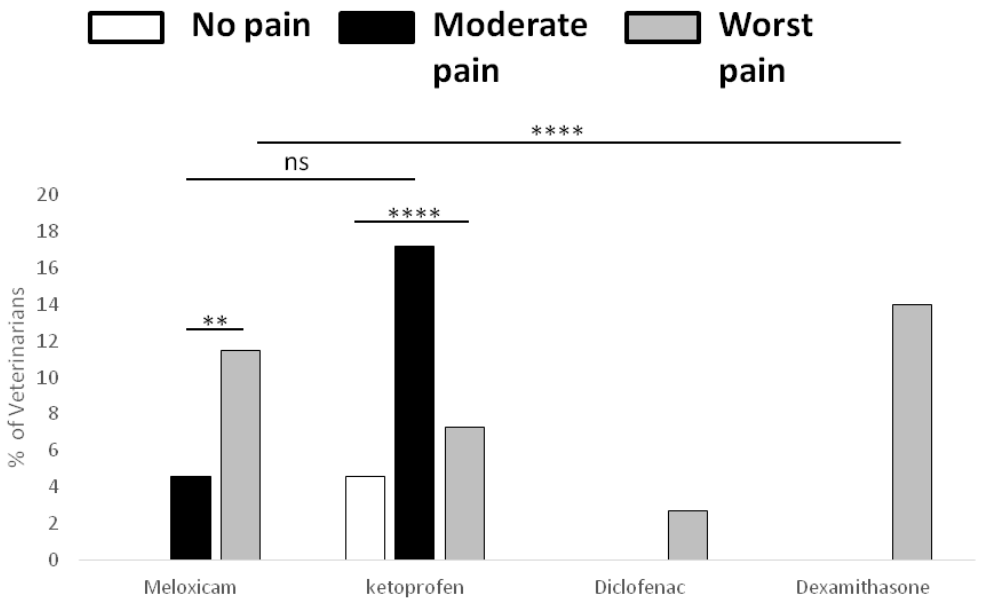

Figure 3 Analgesic uses in different degrees of pain. No analgesics were used in patients with no symptoms of pain. Dexamethasone was used in the most cases of worst pain followed by meloxicam. However, in the cases of moderate pain ketoprofen was the drug of choice in most of the veterinarians. Statistical analysis by Kruskal-Wallis test (Ketoprofen and Worst pain) and Mann Whitney test (Meloxicam and Moderate pain). p**<0.01, ****<0.0001, ns: not significant.

Duration of treatment with analgesics

In dogs, a three days schedule ($p<0.0001$) with ketoprofen ($p<0.0001$), meloxicam ($p<0.001$) and dexamethasone ($p<0.05$) was followed by most of the veterinarians in the current study (Figure 4a). In cats, the scenario is similar except dexamethasone which was used without maintaining a specific duration ($p>0.05$) (Figure 4b). The less frequently used analgesics were prescribed for three or more than three day treatment.

