FACULTY OF VETERINARY MEDICINE
accredited by EAEVE

IEPERSE DIERENARTSENKRING 24/11/2021

CHRONISCHE OA PIJN BIJ DE HOND

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OSTEOARTHRITIS: EEN COMPLEXE AANDOENING

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‘Osteoarthritis is een progressieve degeneratieve gewrichtsaandoening (DJD)’

- komt voor bij meer dan 20% van alle honden
- meest belangrijke chronische aandoening bij de hond
- symptomatische behandeling, geen genezing

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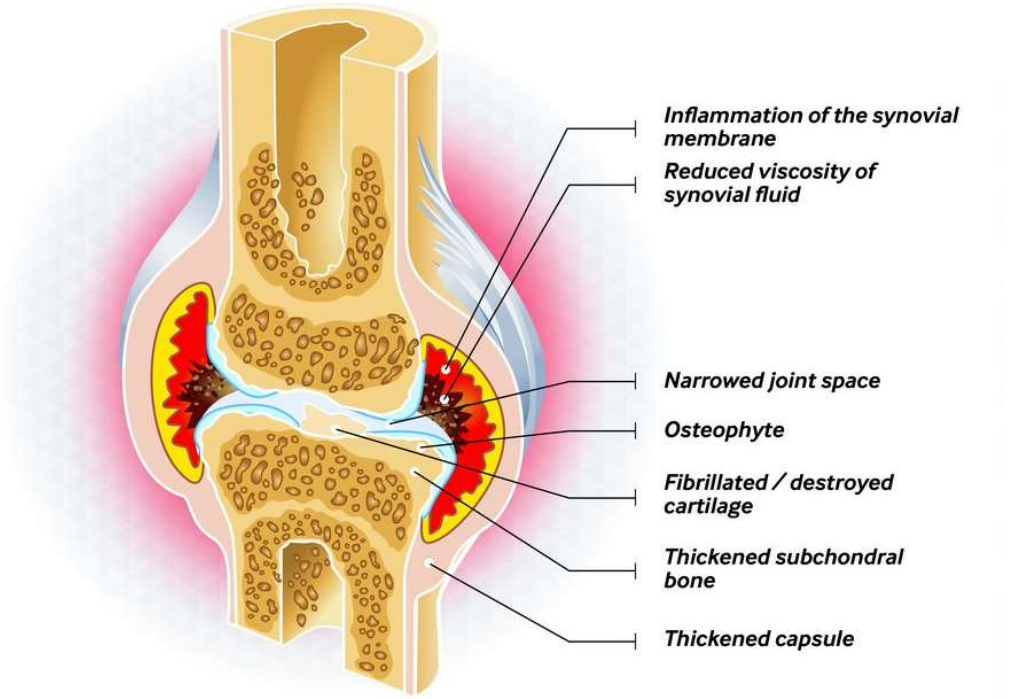
- Alle structuren vh gewricht zijn betrokken:
  - verlies & verminderde functie van het gewrichtskraakbeen
  - bot remodellering (osteofyten vorming)
  - verdikking van het gewrichtskapsel
  - ontsteking van de synoviale membraan



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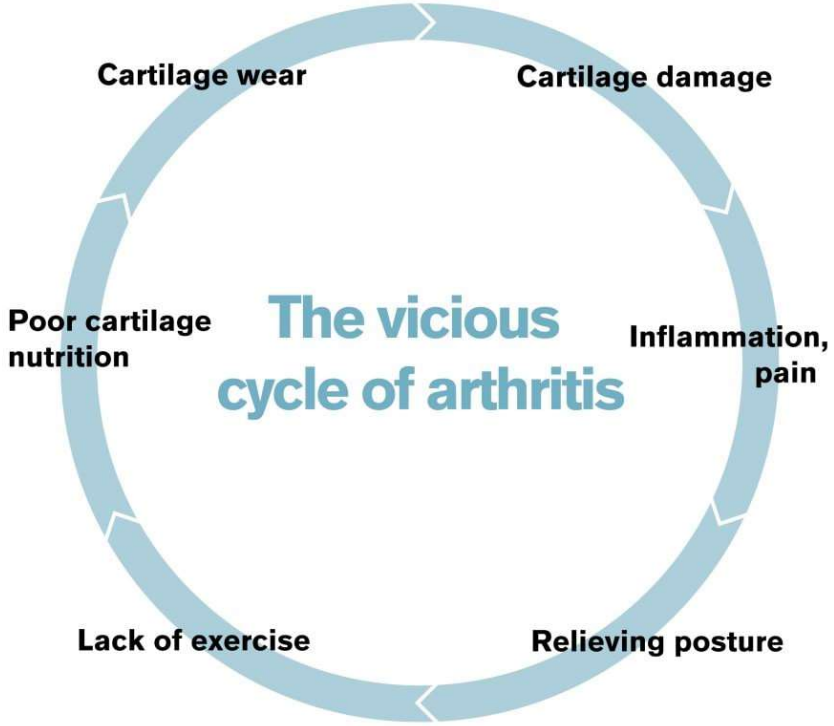
- kenmerken van Osteoarthritis:

  - arthropathie met kraakbeenschade
  - ontsteking!!
  - pijn!!!
  - functionele achteruitgang
  - structurele achteruitgang



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- risicofactoren voor OA:

  - 3035 gescreende artikels
  - 62 finaal geselecteerd als valabel
  - 98% beschreven minstens 1 risicofactor
  - 31% beschreven OA verminderde risicofactoren
  - **6** voornaamste risicofactoren weerhouden

Anderson, K. L., Zulch, H., O'Neill, D. G., Meeson, R. L., & Collins, L. M. (2020). Risk factors for canine osteoarthritis and its predisposing arthropathies: A systematic review. *Frontiers in Veterinary Science*, *7*(April), 1–16.

- voornaamste risicofactoren:
  - lichaamsgewicht
    overgewicht
  - leeftijd
    oud, maar ook jong
  - ras
    specifieke
    gewrichtsaandoeningen
  - genetica
    rasgerelateerd
  - lichaamsbouw
    rasgerelateerd
  - sterilisatie
    significant (bias*)

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Anderson, K. L., Zulch, H., O'Neill, D. G., Meeson, R. L., & Collins, L. M. (2020). Risk factors for canine osteoarthritis and its predisposing arthropathies: A systematic review. *Frontiers in Veterinary Science*, *7*(April), 1–16.

- bijkomende risicofactoren:
  - dieet en voeding
    - grote rassen & snelle groei
  - geboortemaand
    - weer & daglengte: bewegingspatroon
  - externe factoren tijdens 1ste levensfase
  - bewegingsniveau
  - type van beweging als pup

- Symptomen van OA:
  - opgezette gewrichten
  - spierafname
  - PIJN, wat zich bij de hond uit in:
    - minder interesse in wandeling of trager wandelen
    - moeilijk trappen doen of in/uit de auto springen
    - vertraagd rechtkomen uit zit of lig positie
    - algemeen ‘stijve’ indruk tijdens stappen
    - manken
    - likken aan gewrichten
    - gedragsveranderingen (meer of minder aandacht vragen)

OSTEOARTHRITIS & PIJN

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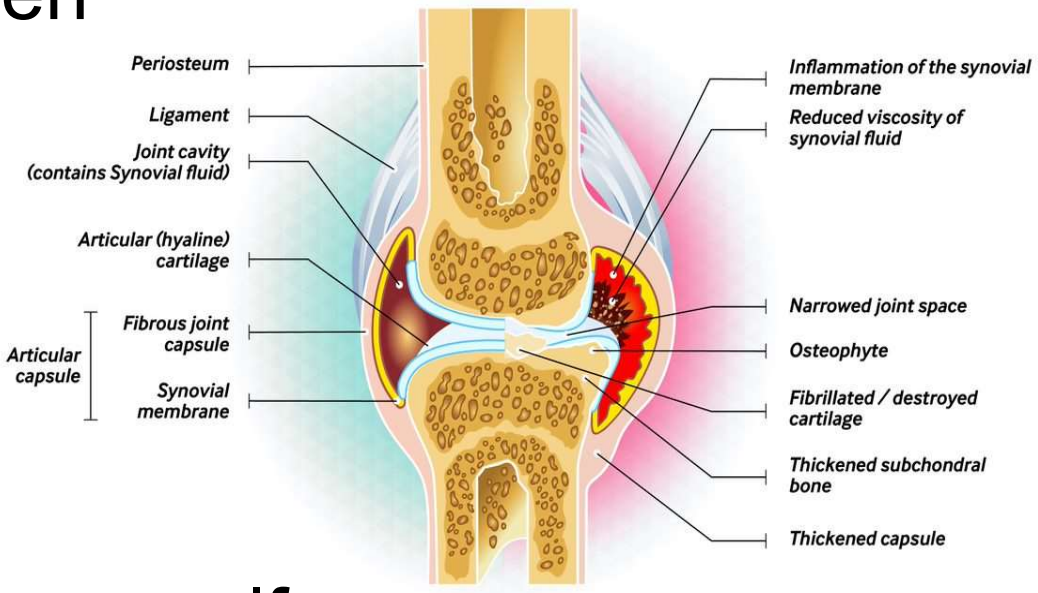
- Waar komt de pijn bij OA vandaan?
  - subchondrale bot & receptoren
  - gewrichtskapsel
  - aangetaste ligamenten
  - synoviaal vocht
  - gewrichtsinstabiliteit



  - <u>niet</u> van het gewrichtskraakbeen zelf

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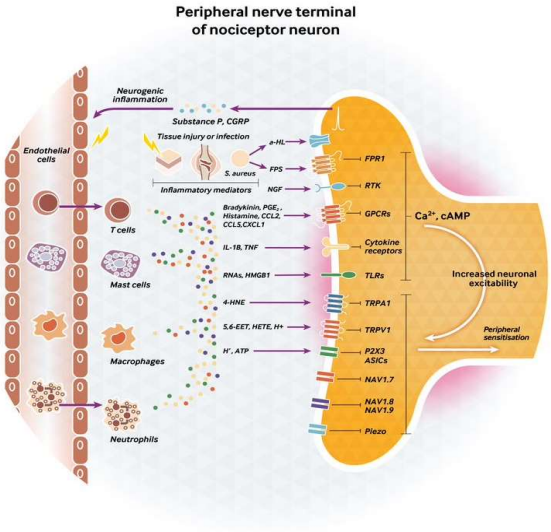
- Gewrichtsletsel geïnduceerde ontstekingsreactie
  - ° ‘ontstekingssoep’ of een chemische pijnstimulus:
    - Cytokines
    - Prostaglandines (PGE_2) & NGF
    - Bradykinin
    - Upregulatie van COX-enzymes
    - Activatie synoviocytes met vorming van degraderende enzymen



°Perifere sensitizatie & overmatige nociceptor activatie

Synovia rijk aan nociceptoren

Nociceptieve pijn

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weefselschade

vrijstelling ontstekingsmediatoren

verlagen drempelwaarde activatie nociceptoren
activatie “slapende nociceptoren”

°perifere sensitizatie

primaire hyperalgesie

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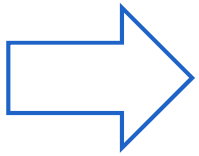
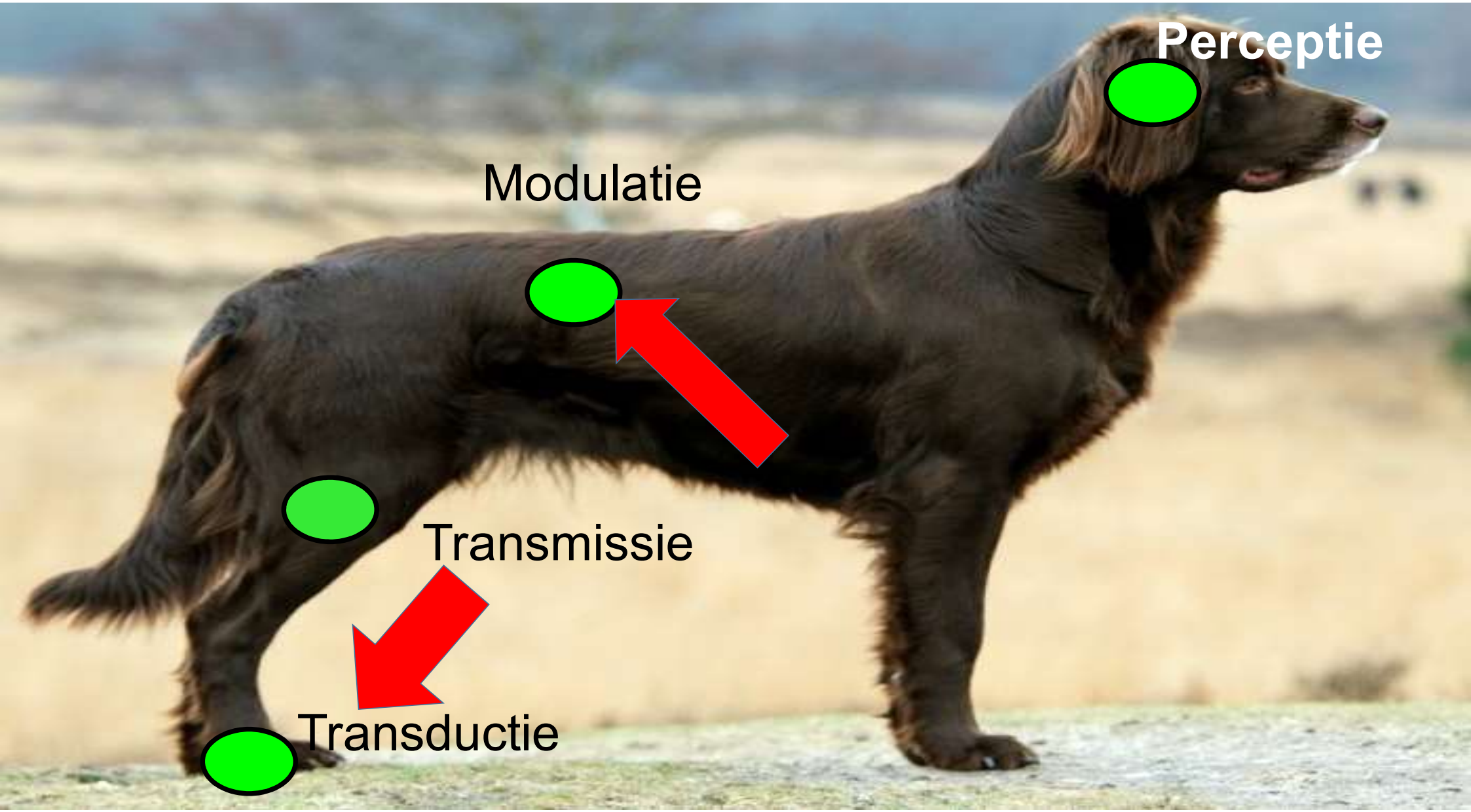
Perifere sensitisatie

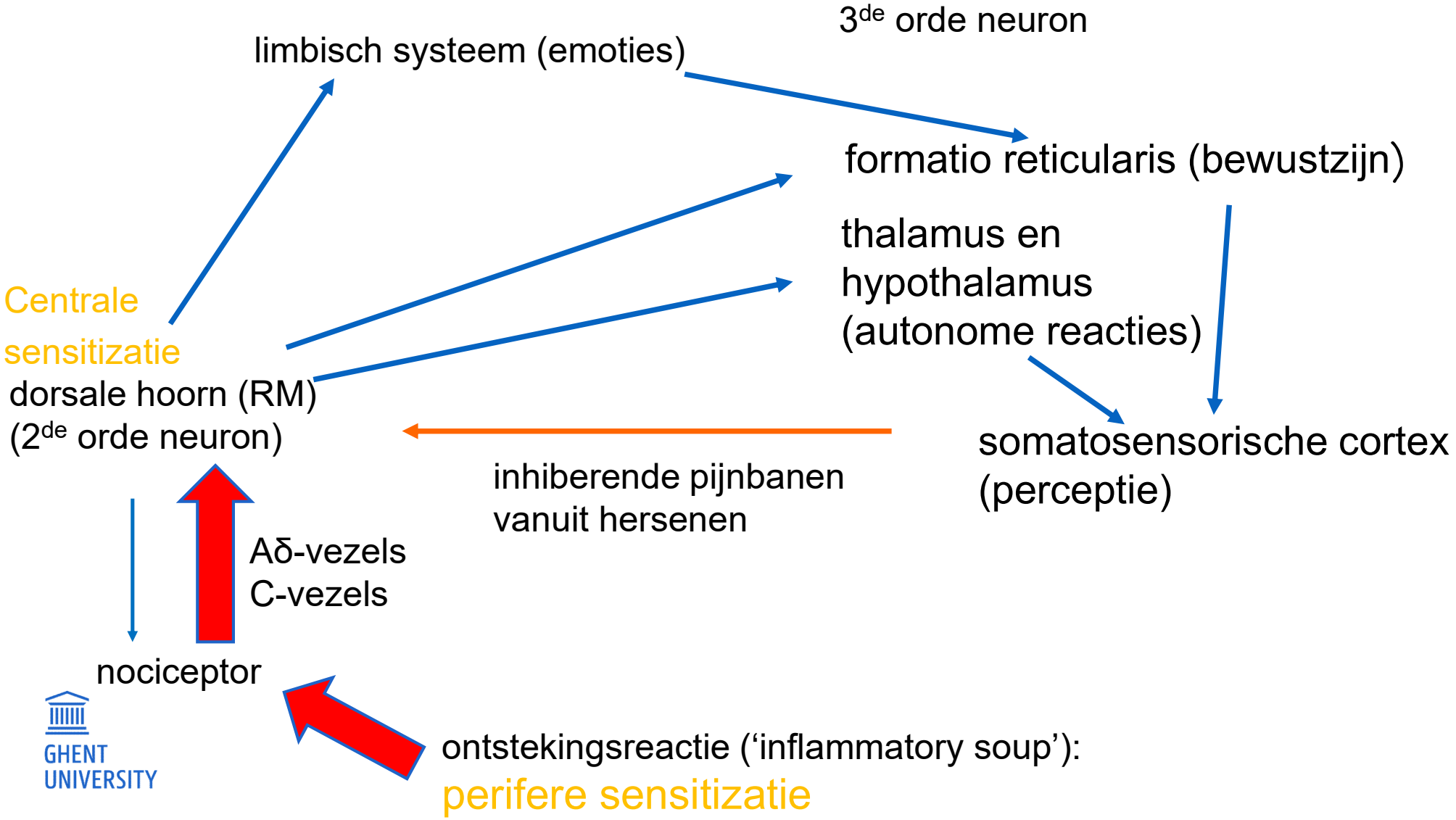
- nociceptie door ontstekingsmediatoren
  - prostaglandines
  - NGF
  - bradykinin
  - histamine

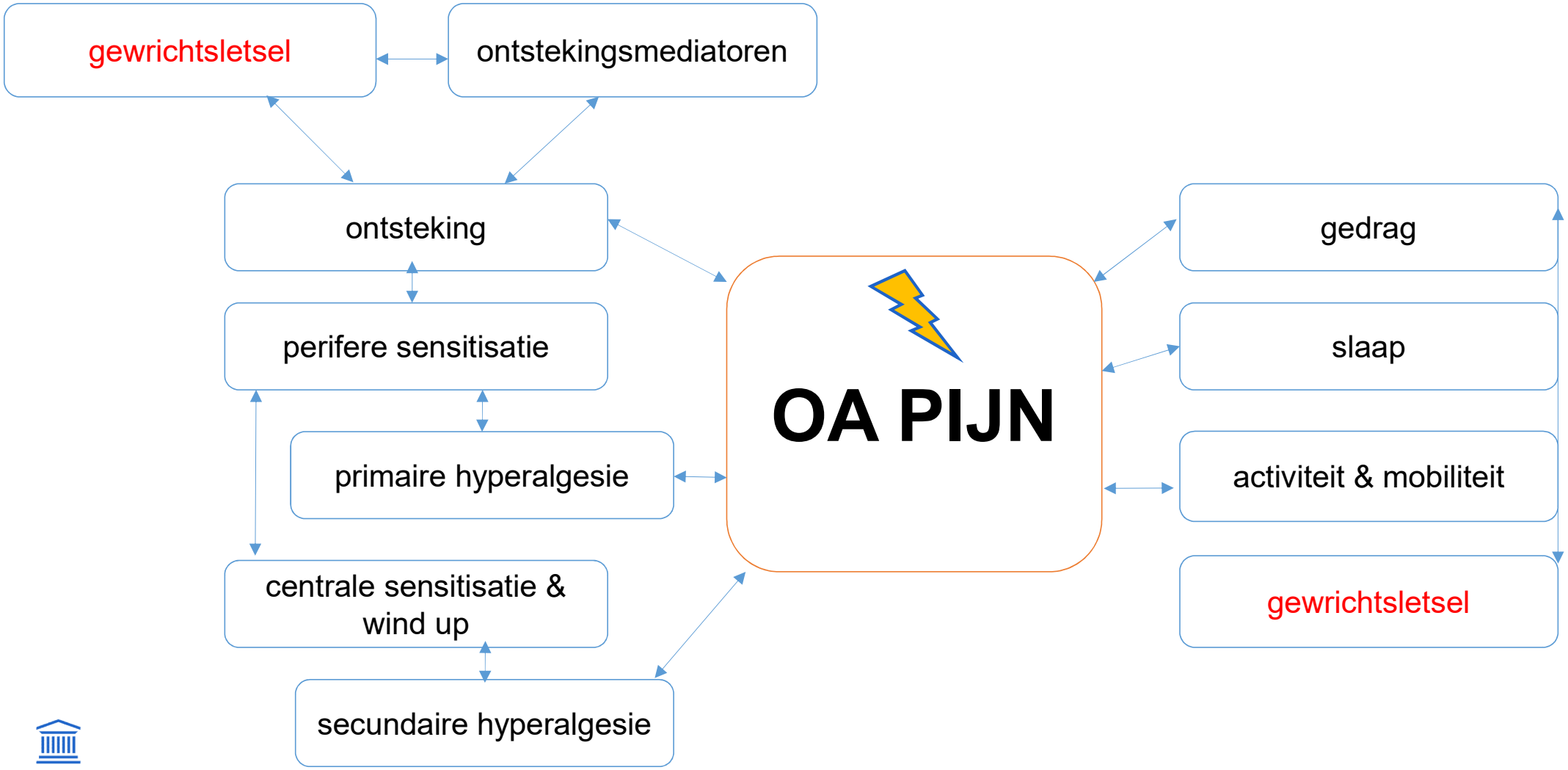


Centrale sensitisatie

- veranderingen in de exciteerbaarheid vd dorsale hoorn in het RM
- verhoogde exciteerbaarheid 2de en 3de orde neuron
- pijnverwerking is veranderd


Perceptie
Modulatie
Transmissie
Transductie


3de orde neuron
limbisch systeem (emoties)
formatio reticularis (bewustzijn)
thalamus en
hypothalamus
(autonome reacties)
Centrale
sensitizatie
dorsale hoorn (RM)
(2de orde neuron)
somatosensorische cortex
(perceptie)
inhiberende pijnbanen
vanuit hersenen
Aδ-vezels
C-vezels
nociceptor
ontstekingsreactie (‘inflammatory soup’):
perifere sensitizatie



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CHRONISCHE PIJN

"Persisterende pijn voor een periode langer dan 3 tot 6 maanden of die langer aanwezig blijft dan de verwachte helingstijd van een niet-kwaadaardig letsel. De oorzaak van de pijn kan, maar kan ook niet meer aanwezig zijn."

Chronische pijn is altijd geassocieerd met subtiele tot heel duidelijke gedragsveranderingen.