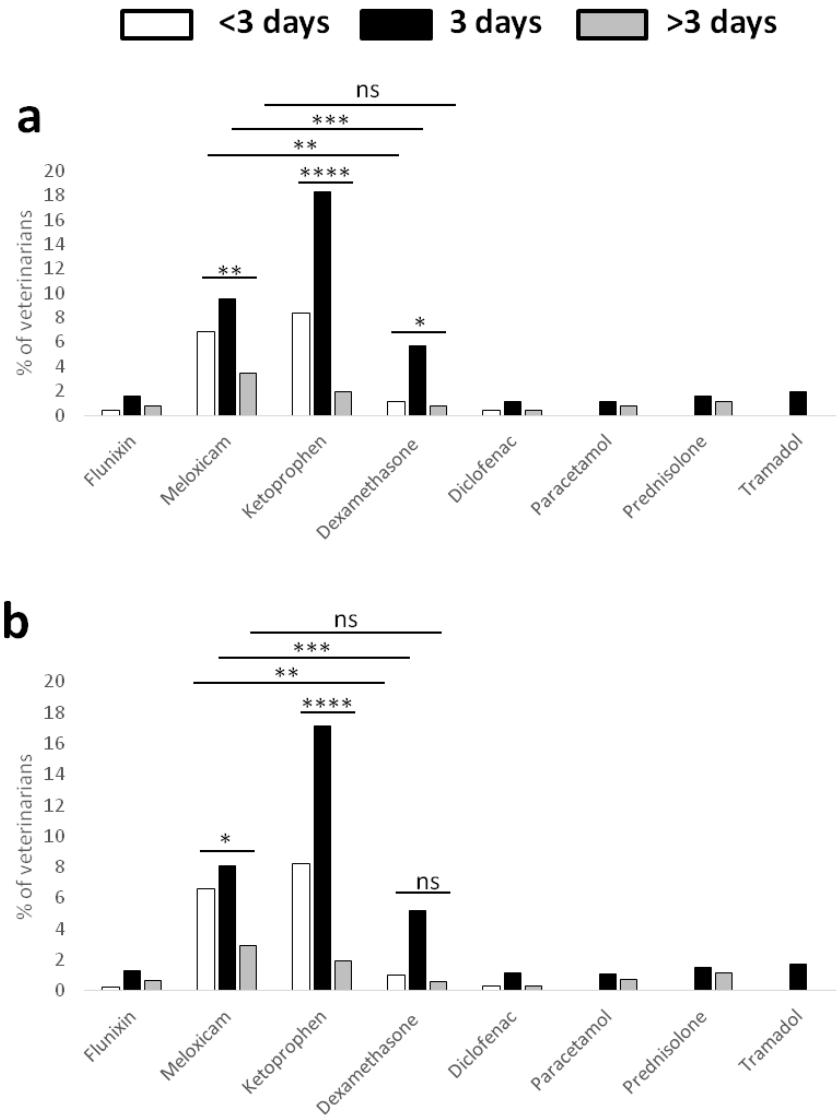

Figure 4 Analgesics used for number of days in dogs and cats. The duration of analgesic therapy is presented for dogs (a) and cats (b). In dogs, meloxicam, kotoprofen and dexamethasone were used for a schedule of three days with few cases of longer duration (a). The scenario is similar in cats (b). However, paracetamol, prednisolone and tramadol were never used for less than three days. Statistical analysis by Kruskal-Wallis test except >3 days of b which was analysed by ANOVA. p*<0.05, **<0.01, ***<0.001, ****<0.0001, ns: not significant.

Analgesic use with/without H2 blockers

H2 blockers are used to reduce side-effects of analgesics. In the current study, we observed that most of the veterinarians used H2 blockers in association with meloxicam, ketoprofen, flunixin, diclofenac sodium and tramadol (Figure 5). The practitioners did not care about the use of H2 blockers when prescribed metamisole, salicylic acid, paracetamol and dexamethasone.