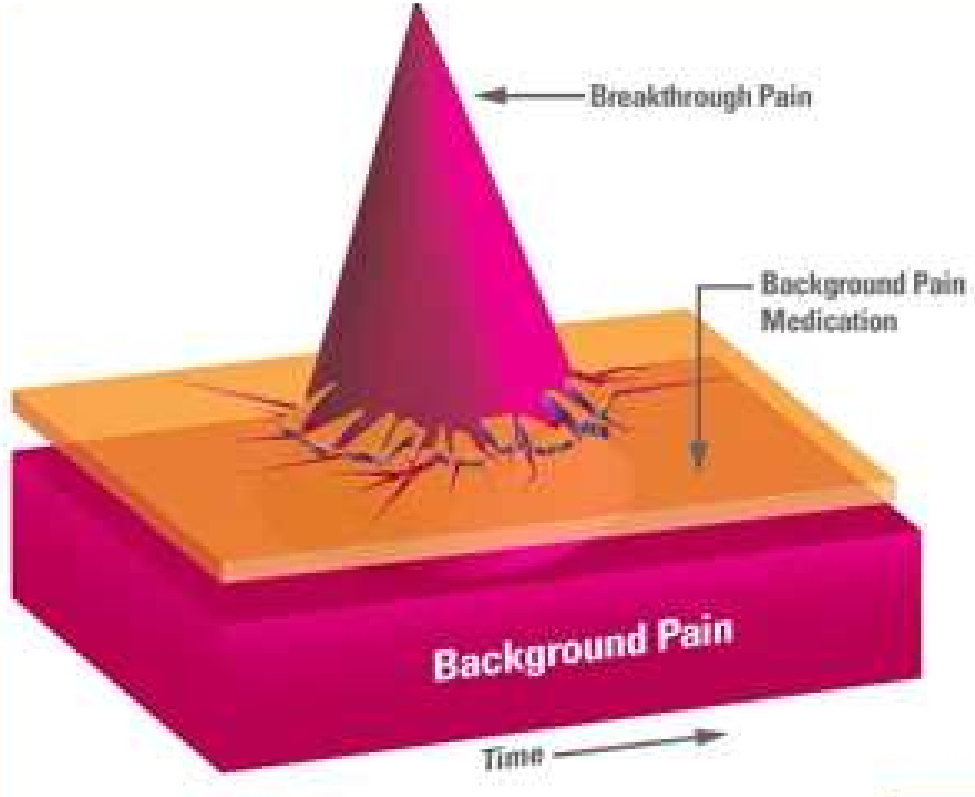
CONCLUSIE PATHOFYSIOLOGIE CHRONISCHE PIJN

- nociceptor functie en transmissie (perifere sensitisatie):
  - verhoogde sensitiviteit van nociceptoren
  - verhoogde hoeveelheid neurotransmitters en receptoren
  - activatie van ‘slapende’ nociceptoren

- gewijzigde verwerking van nociceptieve input thv het ruggemerg (centrale sensitisatie en neuroplasticiteit):
  - celdood van inhibitorische neuronen
  - synaptische remodelering met versterkte transmissie
  - verhoogde sensitiviteit van neuronen in de pijn pathway
  - aanmaak van meer connecties met second-order neuronen in de dorsale hoorn
  - recruitment van zenuwen die normaal niet reageren op pijnlijke stimuli

‘BREAKTHROUGH PAIN’

‘Een abrupte, kortstondige & intense pijn, dewelke de pijnbestrijding die de chronische pijn normaal gezien controleert doorbreekt’



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VIER OORZAKEN ‘BREAKTHROUGH PAIN’

1. onvoldoende therapietrouw
2. ‘end of dose’ analgesie niveau
3. verandering van routine (toename in volume/intensiteit van beweging)
4. progressie van de aandoening

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‘BREAKTHROUGH PAIN’ VOORKOMEN

- continue analgesie is noodzakelijk
  - ontstekingsmediatoren blijven hyperalgesie uitlokken
  - BTP is een aanleiding tot °centrale sensitisatie

- haalbaar doseringsinterval analgesie
  - therapietrouw

- multimodale analgesie aanpak

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HERKENNEN VAN CHRONISCHE OA PIJN

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HERKENNING VAN CHRONISCHE PIJN

- gebaseerd op samenwerking met de eigenaar vh dier
  - zeer belangrijk om deze te motiveren
  - subjectieve beoordeling

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HERKENNING VAN CHRONISCHE PIJN

- zeer moeilijk te herkennen en te kwantificeren
- uitgebreide samenwerking met de eigenaar!
  - kent het normale gedrag van het dier het best
  - kan het dier observeren in een stressvrije omgeving
  - gedetailleerde vragenlijst gebaseerd op herkennen van gedragsveranderingen en gerelateerd aan beoordeling van de levenskwaliteit

HERKENNING VAN CHRONISCHE PIJN

- eerste consultatie bij de dierenarts:
  - gedetailleerde anamnese en observatie (overgang rust-activiteit)
  - klinisch onderzoek
  - locomotorisch onderzoek
    - pijnlijk gebied = laatste dat wordt onderzocht
    - start met lichte aanraking (allodynia)
    - diepe palpatie van spieren en gewrichten

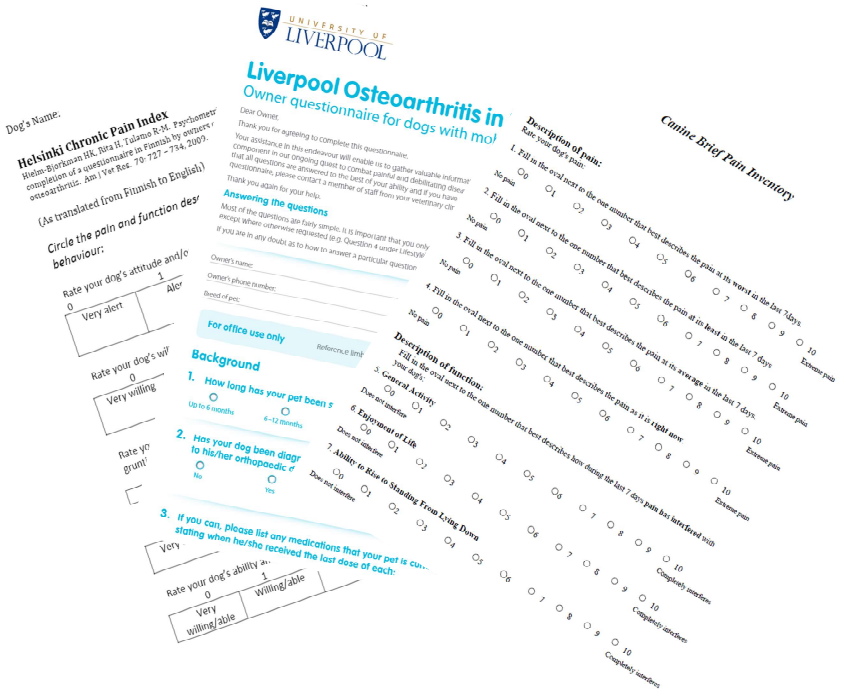
PIJN SCOREN

- Objectief:
  - drukplaatanalyse
  - meting op 1 tijdstip in een vreemde omgeving
  - slechts 1 parameter

- Subjectief:
  - gevalideerde vragenlijsten voor de eigenaar
  - numerieke score op specifieke vragen
  - totaalscore wordt afgewogen tov vorige score
  - typisch 14 dagen interval tussen 2 scores
  - belangrijke tools om efficiëntie behandeling te bepalen

PIJNSCORESYSTEMEN VOOR OA

- Canine Brief Pain Inventory (CBPI)
- Helsinki Chronic Pain Index
- Liverpool OA in Dogs (LOAD)



CANINE BRIEF PAIN INVENTORY

- Pain Severity Score:
  - 4 vragen over pijnintensiteit
    - score 0 (geen pijn) – score 10 (extreme pijn)
- Pain Interference Score:
  - 6 vragen over pijninterferentie met typische functie
    - score 0 (geen interferentie) – score 10 (complete interferentie)
- Overall quality of life score
  - descriptief: slecht tot excellent

CANINE BRIEF PAIN INVENTORY

Description of pain:
Rate your dog's pain:

1. Fill in the oval next to the one number that best describes the pain at its **worst** in the last 7days.

○0 ○1 ○2 ○3 ○4 ○5 ○6 ○ 7 ○ 8 ○ 9 ○ 10

No pain Extreme pain

2. Fill in the oval next to the one number that best describes the pain at its **least** in the last 7 days

○0 ○1 ○2 ○3 ○4 ○5 ○6 ○ 7 ○ 8 ○ 9 ○ 10

No pain Extreme pain

3. Fill in the oval next to the one number that best describes the pain at its **average** in the last 7 days.

○0 ○1 ○2 ○3 ○4 ○5 ○6 ○ 7 ○ 8 ○ 9 ○ 10

No pain Extreme pain

4. Fill in the oval next to the one number that best describes the pain as it is **right now**.

○0 ○1 ○2 ○3 ○4 ○5 ○6 ○ 7 ○ 8 ○ 9 ○ 10

No pain Extreme pain

CANINE BRIEF PAIN INVENTORY

Description of function:

Fill in the oval next to the one number that best describes how during the last 7 days **pain has interfered** with your dog's:

5. **General Activity**

○0 ○1 ○2 ○3 ○4 ○5 ○6 ○ 7 ○ 8 ○ 9 ○ 10

Does not interfere — Completely interferes

6. **Enjoyment of Life**

○0 ○1 ○2 ○3 ○4 ○5 ○6 ○ 7 ○ 8 ○ 9 ○ 10

Does not interfere — Completely interferes

7. **Ability to Rise to Standing From Lying Down**

○0 ○1 ○2 ○3 ○4 ○5 ○6 ○ 7 ○ 8 ○ 9 ○ 10

Does not interfere — Completely interferes

8. **Ability to Walk**

○0 ○1 ○2 ○3 ○4 ○5 ○6 ○ 7 ○ 8 ○ 9 ○ 10

Does not interfere — Completely interferes

9. **Ability to Run**

○0 ○1 ○2 ○3 ○4 ○5 ○6 ○ 7 ○ 8 ○ 9 ○ 10

Does not interfere — Completely interferes

10. **Ability to Climb Stairs, Curbs, Doorsteps, etc.**

○0 ○1 ○2 ○3 ○4 ○5 ○6 ○ 7 ○ 8 ○ 9 ○ 10

Does not interfere — Completely interferes

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CANINE BRIEF PAIN INVENTORY

Overall impression:

11. Fill in the oval next to the one number that best describes your dog's overall quality of life over the last 7 days.

○ Poor ○ Fair ○ Good ○ Very Good ○ Excellent

Brown, D. C., Boston, R. C., Coyne, J. C., & al, (2008). Ability of the canine brief pain inventory to detect response to treatment in dogs with osteoarthritis. Journal of the American Veterinary Medical Association, 233(8), 1278–1283.

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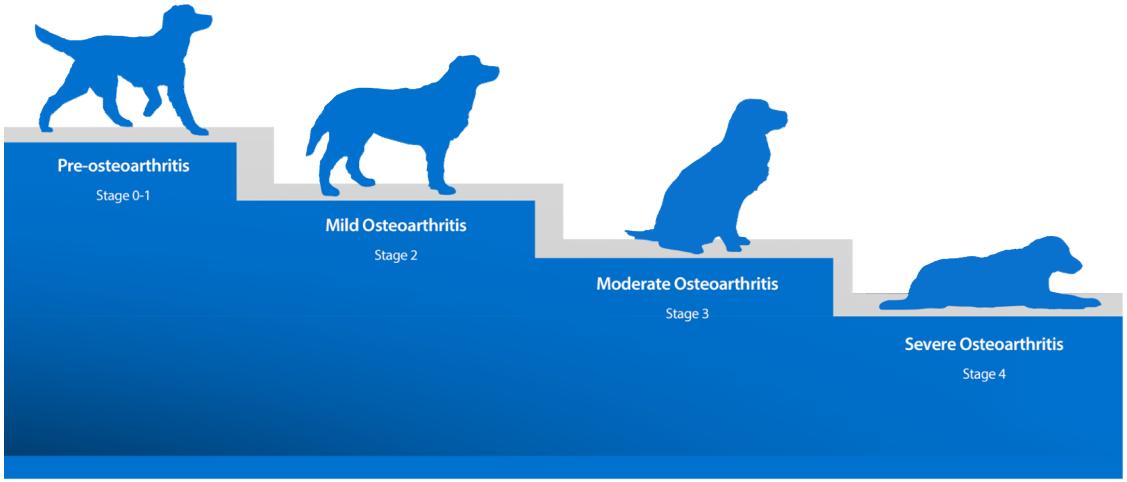
COAST TOOL

- Canine Osteoarthritis Staging Tool (interactieve PDF)

1. Scoor het comfort van de hond
    - Inclusie van een ‘clinical metrology instrument’
2. Scoor de toestand van het gewricht
3. OA stagering wordt gegeven



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BEHANDELEN VAN CHRONISCHE OA PIJN

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BEHANDELING VAN CHRONISCHE OA PIJN

- succes is afhankelijk van:
  - herkenning & scoren van de pijn
  - behandelen van de pijn
  - goede communicatie met de eigenaars over de verwachtingen
  - overwegen van multimodale opties
  - preventie van ‘breakthrough pain’

- gebaseerd op “trial and error”

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BEHANDELING VAN CHRONISCHE OA PIJN

- factoren die de behandelingskeuze beïnvloeden:
  - type en ernst van de pijn
  - stadium aandoening
  - temperament van de patiënt
  - therapietrouw (eigenaar)
  - breakthrough pain
  - behandelingscascade
  - aanwezigheid van neveneffecten
  - kostprijs
  - beschikbaarheid en wil om bijkomende therapieën op te starten

BEHANDELING VAN CHRONISCHE OA PIJN

- gebaseerd op een multimodale aanpak

- klassieke analgetica:
  - NSAID's & piprants

- bijkomende behandelingen:
  - analgetica:
    - paracetamol
    - amantadine
    - gabapentine
    - NMDA-receptor antagonisten
    - monoclonale antistoffen tegen NGF
    - …
  - niet-medicamenteuze behandeling:
    - fysiotherapie & beweging
    - gewichtscontrole
    - nutritionele ondersteuning
    - cannabidiol
    - Intra-articulaire injectie:
      - hyaluronzuur (HA)
      - platelet rich plasma (PRP)
      - mesenchymale stamcellen (MSM)
      - …

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BEHANDELING VAN CHRONISCHE OA PIJN

adjuvant(s)*: kan zowel gewichtscontrole, gecontroleerde beweging, nutritionele ondersteuning, acupunctuur, intra-articulaire opties & fysiotherapie includeren

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NSAIDS

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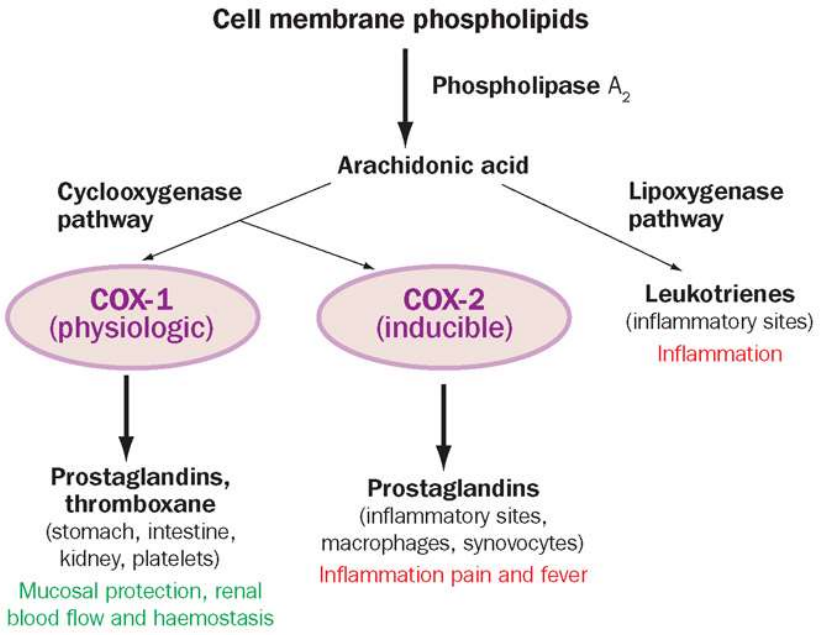
NSAIDS & OA

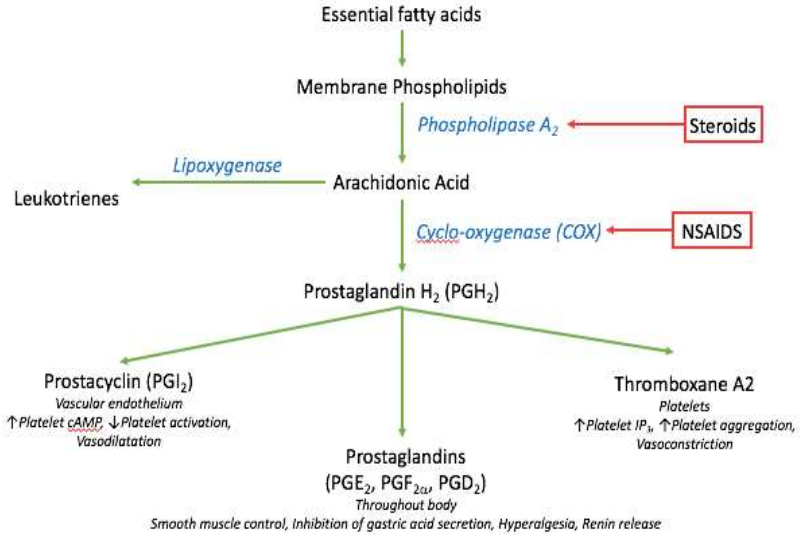
- NSAIDs zijn de hoeksteen van de behandeling van OA, mits er geen tegenindicaties zijn voor hun gebruik.
- Langdurige, efficiënte analgesie zonder sedatie of respiratoire onderdrukking (in tegenstelling tot opioïden)
- Het gebruik van een ‘geschikt’ NSAID is aangewezen (zie verder)

NSAIDS

- Niet steroïdale ontstekingsremmers
- Inhibitie van COX-enzymen
- Grijpen aan op de TRANSDUCTIE in de pijnpathway:
  - Remmen de vorming van prostaglandines
  - Voorkomen de vorming van onder andere PGE2
  - Verminderen nociceptie en primaire hyperalgesie
  - Ook belangrijke neveneffecten mogelijk

NSAIDS





- werkingsmechanisme:
  - ontstekingsremmend, analgetisch, anti-endotoxisch, antithrombotisch, antispasmotisch & antipyretisch
  - directe spinale actie (blokkeren van hyperalgesia)

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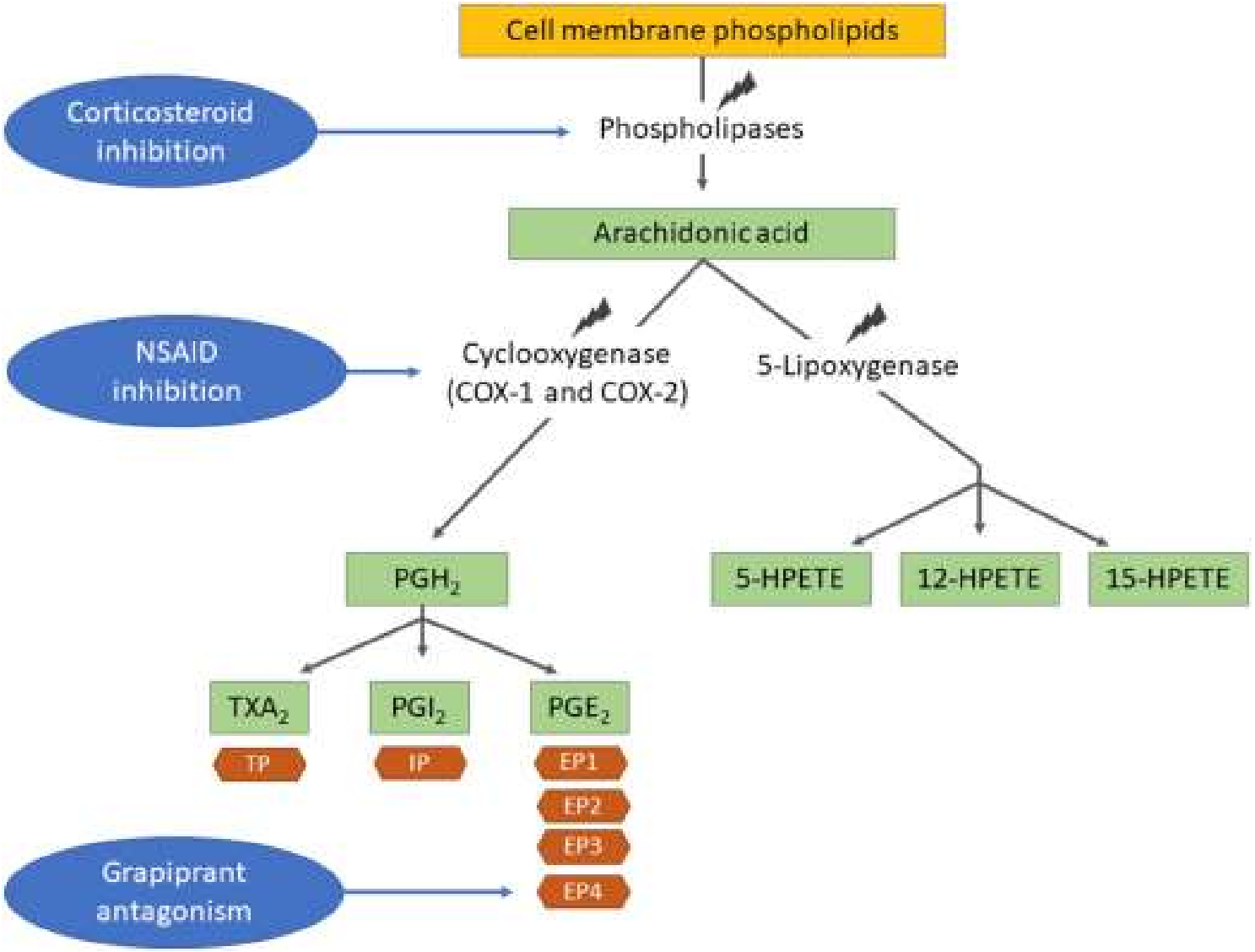

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Monteiro & Steagall 2020 Antiinflammatory Drugs. Vet Clin Small Anim 49 (2019) 993–1011.

COX FYSIOLOGISCHE EFFECTEN

- COX-1: constitutief enzyme

  - PG's hebben homeostatische functies
    - Vasculaire hemostase (TXA2 & PGI2)
      - TXA2: VC en plaatjesaggregatie
      - PGI2: VD en anti-thrombose

COX FYSIOLOGISCHE EFFECTEN

- COX-1: constitutief enzyme

  - PG's hebben homeostatische functies
    - Maagbescherming (PGE2)
      - Verminderde maagzuursecretie
      - Verbeterde maagdoorbloeding
      - Mucusbescherming van de maagmucosa
    - Nierfunctie
      - VD vooral tijdens periodes van hypotensie
      - GFR vrijwaren

COX FYSIOLOGISCHE EFFECTEN

- COX-2: voornamelijk induceerbaar enzyme

  - Komt vooral tot expressie na weefselschade
  - Productie van ontstekingsmediatoren
    - PG's, endotoxines, cytokines en groeifactoren
    - °Perifere sensitisatie van de pijnpathway
    - °Centrale sensitisatie van de pijnpathway (later)
  - ook een constitutieve rol oa in de nierfunctie en herstel van GI-ulcer!!!!

BEHANDELING - NSAIDS

- preferentieel COX2 inhibitie
- MAAR, er moet een balans blijven tussen de COX2/COX1 inhibitie

The safety of nonsteroidal antiinflammatory drugs is not a simple matter of cyclooxygenase selectivity. It is misleading to consider that the type of COX inhibition (ie, COX-2 selectivity and/or COX-1sparing) is the only factor regulating NSAID safety. Both COX-1 and COX-2 have physiologic functions that are impaired during NSAID therapy. Any NSAID has the potential to cause adverse effects and contraindications must be respected before drug administration. However, preferential and selective COX-2 inhibitors have a superior safety profile compared with nonselective COX inhibitors.

Luna SPL, Basilio AC, Steagall PVM, et al. Evaluation of adverse effects of long-termoral administration of carprofen, etodolac, flunixin meglumine, ketoprofen, and meloxicam indogs. Am J Vet Res. 2007;68(3):258-264.