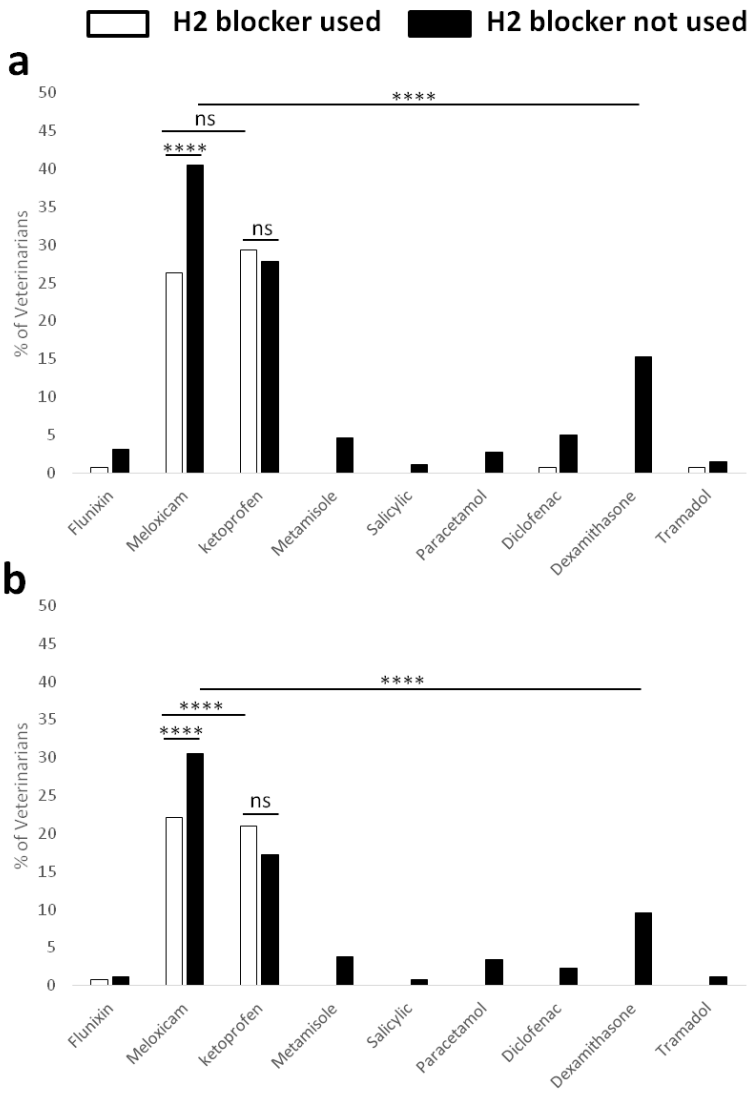

Figure 5 Analgesics used in adjunction with H2 blockers. H2 blockers were used in dogs (a) and cats (b) association with analgesics are presented. In both dogs and cats, most cases were treated with meloxicam without H2 blockers whereas half of the veterinarians used it during ketoprofen. The vets did not choice it during medication with metamisole, salicylic acid, paracetamol and dexamethasone at all (a, b). Statistical analysis by Mann Whitney test except H2 blocker used or not used in Meloxicam, Ketoprofen and Dexamethasone of a and b which were analysed by Kruskal-Wallis test. p****<0.0001, ns: not significant.

Efficacy and side-effects of analgesics

We have collected information on the side-effects observed in the dogs and cats after medication with analgesics and observed that vomition was the mostly seen (Figure 6). Vomition ($p<0.05$) and diarrhea ($p<0.05$) were the prime side-effects of meloxicam and ketoprofen recorded.

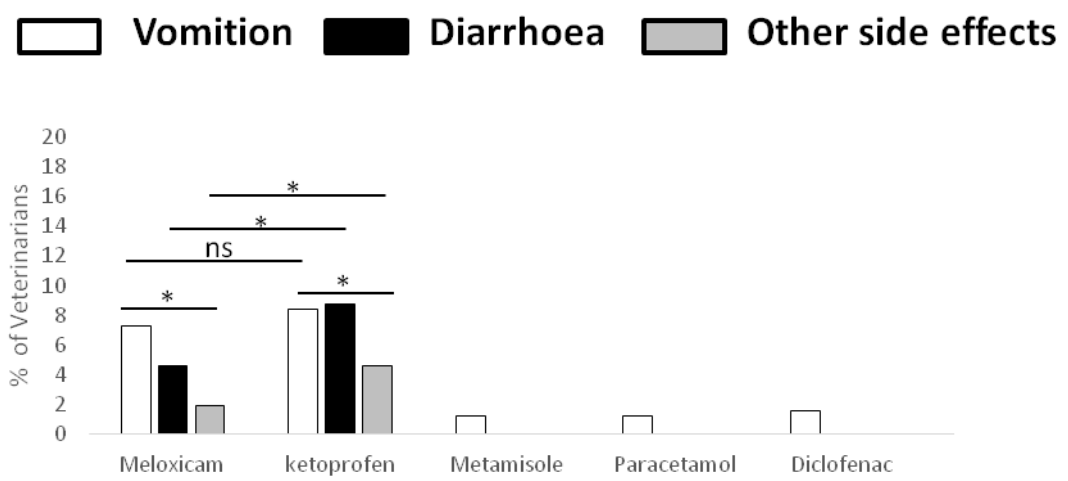

Figure 6 Side effects of analgesics observed. Vomition and diarrhoea were the most common side effects observed during meloxicam and ketoprofen medication. Moreover, vomition was noticed during pain management with metamisole, paracetamol and diclofenac sodium. Statistical analysis by Kruskal-Wallis test (Meloxicam and Ketoprofen), Mann Whitney test (Vomition of Meloxicam and Ketoprofen) and unpaired t test (Diarrhoea of Meloxicam and Ketoprofen, and Others). p*<0.05, ns: not significant.