BEHANDELING – NSAIDS & OA

Drug	Subklasse
Carprofen	**Propionzuur derivaat**
Meloxicam	**Oxicam groep**
Firocoxib	**Coxib groep**
Robenacoxib	**Coxib groep**
Cimicoxib	**Coxib groep**
Mavacoxib	**Coxib groep, maandelijks doseren**
Enflicoxib	**Coxib groep, wekelijks doseren**

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BEHANDELING – NSAIDS & OA

- preferentieel COX-2 inhibitie
  - carprofen
  - meloxicam
    - lange-termijn toediening concentraties (Fe)

- hoog selectieve COX-2 inhibitie (COXIB)
  - enflicoxib (Daxocox®) (Ca, 1x wekelijks)
  - mavacoxib (Trocoxyl®) (Ca, 1x maandelijks)
  - robenacoxib (Onsior®) (Ca and Fe)
  - firoxocib (Previcox®)
  - cimicoxib (Cimalgex®)

BEHANDELING – NSAIDS & OA

NSAIDs voor behandeling van chronische OA pijn bij de hond.

Drug	Dosage form	Dose	Licence duration
Carprofen	20, 50, 100 and 120 mg chewable tablets; 20, 50 and 100 mg tablets	4 mg/kg for seven days, then reduce to 2 mg/kg	No upper limit for duration, although regular veterinary supervision is advised
Meloxicam	1.5 mg/ml oral liquid; 1 and 2.5 mg chewable tablets; oral transmucosal spray	0.2 mg/kg loading dose followed 24 hours later with 0.1 mg/kg once a day. Adjust to lowest effective dose	No upper time limit, although regular veterinary assessment is advised
Cimicoxib	8, 30 and 80 mg chewable tablets	2 mg/kg once a day	Six months for osteoarthritis; beyond this, regular monitoring is required
Ketoprofen	5 and 20 mg tablets	0.25 mg/kg once a day	Up to 30 days, then the patient must be re-examined
Robenacoxib	5, 10, 20 and 40 mg flavoured tablets	1 to 2 mg/kg orally once a day initially and then at the lowest effective dose	No upper time limit at the lowest effective dose
Firocoxib	57 and 227 mg chewable tablets	5 mg/kg orally once a day for osteoarthritis	If used for more than 90 days, the patient requires monitoring
Mavacoxib	6, 20, 30, 75 or 95 mg chewable tablets	2 mg/kg orally, repeated after 14 days and then once monthly. This is not a daily NSAID	Do not exceed seven consecutive doses in a treatment cycle
Daxocox	15, 30, 45, 70, 100 mg chewable tablets	1st dose: 8 mg/kg orally with food 2nd & further doses: 4 mg/kg orally every 7 days This is not a daily NSAID	

NSAIDs voor behandeling van chronische OA pijn bij de kat.

Drug	Dosage form	Dose	Licence duration
Meloxicam	0.5 mg/ml oral solution	0.1 mg/kg oral loading dose once, then 0.05 mg/kg orally once a day	No upper time limit. Discontinue if there is no clinical improvement within 14 days

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BEHANDELING – NSAIDS & OA

- # NSAIDs behoren tot #klassen
- allemaal kunnen ze nevenwerkingen vertonen
- superioriteit tov andere NSAIDs is niet bewezen
- als 1 NSAID niet werkt kan overgeschakeld worden naar een NSAID van een andere klasse
  - respecteer een wash-out periode
    - 4-5 eliminatie half lives = 5-7 dagen
    - langer bij mavacoxib en enflicoxib
  - overweeg toediening gastroprotectiva

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Kukanich, B., Bidgood, T., & Knesl, O. (2012). Clinical pharmacology of nonsteroidal anti-inflammatory drugs in dogs. *Veterinary Anaesthesia and Analgesia*, *39*(1), 69–90. https://doi.org/10.1111/j.1467-2995.2011.00675.x

BEHANDELING - NSAIDS & OA

- Langdurige toediening vereist dikwijls het zoeken naar de laagst effectieve dosis en het langste doseringsinterval
  - Maar dosisreductie minder efficiënt dan continue toediening (meer patiënten vallen uit)
  - Dosisreductie met behoud van efficiëntie is mogelijk (verhinder toediening van <60% van de initiële dosis)

Wernham, B. G. J., Trumpatori, B., Hash, J., Lipsett, J., Davidson, G., Wackerow, P., et al. (2011). Dose Reduction of Meloxicam in Dogs with Osteoarthritis-Associated Pain and Impaired Mobility. J Vet Intern Med, 25(6), 1298–1305.

NSAIDS NEVENEFFECTEN

- Incidentie neveneffecten:
  - geen robuste data beschikbaar over de lange termijn veiligheid van NSAID toediening bij honden.
  - de echte incidentie van neveneffecten is dus onbekend.
  - gebrek aan melding van neveneffecten door de eigenaar
  - sommige neveneffecten worden getolereerd

Hunt, J. R., Dean, R. S., Davis, G. N. D., & Murrell, J. C. (2015). An analysis of the relative frequencies of reported adverse events associated with NSAID administration in dogs and cats in the United Kingdom. *Veterinary Journal*, *206*(2), 183–190. https://doi.org/10.1016/j.tvjl.2015.07.025

NSAIDS NEVENEFFECTEN

- GI-irritatie (braken, (bloederige)diarree), ulceratie & sterfte
- anorexie
- lethargie
- nierinsufficiëntie (komt zelden voor)
- verlengde bloedingstijden door verminderde bloedplaatjesaggregatie (komt zelden voor)

Lawson, A. (2019). Monitoring side effects of long-term NSAID use in dogs with chronic osteoarthritis. *In Practice*, *41*(4), 148–154. https://doi.org/10.1136/inp.l1506

Hunt, J. R., Dean, R. S., Davis, G. N. D., & Murrell, J. C. (2015). An analysis of the relative frequencies of reported adverse events associated with NSAID administration in dogs and cats in the United Kingdom.

NSAIDS NEVENEFFECTEN

- Leverfalen (komt zelden voor)
  - extensieve hepatische klaring
  - Idiosyncratisch hepatotoxicosis (onafhankelijk van de dosis) 1/1000 tot 1/10.000
    - beschreven bij carprofen
    - verhoging van leverenzymen & bilirubine
  - Intrinsiek (dosis afhankelijk)

- Samenvatting NSAIDs:
  - inhibitie van COX enzymes
    - remt homeostatische effecten (GI, renaal, vasculair)
    - ontstekingsremmend & analgetisch
  - analgetische effect is vooral individuafhankelijk
  - risico op neveneffecten bestaat altijd en bij elke NSAID!
  - risico op neveneffecten is individuafhankelijk.

NSAIDS SCREENING

- Het is aan te raden om baseline serumbiochemie nier- & leverwaarden te bepalen alvorens een langdurige NSAID therapie te starten = SCREENING.
- Vervolgens:
  - Op regelmatige basis hercontroles
  - Eigenaars motiveren om neveneffecten op te volgen

Chalifoux, N. V., Kaiman, G., Drobatz, K. J., & Thawley, V. J. (2020). Evaluation of renal and hepatic blood value screening before non-steroidal anti-inflammatory drug administration in dogs. *Journal of Small Animal Practice*, 1–7. https://doi.org/10.1111/jsap.13230

Kukanich, B., Bidgood, T., & Knesl, O. (2012). Clinical pharmacology of nonsteroidal anti-inflammatory drugs in dogs. *Veterinary Anaesthesia and Analgesia*, *39*(1), 69–90. https://doi.org/10.1111/j.1467-2995.2011.00675.x

NSAIDS SCREENING

Chalifoux, N. V., Kaiman, G., Drobatz, K. J., & Thawley, V. J. (2021). Evaluation of renal and hepatic blood value screening before non-steroidal anti-inflammatory drug administration in dogs. *Journal of Small Animal Practice 62*, 12-18.

- Doel?
  - Evalueren van de samenhang tussen signalement, historiek en klinisch onderzoek & afwijkende nier- en leverwaarden voor het toedienen van NSAIDs aan honden

- Welke parameters?
  - Nierinsufficiëntie
    - Ureum & Creatinine
  - Hepatocellulaire schade & galstase
    - Alanine aminotransferase (ALT)
    - Aspartate aminotransferase (AST)
    - Alkaline phosphatase (ALP)

NSAIDS SCREENING

- bevindingen retrospectieve studie (n=81 honden):
  - 67% van de honden >8 jaar had gestegen lever- of nierwaarden
  - 20% van de honden <8 jaar had gestegen lever- of nierwaarden
  - 9% had gestegen nierwaarden
  - 53% had een stijging in minstens 1 leverwaarde
  - 56% had een stijging in minstens 1 nier- of leverwaarde
  - 78% d'artsen schreef toch een NSAID voor ondanks afwijkingen

Chalifoux, N. V., Kaiman, G., Drobatz, K. J., & Thawley, V. J. (2021). Evaluation of renal and hepatic blood value screening before non-steroidal anti-inflammatory drug administration in dogs. *Journal of Small Animal Practice 62*, 12-18.

NSAIDS SCREENING

- bevindingen studie:
  - Een leeftijdsgrens van 8 jaar is een potentiële predictor voor milde afwijkingen in lever- en nierwaarden, die een invloed kunnen hebben op het voorschrijven van NSAIDs.

  - Vooral afwijkende leverwaarden weerhielden d'artsen ervan om NSAIDs voor te schrijven

Chalifoux, N. V., Kaiman, G., Drobatz, K. J., & Thawley, V. J. (2021). Evaluation of renal and hepatic blood value screening before non-steroidal anti-inflammatory drug administration in dogs. *Journal of Small Animal Practice 62*, 12-18.

!CONTRAINDICATIES VOOR NSAIDS!

- geschiedenis van GI aandoeningen
- NSAID intolerantie (ander type NSAID is wel een optie)
- ongecontroleerde nier- of leveraandoeningen
- anemie
- coagulopathie
- hypovolemie of dehydratatie
- hypotensie

!CONTRAINDICATIES VOOR NSAIDS!

- heel erg belangrijk om dierenartsen/eigenaars in te lichten over:
  - welke neveneffecten te verwachten
  - onmiddellijk stoppen met toediening van een NSAID wanneer neveneffecten zich voordoen
  - screening bij lange termijn toediening van NSAIDS
  - follow-up van de patiënt in chronische pijnconsultaties

BEHANDELING - NSAIDS

- strategie om de veiligheid te verhogen:
  - eigenaar moet geschreven instructies voor het verantwoordelijk gebruik van NSAIDs krijgen
  - vermeld steeds te stoppen met de behandeling wanneer er GI problemen optreden
  - doe een klinisch en bloed onderzoek vooraleer je een voorschrift herhaalt
  - geef maagbeschermers aan risico-patiënten

BEHANDELING - NSAIDS

- strategie om de veiligheid te verhogen:
  - niet gebruiken bij GI-aandoeningen, verminderde nierfunctie, stollingsproblemen
  - combineer NOOIT NSAIDs en corticosteroïden
  - combineer geen klassieke NSAIDs met grapiprant
  - wash-out periode van 1-2 weken tussen verschillende NSAIDs (afhankelijk van molecule)

GRAPIPRANT
EEN ATYPISCH NSAID

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BEHANDELING - GRAPIPRANT

- Galliprant 20, 60, 100 mg tabletten
- niet COX-inhiberende ontstekingsremmer
- behoort tot de klasse van de NSAIDs
- behandeling van milde tot matige OA bij de hond
- selectieve PGE_2, EP4 receptor antagonist
  - effecten van PGE_2 op de EP4 receptor
    - vasodilatatie
    - angiogenese
    - synthese van ontstekingsmediatoren

- vermindert nociceptie en ontsteking

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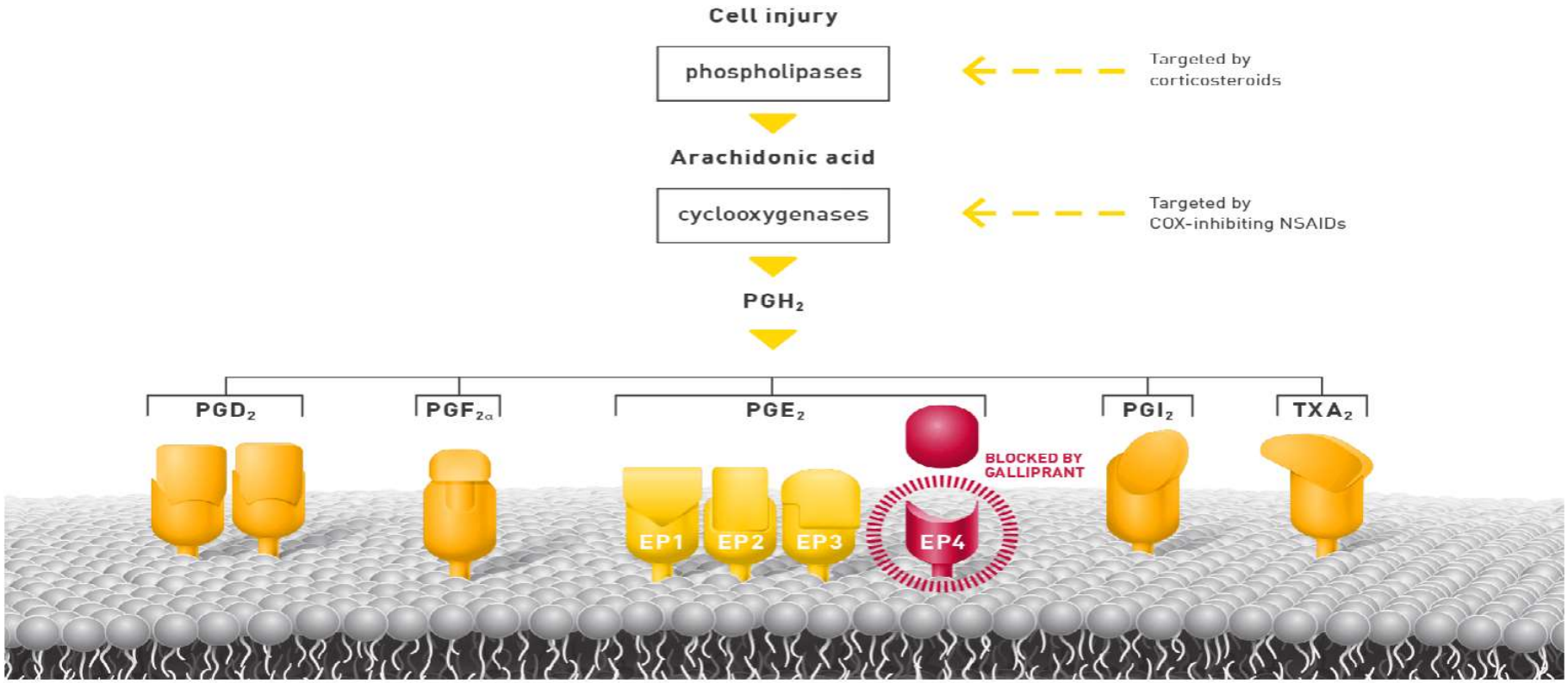
BEHANDELING - GRAPIPRANT



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BEHANDELING - GRAPIPRANT

- behandeling van milde tot matige OA
- dosis: 2 mg/kg SID nuchter
- niet samen met NSAIDs & wash-out respecteren
- veldstudies tot 28 dagen gebaseerd op de CBPI
  - succespercentage vs placebo:
    - 51.3% (120/235) vs 35.5% (82/231)

BEHANDELING - GRAPIPRANT

- tegenindicaties:
  - niet bij honden <9 maanden of <3.6 kg
  - niet bij drachtige of lacterende honden
  - voorzichtigheid bij:
    - GI aandoeningen
    - Leveraandoeningen
    - CV aandoeningen
    - nieraandoeningen

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BEHANDELING - GRAPIPRANT

- neveneffecten:
  - braken
  - platte stoelgang
  - diarree (soms hemorragisch)
  - anorexie
  - lichte daling van serum albumine en plasma proteïnen

BEHANDELING - GRAPIPRANT

J Vet Intern Med. 2016 May;30(3):756-63. doi: 10.1111/jvim.13948. Epub 2016 Apr 13.

A Prospective, Randomized, Masked, Placebo-Controlled Multisite Clinical Study of Grapiprant, an EP4 Prostaglandin Receptor Antagonist (PRA), in Dogs with Osteoarthritis.

Rausch-Derra L[1], Huebner M[2], Wofford J[1], Rhodes L[1].

Author information

1 Aratana Therapeutics, Leawood, KS.
2 ClinData Services, Ft. Collins, CO.

Abstract

BACKGROUND: This study evaluated the effectiveness and safety of grapiprant for treatment of pain in dogs with osteoarthritis (OA).

HYPOTHESIS/OBJECTIVES: Grapiprant will relieve pain as measured by the owner's and veterinarian's evaluation of pain in dogs with OA. Another objective was evaluation of the safety of grapiprant.

ANIMALS: Two hundred and eighty-five client-owned dogs with OA were enrolled and treated with grapiprant or placebo with 262 cases (N = 131 in each group) evaluable for the effectiveness analysis.

METHODS: In this prospective, randomized, masked, placebo-controlled study dogs were treated daily with grapiprant (2 mg/kg) per OS or placebo. Owners completed an evaluation using the Canine Brief Pain Inventory (CBPI) on days 0, 7, 14, 21, and 28. Success was defined as improvement in the CBPI. Veterinary assessments were made on screening and days 14 and 28. Safety was evaluated by physical examination, evaluation of clinical pathology results, and owner observations.

RESULTS: Grapiprant treatment improved pain compared to placebo on day 28 (48.1 and 31.3% treatment successes respectively; P = .0315). The pain interference score (PIS) and pain severity score (PSS) improved in the grapiprant group compared to placebo (P = .0029 and 0.0022, respectively). Veterinary assessments were significantly better in the grapiprant-treated dogs (P = .0086). Grapiprant generally was well tolerated, but a higher percentage of treated dogs (17.02%) had occasional vomiting as compared to the placebo group (6.25%).

CONCLUSIONS AND CLINICAL IMPORTANCE: Grapiprant is an effective treatment for alleviation of pain in dogs with OA, and represents a modality of treatment that may be better tolerated than current options.

BEHANDELING - GRAPIPRANT

BMC Vet Res. 2019 Aug 29;15(1):309. doi: 10.1186/s12917-019-2052-0.

Assessment of the efficacy of firocoxib (Previcox®) and grapiprant (Galliprant®) in an induced model of acute arthritis in dogs.

de Salazar Alcalá AG[1], Gioda L[1], Dehman A[2], Beugnet F[3].

Author information

1 Avogadro LS, Parc de Génibrat, 31470, Fontenilles, France.
2 Hyphen-stat, 195, route d'Espagne BP13669, 31036, Toulouse Cedex 1, France.
3 Boehringer Ingelheim Animal Health, 29, avenue Tony Garnier, 69007, Lyon, France. frederic.beugnet@boehringer-ingelheim.com.

Abstract

BACKGROUND: Non-steroidal anti-inflammatory drugs (NSAIDs) are an important tool in the management of canine osteoarthritis, with the most recent introduction into the category being grapiprant, a piprant that selectively targets the EP4 prostaglandin receptor. To date there have been no efficacy studies comparing grapiprant with other NSAIDs. A randomized, two-sequence, assessor-blinded study involving two separate experiments was undertaken to measure the potency and persistence of acute pain control over 24 h resulting from a single oral dose of either firocoxib (Previcox®) or grapiprant (Galliprant®) in an acute arthritis model.

RESULTS: Force-plate derived lameness ratios (0, no force recorded on the plate; 1, normal force) for the untreated group remained at 0 for most post-arthritis induction (PAI) assessments in both experiments. Throughout Experiment 1, mean PAI lameness ratios of the firocoxib-treated group remained at or above 0.80. In the grapiprant-treated group, ratios were 0 at 5 and 7 h PAI (7 and 9 h post-treatment), and 0.16 at 10 h PAI (12 h post-treatment). For lameness ratios, relative to the firocoxib group, the control and grapiprant group ratios were significantly lower at each PAI assessment ($p \leq 0.026$ and $p < 0.001$, respectively), except at 1.5 h PAI at which acute pain was still not installed in untreated control dogs. In Experiment 2 the mean lameness ratios for the control group were 0 at 3, 5 and 7 h PAI, and in the grapiprant group at 5, 7 and 10 h PAI (i.e., 19, 21, and 24 h post-treatment). In the firocoxib group the lowest mean lameness ratio of 0.36 occurred at 3 h PAI (i.e. 17 h post-treatment). Except at 1.5 and 3 h PAI (i.e. 15.5 and 17 h post-treatment), due to the needed time for pain to install in the untreated control dogs, the lameness ratio differences between the firocoxib and both the control and grapiprant groups were significant at all assessments ($p \leq 0.033$ for both groups). No significant differences were detected between the grapiprant and control groups in either experiment.

CONCLUSIONS: Firocoxib treatment prior to induction of arthritis in dogs resulted in a high level of analgesia from the first post-treatment assessment at 1.5 h through 24 h post-treatment. The reduction in lameness provided by firocoxib was consistently superior to that provided by grapiprant, which was not significantly different from untreated controls.

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PARACETAMOL

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BEHANDELING - PARACETAMOL

- Paracetamol (nooit bij katten!)

  - werkt op het niveau van het ruggemerg
    - COX inhibitie
    - opioid receptor
    - serotonine receptor
    - cannabinoid systeem

BEHANDELING- PARACETAMOL

- Paracetamol (nooit bij katten!)
  - eerste keuze bij chronisch nierfalen
  - dosering ALLEEN HOND!!:
    - 10-15 mg/kg BID
    - nauwe therapeutische breedte
  - weinig gecontroleerde studies, geen voor chronische pijn en multimodale aanpak
  - wordt soms gebruikt voor de behandeling van breakthrough pain bij OA (voor een korte periode)

BEHANDELING - PARACETAMOL

- **Clinical evaluation of postoperative analgesia, cardiorespiratory parameters and changes in liver and renal function tests of paracetamol compared to meloxicam and carprofen in dogs undergoing ovariohysterectomy. Hernández-Avalos et al. 2020.**
  PLoS One 2020 Feb 14;15(2):e0223697 doi: 10.1371/journal.pone.0223697.

Paracetamol was as effective as meloxicam and carprofen for post-surgical analgesia in bitches subjected to elective ovariohysterectomy. The present study demonstrates that paracetamol may be considered a tool for the effective treatment of acute perioperative pain in dogs.

- **Comparing paracetamol/codeine and meloxicam for postoperative analgesia in dogs: a non-inferiority trial. Pacheco et al. 2020.**
  Vet Rec. 2020 Oct 17;187(8):e61. doi: 10.1136/vr.105487. Epub 2020 Jan 3. PMID: 31900324.

Paracetamol/codeine is a useful perioperative analgesic that within the context of the perioperative analgesia regimen studied (methadone premedication, buprenorphine for the first 24 hours after surgery) shows non-inferiority to the NSAID meloxicam.