Discussion

Analgesics are used to combat pain when it is severe and unbearable. These drugs are also prescribed during perioperative and surgical procedures. Different analgesics have specific actions on different tissues injured and duration of pain management needed. Although not all analgesic drugs are free from side effects, these are frequently prescribed in pet dogs and cats as pain relief. However, it is worth beneficial to know the specific analgesic use for specific cases for effective pain management by minimizing the adverse effects. The present study was designed to investigate the current scenario of analgesics use in pet dogs and cats for pain management by registered veterinarians in Bangladesh. We also have collected information of the veterinarians interviewed to analyse the current situation of veterinary practice with special emphasis on pet dogs and cats. It was observed that the veterinary practice on pets is still dominated by the young male vets with experiences of less than 10 years that is completely different to developed countries like Canada (Hewson et al. 2006). These indicate that most of the older and experienced vets are still practice on farm animals and poultry. Moreover, most of the vets interviewed have graduated from CVASU followed by BAU. This might be due to fact that the study was based in Chattogram. The study also revealed that the majority of vets use their academic knowledge during prescribing analgesics rather than drug information leaflets and internet enlightening use of memory of undergraduate and postgraduate knowledge in practice.

The results of the study revealed that meloxicam and ketoprofen are the first and subsequent choice among NSAIDs followed by dexamethasone as steroid and tramadol as opioid by most of the veterinarians as pain relief in both dogs and cats (Figure 1 and 2). The drugs were used mostly in medical cases with however; meloxicam, ketoprofen and dexamethasone only were used in surgical cases which are similar to the trends in France and Brazil (Hugonnard et al. 2004, Lorena et al. 2014). The least prescribed analgesics were flunixin, metamisole, salicylic acid and prednisolone. In South Africa, the drugs most commonly used for the treatment of pain

in general practice are flunixin meglumine followed by phenylbutazone with the least common are aspirin, pethidine, ibuprofen, xylazine and meloxicam (Joubert 2001). Although paracetamol and diclofenac sodium are not used in dogs and cats as they are toxic and cause serious illness, a number of veterinarians still suggest these drugs in different medical conditions.

Meloxicam and ketoprofen were the primarily prescribed analgesic for skeletal, muscular and soft tissue injuries reported in the present study (Figure 3). The most commonly used opioids and NSAIDs are tramadol and meloxicam reported by Brazilian and Colombian veterinarians surveys (Morales-Vallecilla et al. 2019). This differs from some North American and European surveys, where butorphanol and/or buprenorphine appear to be the most popular opioid (Capner et al. 1999). Several other studies in different countries reported similar trends of analgesics use in different orthopaedic and soft tissue surgeries (Deneuche et al. 2004, Hugonnard et al. 2004, Lafuente et al. 2005, Leece et al. 2005, Hewson et al. 2006). The study also reported that dexamethasone was used by majority of the vets when pain is the worst. Hermeto et al. (2017) reported epidural injection of dexamethasone in association with lignocaine significantly extends the postoperative analgesia after ovariohysterectomy in dogs. The current study also revealed that most of the analgesics were used in dogs and cats were for maximum three-days and for longer duration in few cases (Figure 4). Luna et al. (2007) reported that meloxicam has lowest frequency of gastrointestinal adverse effects in long-term use compared to flunixin and ketoprofen. Alves et al. (2018) also reported effective management of chronic back pain in dogs by using dexamethasone upto four-months. However, Joubert (2001) recommended single application of analgesics to minimize the side effects of analgesics. In another study, Varrassi et al. (2017) suggested tramadol in the management of moderate to severe acute pain in different tissue injury.

Histamin (H)-2 blockers are used to prevent adverse effects of NSAIDs and treatment of peptic ulcer disease and its complications (Lukas , Savarino et al. 2018, Scally et al. 2018). In the current study, none of the vets used this drug when prescribed

metamisole, salicylic acid, paracetamol and in some cases of diclofenac sodium and tramadol (Figure 5). Whereas, Hunt et al. (2015) clearly stated that H2 blocker should be used to prevent the side effects of NSAIDs. Moreover, diarrhea and vomiting were recorded as the mostly observed side effects following meloxocam and ketoprofen medication with diarrhea after metamisole, paracetamol and diclofenac sodium (Figure 6). Monteiro-Steagall et al. (2013) reported similar results in dogs in 35 studies. However, Luna et al. (2007) reported gastro-intestinal bleeding following long-term medication with carprofen, etodolac, flunixin meglumine, ketoprofen, and meloxicam in dogs.