BEDINVETMAB
LIBRELA

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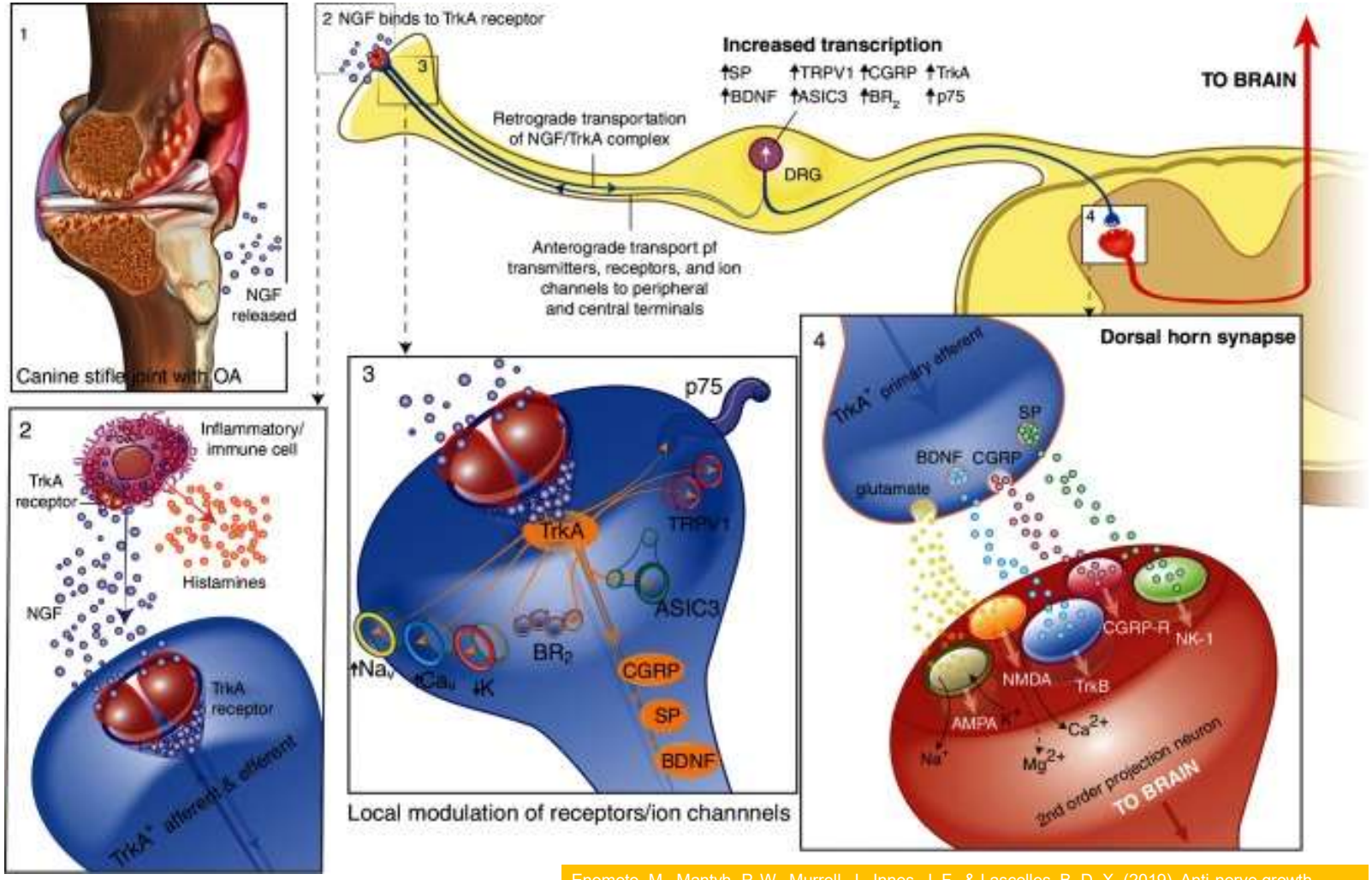
BEHANDELING – LIBRELA (BEDINVETMAB)

- Librela (bedinvetmab)
  - Canine monoclonale antistof tegen NGF
  - behandeling van OA pijn
  - NGF activeert de TrkA receptor, belangrijk voor pijn bij OA
    - perifere sensitisatie: meer NGF & threshold reductie nociceptoren
    - centrale sensitisatie: verandert dorsale hoorn gene expression & versterkt glutamaat transmissie

BEHANDELING – LIBRELA (BEDINVETMAB)



Enomoto, M., Mantyh, P. W., Murrell, J., Innes, J. F., & Lascelles, B. D. X. (2019). Anti-nerve growth factor monoclonal antibodies for the control of pain in dogs and cats. *Veterinary Record*, *184*(1), 1–14. https://doi.org/10.1136/vr.104590

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BEHANDELING – LIBRELA (BEDINVETMAB)

- Librela (bedinvetmab)
  - 0.5-1 mg/kg SC per maand
  - 3 maanden veldstudie:
    - succes na dosis 1 (CBPI):

      43.5% Librela vs. 16.9% placebo
  - Steady state concentratie na 2 doses

BEHANDELING – LIBRELA (BEDINVETMAB)

- Librela (bedinvetmab)
  - kan samen worden toegediend met een NSAID
    - getest met carprofen, maar teststudie enkel gedurende 2 weken!
    - bij de mens: snel progressieve OA na combi!

  - positief effect op de 3 componenten van de CBPI:
    - ernst van de pijn
    - interferentie pijn met typische activiteiten
    - quality of life

  - focust ook op het verhinderen van centrale sensitizatie
  - gaat waarschijnlijk worden ingezet bij de refractaire OA patiënten

TRAMADOL

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BEHANDELING – TRAMADOL

- Tramadol

  - synthetisch codeine analoog
  - 1/10de potentie van morfine
  - zwakke μ-receptor agonist (40%)
    - (+)-enantiomeer van tramadol en M1 metaboliet
  - inhibitie van norepinephrine reuptake (20%)
    - (-)-enantiomeer van tramadol
  - inhibitie van serotonine reuptake (20%)
    - (+)-enantiomeer van tramadol
  - stimuleert descenderende inhibitorische pijn pathways

BEHANDELING – TRAMADOL

- Tramadol
  - opioid analgetisch effect is afhankelijk van de vorming van de M1-metaboliet
  - CYP450 enzyme is verantwoordelijk hiervoor
  - interspecies, intraspecies en interindividuele variatie in analgetische potentie wordt veroorzaakt door verschillen in metabolisatie
  - mens: CYP2D6: ‘poor metabolizers’ resulteert in minder goede analgesie

BEHANDELING – TRAMADOL

- Tramadol
  - M1 synthese bij de hond is lager dan de concentraties die geassocieerd worden met analgesie bij de mens
  - M1 synthese bij de kat is vergelijkbaar met concentraties die geassocieerd worden met analgesie bij de mens
  - orale toediening van tramadol bij de hond voor een periode langer dan 1 week kan resulteren in een reductie van de plasma concentratie te wijten aan een ongekend mechanisme

BEHANDELING – TRAMADOL

- Tramadol
  - dosis hond: 2-5 mg/kg bid tot qid, variabele efficiëntie!
  - dosis kat: 2-4 mg/kg bid (mindere metabolisatie, lagere klaring) (off-label)

Am J Vet Res. 2009 Dec;70(12):1465-70. doi: 10.2460/ajvr.70.12.1465.

Effects of tramadol hydrochloride on the thermal threshold in cats.

Pypendop BH[1], Siao KT, Ilkiw JE.

  - aandacht: serotonine syndroom! wanneer samen gebruikt wordt met SSRI's, MAOI's, tricyclische antidepressiva!

BEHANDELING – TRAMADOL

- Tramadol
  - neveneffecten (vooral bij de kat):
    - sedatie
    - dysphorie
    - braken/diarree bij de hond
  - niet combineren met MAO-inhibitoren/SSRI's

- Tapentadol
  - toekomst: efficiëntie is onafhankelijk van metabolieten
  - nog geen aanbevolen dosering beschikbaar

BEHANDELING - TRAMADOL

Efficacy of tramadol for postoperative pain management in dogs: systematic review and meta-analysis. Donati et al. 2021.
VAA; February 09, 2021DOI:https://doi.org/10.1016/j.vaa.2021.01.003

Overall 26 RCTs involving 848 dogs were included. Tramadol administration probably results in a lower need for rescue analgesia *versus* no treatment or placebo [moderate CoE; relative risk (RR): 0.47; 95% confidence interval (CI): 0.26–0.85; I^2 = 0%], and may result in a lower need for rescue analgesia *versus* buprenorphine (low CoE; RR: 0.50; 95% CI: 0.20–1.24), codeine (low CoE; RR: 0.75; 95% CI: 0.16–3.41) and nalbuphine (low CoE; RR: 0.05; 95% CI: 0.00–0.72). However, tramadol administration may result in an increased requirement for rescue analgesia *versus* methadone (low CoE; RR: 3.45; 95% CI: 0.66–18.08; I^2 = 43%) and COX inhibitors (low CoE; RR: 2.27; 95% CI: 0.68–7.60; I^2 = 45%). Compared with multimodal therapy, tramadol administration may make minimal to no difference in the requirement for rescue analgesia (low CoE; RR: 1.12; 95% CI: 0.48–2.60; I^2 = 0%). Adverse events were inconsistently reported and the CoE was very low. The overall CoE of the analgesic efficacy of tramadol for postoperative pain management in dogs was low or very low, and the main reasons for downgrading the evidence were risk of bias and imprecision.

CoE=Certainty of Evidence

BEHANDELING – TRAMADOL

J Am Vet Med Assoc. 2018 Feb 15;252(4):427-432. doi: 10.2460/javma.252.4.427.

Lack of effectiveness of tramadol hydrochloride for the treatment of pain and joint dysfunction in dogs with chronic osteoarthritis.

Budsberg SC, Torres BT, Kleine SA, Sandberg GS, Berjeski AK.

Abstract

OBJECTIVE To investigate the effectiveness of tramadol for treatment of osteoarthritis in dogs. DESIGN Randomized, blinded, placebo-controlled crossover study. ANIMALS 40 dogs with clinical osteoarthritis of the elbow or stifle joint. PROCEDURES Dogs orally received 3 times/d (morning, midday, and night) for a 10-day period each of 3 identically appearing treatments (placebo; carprofen at 2.2 mg/kg [1 mg/lb], q 12 h [morning and night], with placebo at midday; or tramadol hydrochloride at 5 mg/kg [2.3 mg/lb], q 8 h) in random order, with treatment sessions separated by a minimum 7-day washout period. Vertical ground reaction forces (vertical impulse [VI] and peak vertical force [PVF]) were measured and Canine Brief Pain Inventory (CBPI) scores assigned prior to (baseline) and at the end of each treatment period. Repeated-measures ANOVA was performed to compare VI and PVF data among and within treatments, and the χ^2 test was used to compare proportions of dogs with a CBPI-defined positive response to treatment. RESULTS 35 dogs completed the study. No significant changes from baseline in VI and PVF were identified for placebo and tramadol treatments; however, these values increased significantly with carprofen treatment. Changes from baseline in VI and PVF values were significantly greater with carprofen versus placebo or tramadol treatment. A significant improvement from baseline in CBPI scores was identified with carprofen treatment but not placebo or tramadol treatment. CONCLUSIONS AND CLINICAL RELEVANCE 10 days of treatment with tramadol as administered (5 mg/kg, PO, q 8 h) provided no clinical benefit for dogs with osteoarthritis of the elbow or stifle joint.

BEHANDELING - TRAMADOL

Vet Anaesth Analg. 2017 Mar;44(2):309-316. doi: 10.1016/j.vaa.2016.02.003. Epub 2017 Jan 7.

Influence of tramadol on acute thermal and mechanical cutaneous nociception in dogs.

Schütter AF[1], Tünsmeyer J[2], Kästner SBR[2].

Author information

Abstract

OBJECTIVE: The aim of the study was to evaluate the influence of tramadol on acute nociception in dogs.

STUDY DESIGN: Experimental, blinded, randomized, crossover study.

ANIMALS: Six healthy laboratory Beagle dogs.

METHODS: Dogs received three treatments intravenously (IV): isotonic saline placebo (P), tramadol 1 mg kg^{-1} (T1) and tramadol 4 mg kg^{-1} (T4). Thermal thresholds were determined by ramped contact heat stimulation (0.6 °C $second^{-1}$) at the lateral thoracic wall. Mechanical thresholds (MT) were measured using a probe containing three blunted pins which were constantly advanced over the radial bone, using a rate of force increase of 0.8 N $second^{-1}$. Stimulation end points were defined responses (e.g. skin twitch, head turn, repositioning, vocalization) or pre-set cut-out values (55 °C, 20 N). Thresholds were determined before treatment and at predetermined time points up to 24 hours after treatment. At each measurement point, blood was collected for determination of O-desmethyltramadol concentrations. The degree of sedation and behavioural side effects were recorded. Data were analysed by one-way anova and two-way anova for repeated measurements.

RESULTS: Thermal nociception was not influenced by drug treatment. Mechanical nociception was significantly increased between P and T1 at 120 and 240 minutes, and between P and T4 at 30, 60, 240 and 420 minutes. T1 and T4 did not differ. O-desmethyltramadol (M1) maximum plasma concentrations (C_{max}) were 4.2±0.8 ng mL^{-1} and 14.3±2.8 ng mL^{-1} for T1 and T4, respectively. Times to reach maximum plasma concentrations (T_{max}) were 27.6±6.3 minutes for T1 and 32.1±7.8 minutes for T4. No sedation occurred. There were signs of nausea and mild to moderate salivation in both groups.

CONCLUSION AND CLINICAL RELEVANCE: Tramadol was metabolized marginally to O-desmethyltramadol and failed to produce clinically relevant acute antinociception. Therefore, the use of tramadol for acute nociceptive pain is questionable in dogs.

BEHANDELING - TRAMADOL

Am J Vet Res. 2015 Sep;76(9):763-70. doi: 10.2460/ajvr.76.9.763.