Limitations

In this study, a total of 262 vets were interviewed where most of them graduated from CVASU and BAU. It would be better if we could involve more vets from different institutions as currently, there are more than 10 veterinary schools in Bangladesh. Moreover, detail information on analgesic use in specific medical and surgical cases, different age and health condition of pets with doses and exact duration, and finally, the details of adverse effects could improve the study.

Conclusions

The current study revealed that meloxicam is the mostly recommended analgesic in pain management of dogs and cats irrespective of tissues injured followed by ketoprofen. However, dexamethasone is the primary choice when the pain is severe. This study will convey message to the pet practitioners in suggesting appropriate pain relief having least side effects.

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Appendix 1

Questionnaire used during data collection

Use of analgesics in dogs and cats by Bangladeshi veterinarians

Information of veterinarian

Name:	Designation:	Date:
Working organisation:	Working district:	
School of graduation:		
Year of graduation:		
Source of knowledge about analgesics:		

Information on use of analgesics

Analgesics	Species		Nature of the case		Tissue affected			Severity of pain	Dose	Frequency	Route (i/m, i/v, s/c)	Duration	H2 blocker used			Efficacy	Side effects		
	Dog	Cat	Medicine	Surgery	Skeletal	Muscular	Soft tissue	(Zero pain, 10=worst pain)	(mg/kg BW)			(days)	Ranitidine	Omeprazole	Others (....	(0=not effective, 5=excellent)	Vomiting	Diarrhoea	Others (....
NSAIDS																			
Flunixin																			
Meloxicam																			
Ketoprofen																			
Metamisole																			
Salicylic acid																			
Aspirin																			
Paracetamol																			
Ibuprofen																			
Diclofenac Na																			
Others (.....)																			
Steroids																			
Dexamethasone																			
Prednisolone																			
Dexa + Pred																			
Others (.....)																			
Opioids																			
Butorphanol																			
Meperidine																			
Tramadol																			
Others (.....)																			

Appendix 2

Statistical analysis

Figure 1.a Meloxicam: Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	109.4
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	0.0061
Exact or approximate P value?	Exact
P value summary	**
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	3870 , 3390
Mann-Whitney U	1560

Figure 1.a Ketoprofen: Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	40.34
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	<0.0001
Exact or approximate P value?	Exact
P value summary	****
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	3819 , 2736
Mann-Whitney U	1083

Figure 1.a Meloxicam, Ketoprofen (Dog): Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	179.8
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	0.2437
Exact or approximate P value?	Exact
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	3720 , 3540
Mann-Whitney U	1710

Figure 1.a Meloxicam, Ketoprofen (Cat): Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	51.49
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	<0.0001
Exact or approximate P value?	Exact
P value summary	****
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	3094 , 2366
Mann-Whitney U	988

Figure 1.a Dexamethasone: Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	11.13
P value	0.0038
Passed normality test (alpha=0.05)?	No
P value summary	**

Mann Whitney test	
P value	0.0169
Exact or approximate P value?	Exact
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	277.5 , 187.5
Mann-Whitney U	67.50

Figure 1.b Meloxicam: Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	69.00
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	0.0026
Exact or approximate P value?	Exact
P value summary	**
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	2444 , 2021
Mann-Whitney U	893

Figure 1.b Ketoprofen: Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	78.24
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	0.2368
Exact or approximate P value?	Exact
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	899 , 812
Mann-Whitney U	377

Figure 1.b Dexamethasone: Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	11.76
P value	0.0028
Passed normality test (alpha=0.05)?	No
P value summary	**

Mann Whitney test	
P value	0.0902
Exact or approximate P value?	Exact
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	148.5 , 104.5
Mann-Whitney U	38.50

Figure 1.b Meloxicam, Ketoprofen (Dog): Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	26.89
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	<0.0001
Exact or approximate P value?	Exact
P value summary	****
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	2656 , 1810
Mann-Whitney U	681.5

Figure 1.a Meloxicam, Ketoprofen (Cat): Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	32.27
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	0.0002
Exact or approximate P value?	Exact
P value summary	***
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	1691 , 1235
Mann-Whitney U	494

Figure 1.c Meloxicam: Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	27.12
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	0.0463
Exact or approximate P value?	Exact
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	418 , 323
Mann-Whitney U	133

Figure 1.c Ketoprofen: Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	20.53
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	<0.0001
Exact or approximate P value?	Exact
P value summary	****
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	958.5 , 526.5
Mann-Whitney U	148.5

Figure 1.c Dexamethasone: Normality test and Unpaired t test

Test for normal distribution	
D'Agostino & Pearson test	
K2	3.672
P value	0.1594
Passed normality test (alpha=0.05)?	Yes
P value summary	ns

Unpaired t test	
P value	0.1340
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.732, df=6

Figure 1.c Meloxicam, Ketoprofen (Dog): Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	11.50
P value	0.0032
Passed normality test (alpha=0.05)?	No
P value summary	**

Mann Whitney test	
P value	0.0243
Exact or approximate P value?	Exact
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	648 , 837
Mann-Whitney U	270

Figure 1.c Meloxicam, Ketoprofen (Cat): Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	30.23
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	0.2222
Exact or approximate P value?	Exact
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	224 , 182
Mann-Whitney U	77

Figure 2.a Meloxicam: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	8.560
P value	0.0138
Passed normality test (alpha=0.05)?	No
P value summary	*
Number of values	36

Kruskal-Wallis test	
P value	0.0045
Exact or approximate P value?	Approximate
P value summary	**
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	10.82
Data summary	
Number of treatments (columns)	3
Number of values (total)	48

Figure 2.a Ketoprofen: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	25.25
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****
Number of values	48

Kruskal-Wallis test	
P value	0.0045
Exact or approximate P value?	Approximate
P value summary	**
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	10.82
Data summary	
Number of treatments (columns)	3
Number of values (total)	48

Figure 2.a Skeletal tissue: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	173.1
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****
Number of values	48

Table Analyzed	Data 2
Kruskal-Wallis test	
P value	<0.0001
Exact or approximate P value?	Approximate
P value summary	****
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	27.16
Data summary	
Number of treatments (columns)	3
Number of values (total)	48

Figure 2.a Muscular tissue: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	23.47
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****
Number of values	24

Table Analyzed	Data 2
Kruskal-Wallis test	
P value	<0.0001
Exact or approximate P value?	Approximate
P value summary	****
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	13.58
Data summary	
Number of treatments (columns)	3
Number of values (total)	24

Figure 2.a Soft tissue: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	11.13
P value	0.0038
Passed normality test (alpha=0.05)?	No
P value summary	**
Number of values	30

Table Analyzed	Data 2
Kruskal-Wallis test	
P value	0.0892
Exact or approximate P value?	Approximate
P value summary	ns
Do the medians vary signif. (P < 0.05)?	No
Number of groups	3
Kruskal-Wallis statistic	4.833
Data summary	
Number of treatments (columns)	3
Number of values (total)	30

Figure 2.b Meloxicam: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	8.969
P value	0.0113
Passed normality test (alpha=0.05)?	No
P value summary	*
Number of values	24

Table Analyzed	Data 6
Kruskal-Wallis test	
P value	0.0430
Exact or approximate P value?	Approximate
P value summary	*
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	6.295
Data summary	
Number of treatments (columns)	3
Number of values (total)	24

Figure 2.b Ketoprofen: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	14.62
P value	0.0007
Passed normality test (alpha=0.05)?	No
P value summary	***
Number of values	36

Table Analyzed	Data 6
Kruskal-Wallis test	
P value	0.0090
Exact or approximate P value?	Approximate
P value summary	**
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	9.418
Data summary	
Number of treatments (columns)	3
Number of values (total)	36

Figure 2.b Skeletal tissue: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	2492
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****
Number of values	36

Table Analyzed	Data 6
Kruskal-Wallis test	
P value	0.0001
Exact or approximate P value?	Approximate
P value summary	***
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	18.15
Data summary	
Number of treatments (columns)	3
Number of values (total)	36

Figure 2.b Muscular tissue: Normality test and Mann Whitney test

D'Agostino & Pearson test	
K2	9.705
P value	0.0078
Passed normality test (alpha=0.05)?	No
P value summary	**

Mann Whitney test	
P value	0.2000
Exact or approximate P value?	Exact
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	80 , 56
Mann-Whitney U	20

Figure 2.b Soft tissue: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	36.79
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****
Number of values	24

Table Analyzed	Data 6
Kruskal-Wallis test	
P value	0.5929
Exact or approximate P value?	Approximate
P value summary	ns
Do the medians vary signif. (P < 0.05)?	No
Number of groups	3
Kruskal-Wallis statistic	1.045
Data summary	
Number of treatments (columns)	3
Number of values (total)	24

Figure 3.Meloxicam: Normality test and Mann Whitney test

D'Agostino & Pearson test	
K2	7.387
P value	0.0249
Passed normality test (alpha=0.05)?	No
P value summary	*

Mann Whitney test	
P value	0.0046
Exact or approximate P value?	Exact
P value summary	**
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	108 , 192
Mann-Whitney U	30

Figure 3.Ketoprofen: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	966.1
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****
Number of values	54

Kruskal-Wallis test	
P value	<0.0001
Exact or approximate P value?	Approximate
P value summary	****
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	21.64
Data summary	
Number of treatments (columns)	3
Number of values (total)	54

Figure 3.Moderate pain: Normality test and Mann Whitney test

D'Agostino & Pearson test	
K2	16.49
P value	0.0003
Passed normality test (alpha=0.05)?	No
P value summary	***

Mann Whitney test	
P value	0.4615
Exact or approximate P value?	Exact
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	45.50 , 59.50
Mann-Whitney U	17.50

Figure 3.Worst pain: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	779.4
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****
Number of values	72

Kruskal-Wallis test	
P value	<0.0001
Exact or approximate P value?	Approximate
P value summary	****
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	4
Kruskal-Wallis statistic	29.99

Figure 4.a Meloxicam: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	19.18
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****
Number of values	30

Kruskal-Wallis test	
P value	0.0047
Exact or approximate P value?	Approximate
P value summary	**
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	10.73

Figure 4.a Ketoprofen: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	854.4
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****
Number of values	54

Kruskal-Wallis test	
P value	<0.0001
Exact or approximate P value?	Approximate
P value summary	****
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	28.54

Figure 4.a Dexamethasone: Normality test and Kruskal-Wallis test

D'Agostino & Pearson test	
K2	32.32
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****
Number of values	18

Kruskal-Wallis test	
P value	0.0364
Exact or approximate P value?	Exact
P value summary	*
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	6.800

Figure 4.a <3 Days: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	7.387
P value	0.0249
Passed normality test (alpha=0.05)?	No
P value summary	*
Number of values	24

Kruskal-Wallis test	
P value	0.0025
Exact or approximate P value?	Approximate
P value summary	**
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	11.98

Figure 4.a 3 Days: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	228.5
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****
Number of values	54

Kruskal-Wallis test	
P value	0.0002
Exact or approximate P value?	Approximate
P value summary	***
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	17.46

Figure 4.a >3 Days: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	5.409
P value	0.0669
Passed normality test (alpha=0.05)?	Yes
P value summary	ns
Number of values	9

Kruskal-Wallis test	
P value	>0.9999
Exact or approximate P value?	Exact
P value summary	ns
Do the medians vary signif. (P < 0.05)?	No
Number of groups	3
Kruskal-Wallis statistic	1.143

Figure 4.b Meloxicam: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	6.333
P value	0.0422
Passed normality test (alpha=0.05)?	No
P value summary	*
Number of values	24

Kruskal-Wallis test	
P value	0.0114
Exact or approximate P value?	Approximate
P value summary	*
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	8.944

Figure 4.b Ketoprofen: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	911.2
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****
Number of values	51

Kruskal-Wallis test	
P value	<0.0001
Exact or approximate P value?	Approximate
P value summary	****
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	26.39

Figure 4.b Dexamethasone: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	15.52
P value	0.0004
Passed normality test (alpha=0.05)?	No
P value summary	***
Number of values	15

Kruskal-Wallis test	
P value	0.2008
Exact or approximate P value?	Exact
P value summary	ns
Do the medians vary signif. (P < 0.05)?	No
Number of groups	3
Kruskal-Wallis statistic	4.667

Figure 4.b <3Days: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	7.387
P value	0.0249
Passed normality test (alpha=0.05)?	No
P value summary	*
Number of values	24

Kruskal-Wallis test	
P value	0.0025
Exact or approximate P value?	Approximate
P value summary	**
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	11.98

Figure 4.b 3Days: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	865.6
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****
Number of values	51

Kruskal-Wallis test	
P value	0.0002
Exact or approximate P value?	Approximate
P value summary	***
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	16.61

Figure 4.b >3Days: Normality test and ANOVA test

Test for normal distribution	
D'Agostino & Pearson test	
K2	5.409
P value	0.0669
Passed normality test (alpha=0.05)?	Yes
P value summary	ns
Number of values	9

ANOVA summary	
F	0.5000
P value	0.6297
P value summary	ns
Significant diff. among means (P < 0.05)?	No
R square	0.1429

Figure 5.a Meloxicam: Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	28.09
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	<0.0001
Exact or approximate P value?	Exact
P value summary	****
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	1340 , 1900
Mann-Whitney U	520

Figure 5.a Meloxicam, Ketoprofen (Dog): Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	96.75
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	0.4912
Exact or approximate P value?	Exact
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	884.5 , 826.5
Mann-Whitney U	391.5

Figure 5.a H2 blocker (Meloxicam, Ketoprofen): Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	78.24
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	0.2368
Exact or approximate P value?	Exact
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	812 , 899
Mann-Whitney U	377

Figure 5.a H2 blocker not used (Meloxicam, Ketoprofen & Dexamethasone): Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	132.9
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Kruskal-Wallis test	
P value	<0.0001
Exact or approximate P value?	Approximate
P value summary	****
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	35.82

Figure 5.b Meloxicam: Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	874.7
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	<0.0001
Exact or approximate P value?	Exact
P value summary	****
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	510 , 1320
Mann-Whitney U	45

Figure 5.b Ketoprofen: Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	49.75
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	0.2308
Exact or approximate P value?	Exact
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	440 , 380
Mann-Whitney U	170

Figure 5.b H2 blocker (Meloxicam, Ketoprofen): Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	835.6
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	<0.0001
Exact or approximate P value?	Exact
P value summary	****
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	240 , 580
Mann-Whitney U	30

Figure 5.b H2 blocker not used (Meloxicam, Ketoprofen & Dexamethasone): Normality test and Kruskal -Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	1368
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Kruskal-Wallis test	
P value	<0.0001
Exact or approximate P value?	Approximate
P value summary	****
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	31.51

Figure 6. Meloxicam: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	27.21
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Kruskal-Wallis test	
P value	0.0101
Exact or approximate P value?	Approximate
P value summary	*
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	9.200

Figure 6. Ketoprofen: Normality test and Kruskal-Wallis test

Test for normal distribution	
D'Agostino & Pearson test	
K2	14.64
P value	0.0007
Passed normality test (alpha=0.05)?	No
P value summary	***

Kruskal-Wallis test	
P value	0.0101
Exact or approximate P value?	Approximate
P value summary	*
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	9.200

Figure 6. Vomition (Meloxicam, Ketoprofen): Normality test and Mann Whitney test

Test for normal distribution	
D'Agostino & Pearson test	
K2	42.97
P value	<0.0001
Passed normality test (alpha=0.05)?	No
P value summary	****

Mann Whitney test	
P value	>0.9999
Exact or approximate P value?	Exact
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
Sum of ranks in column A,B	64 , 72
Mann-Whitney U	28

Figure 6. Diarrhoea (Meloxicam, Ketoprofen): Normality test and Unpaired t test

Test for normal distribution	
D'Agostino & Pearson test	
K2	4.879
P value	0.0872
Passed normality test (alpha=0.05)?	Yes
P value summary	ns

Unpaired t test	
P value	0.0192
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=2.646, df=14

Figure 6. Other: Normality test and Unpaired t test

Test for normal distribution	
D'Agostino & Pearson test	
K2	3.350
P value	0.1873
Passed normality test (alpha=0.05)?	Yes
P value summary	ns

Unpaired t test	
P value	0.0400
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=2.449, df=8