Pharmacokinetics of hydrocodone and tramadol administered for control of postoperative pain in dogs following tibial plateau leveling osteotomy.

Benitez ME, Roush JK, KuKanich B, McMurphy R.

Abstract

OBJECTIVE: To evaluate the pharmacokinetics of hydrocodone (delivered in combination with acetaminophen) and tramadol in dogs undergoing tibial plateau leveling osteotomy (TPLO).

ANIMALS: 50 client-owned dogs.

PROCEDURES: Dogs were randomly assigned to receive tramadol hydrochloride (5 to 7 mg/kg, PO, q 8 h; tramadol group) or hydrocodone bitartrate-acetaminophen (0.5 to 0.6 mg of hydrocodone/kg, PO, q 8 h; hydrocodone group) following TPLO with standard anesthetic and surgical protocols. Blood samples were collected for pharmacokinetic analysis of study drugs and their metabolites over an 8-hour period beginning after the second dose of the study medication.

RESULTS: The terminal half-life, maximum serum concentration, and time to maximum serum concentration for tramadol following naïve pooled modeling were 1.56 hours, 155.6 ng/mL, and 3.90 hours, respectively. Serum concentrations of the tramadol metabolite O-desmethyltramadol (M1) were low. For hydrocodone, maximum serum concentration determined by naïve pooled modeling was 7.90 ng/mL, and time to maximum serum concentration was 3.47 hours. The terminal half-life for hydrocodone was 15.85 hours, but was likely influenced by delayed drug absorption in some dogs and may not have been a robust estimate. Serum concentrations of hydromorphone were low.

CONCLUSIONS AND CLINICAL RELEVANCE: The pharmacokinetics of tramadol and metabolites were similar to those in previous studies. Serum tramadol concentrations varied widely, and concentrations of the active M1 metabolite were low. Metabolism of hydrocodone to hydromorphone in dogs was poor. Further study is warranted to assess variables that affect metabolism and efficacy of these drugs in dogs.

BEHANDELING - TRAMADOL

- plaats voor tramadol in pijnbehandeling
  - korte termijn post-operatieve acute pijnbehandeling
    - ter vervanging van opiaten (‘at home’ treatment)
  - ‘breakthrough pain’ behandeling voor korte periode
    - osteoarthritis
  - effect is patiëntafhankelijk
  - multimodale pijnbestrijding (meer studies nodig)

NMDA - ANTAGONISTEN

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BEHANDELING – NMDA-ANTAGONISTEN

- werkingsmechanisme:
  - NMDA-receptoren (excitatorisch glutamaat) worden geactiveerd na sterke of langdurige activatie van Aδ- en C-vezels
  - NMDA-receptor blokkade op het niveau van de dorsale hoorn (ruggemerg)
  - preventief of curatief

BEHANDELING – NMDA-ANTAGONISTEN

- Ketamine
  - NMDA-receptor antagonist
  - agonistisch effect op kappa en delta-receptoren
  - inhibitie van noradrenaline re-uptake

  - LD: 0.1-0.5 mg/kg
  - CRI: 10-20 µg/kg/minuut (of zelfs hoger)
  - niet als alleenstaande therapie: deel van een multimodale analgetische aanpak
    - combinatie met lidocaine, opiaten, NSAID's, tramadol

BEHANDELING – NMDA-ANTAGONISTEN

- Ketamine
  - per-operatief: 0.6 mL (60 mg) ketamine in 1L NaCl 0.9% toegediend aan 10 mL/kg/u resulteert in 10 µg/kg/minuut
  - post-operatief: 0.6 mL (60 mg) ketamine LG in 1L NaCl 0.9% toegediend aan 2 mL/kg/u resulteert in 2 µg/kg/minuut

- Methadone (parenteraal)

  - eerste keuze opioid om NP te behandelen
  - µ-receptor agonist
  - inhibitie van noradrenaline re-uptake
  - NMDA-receptor antagonist (d-methadone)

BEHANDELING – NMDA-ANTAGONISTEN

- Amantadine (Amantan®)
  - anti-viraal geneesmidel/ gebruikt voor de behandeling van Parkinson
  - orale NMDA-receptor antagonist voor Stap 2 OA behandeling
  - dopamine agonist
  - dosisreductie van en synergistisch effect met opioiden
  - dosis hond: 3-5 mg/kg sid
  - dosis kat: 1-4 mg/kg sid
  - neveneffecten:
    - angst/rusteloosheid
    - droge mond
    - gedragsveranderingen bij hoge doseringen (15 mg/kg)

BEHANDELING – NMDA ANTAGONISTEN

J Vet Intern Med. 2008 Jan-Feb;22(1):53-9. doi: 10.1111/j.1939-1676.2007.0014.x.

Amantadine in a multimodal analgesic regimen for alleviation of refractory osteoarthritis pain in dogs.

Lascelles BD[1], Gaynor JS, Smith ES, Roe SC, Marcellin-Little DJ, Davidson G, Boland E, Carr J.

Author information

Abstract

BACKGROUND: Nonsteroidal anti-inflammatory drugs (NSAIDs) do not always provide sufficient pain relief in dogs with osteoarthritis (OA).

HYPOTHESIS: The use of amantadine in addition to NSAID therapy will provide improved pain relief when compared with the use of nonsteroidal analgesics alone in naturally occurring OA in dogs.

ANIMALS: Thirty-one client-owned dogs with pelvic limb lameness despite the administration of an NSAID.

METHODS: The study was randomized, blinded, and placebo controlled with parallel groups (days 21-42). On day 0, analgesic medications were discontinued. On day 7, all dogs received meloxicam for 5 weeks. On day 21, all dogs received amantadine (3-5 mg/kg once daily per os) or placebo for 21 days, in addition to receiving meloxicam. Assessments were performed before the study and on days 7, 21, and 42. Primary outcome measures were blinded owner assessments of activity using client-specific outcome measures (CSOM) on days 0, 7, 21, and 42. Data were analyzed by a mixed model approach.

RESULTS: For CSOM activity, there was a significant time by treatment effect (P=.009). On the basis of the planned post hoc t-tests of postrandomization means, there was a significant difference between treatment groups on day 42 (P=.030), with the amantadine group being more active.

CONCLUSIONS AND CLINICAL IMPORTANCE: In dogs with osteoarthritic pain refractory to an NSAID, physical activity is improved by the addition of amantadine. Amantadine might be a useful adjunct therapy for the clinical management of canine osteoarthritic pain.

ANTIEPILEPTICA
GABAPENTINE
PREGABALINE

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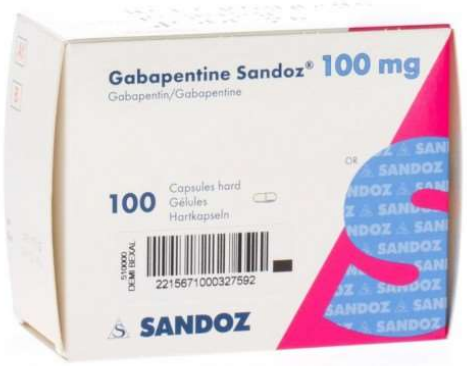
BEHANDELING - ANTIEPILEPTICA

- Gabapentine

  - anti-epileptisch geneesmiddel, GABA-analoog
  - anticonvulsief, anxiolytisch, analgetisch effect

  - blokkeert calcium-kanalen op spinaal en supraspinaal niveau
  - reduceert glutamaat (excitatoire neurotransmitter) vrijstelling
  - moduleert activiteit van post-synaptische glutamaat receptoren

  - blokkeert centrale sensitizatie
  - activeert descenderend NE-systeem



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BEHANDELING - ANTIEPILEPTICA

- Gabapentine
  - combineer met NSAID in acute fase
  - later solo therapie eventueel mogelijk
  - dosis = geëxtrapoleerd van de mens
  - gesuggereerde start dosis:
    - Ca: 5-25 mg/kg bid of tid
    - Fe: 5-10 mg/kg tid

BEHANDELING - ANTIEPILEPTICA

- Gabapentine
  - titreer op effect (dosis range: 2.5-50 mg/kg)
  - lange termijn behandeling kan noodzakelijk zijn (weken tot maanden)
  - sedatie is dosis afhankelijk (geen sedatie bij kat)
  - normale nierfunctie is noodzakelijk (klaring)

BEHANDELING - ANTIEPILEPTICA

- Pregabaline
  - GABA-analoog
  - zelfde mechanisme als Gabapentine
  - bijkomend effect op voltage-gated kalium kanalen
  - dosis: Ca: 3-4 mg/kg qid (anecdotisch)

TRICYCLISCHE ANTIDEPRESSIVA

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BEHANDELING – TRICYCLISCHE ANTIDEPRESSIVA

Tricyclische antidepressiva gebruikt voor de behandeling van chronische pijn bij hond en kat.

Drug	Dog	Cat	Comments
Amitriptyline	1 to 2 mg/kg orally every 12 hours	0.5 to 1 mg/kg orally every 24 hours	
Imipramine	0.5 mg/kg orally every 12 to 24 hours	0.5 to 1 mg/kg orally every 12 to 24 hours	
Clomipramine	None	None	Not generally considered useful in pain management. The serotonin effect is greater than the adrenergic effect

BEHANDELING – TRICYCLISCHE ANTIDEPRESSIVA

- werkingsmechanisme:
  - inhibitie van de re-uptake van noradrenaline/serotonine
  - verhogen de endogene opioid spiegels, wat kan leiden tot veranderingen in opioid receptor densiteit
  - effect op NMDA-receptoren met vermindering van wind-up
  - combinatie met andere analgetica
  - effect na 2 dagen

BEHANDELING – TRICYCLISCHE ANTIDEPRESSIVA

- neveneffecten:
  - tachycardie
  - gewichtstoename
  - sedatie
  - serotonine syndroom

BEHANDELING – TRICYCLISCHE ANTIDEPRESSIVA

Aust Vet J. 2009 Jan-Feb;87(1):45-50. doi: 10.1111/j.1751-0813.2008.00379.x.

Clinical diagnosis and treatment of suspected neuropathic pain in three dogs.

Cashmore RG[1], Harcourt-Brown TR, Freeman PM, Jeffery ND, Granger N.

Author information

Abstract

Three dogs were referred to The Queen's Veterinary School Hospital at University of Cambridge for chronic behavioural or locomotor disorders associated with pain. All three had been unsuccessfully treated with conventional analgesics, including non-steroidal anti-inflammatory drugs, glucocorticoids and opiate agonists, prior to referral, with minimal or no response. They were investigated by neurological examination plus conventional ancillary diagnostic tests and therapeutic drug trials. Ruling out other causes of pain and applying previously well-described criteria, each case was diagnosed as consistent with neuropathic pain, a poorly recognised condition in domestic dogs. Treatment with the tricyclic antidepressant drug, amitriptyline, or the antiepileptic drug, gabapentin, resulted in either a dramatic improvement or full resolution of clinical signs in all cases.

Aust Vet J. 2006 Mar;84(3):83-6.

Neuropathic pain in a cat post-amputation.

O'Hagan BJ[1].

Author information

Abstract

Phantom limb pain is a form of neuropathic pain experienced by human patients who have had amputations. To date there are no reported cases of phantom limb pain in the veterinary literature. A cat presented with signs consistent with neuropathic or phantom limb pain 42 days after iatrogenic sciatic nerve injury and 38 days after subsequent hind limb amputation. Multimodal analgesic therapy resulted in resolution of signs of pain.

NIET FARMACOLOGISCHE ADJUVANTIA

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BIJKOMENDE BEHANDELINGSOPTIES

- acupunctuur/electroacupunctuur
  - stimulatie van specifieke anatomische punten
  - stimulatie Aδ-vezels, onderdrukking C-vezels
  - opregulatie messenger RNA voor pre-encephalin (verantwoordelijk voor de lange termijn effecten van acupunctuur)
  - vermindert spierspasmen

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BIJKOMENDE BEHANDELINGSOPTIES

- acupunctuur/electroacupunctuur
  - anxiolyse, verbeterde heling, antinausea
  - vrijstelling van verschillende neurotransmitters (endogene opioiden)
  - versterken van de inhibitorische pijnsystemen
  - geen neveneffecten!!
  - STERK aangeraden voor de behandeling van neuropatische pijn en OA: CENTRALE PIJN
  - 2-3 maal/week, gedurende 3-4 weken en re-evalueer

BIJKOMENDE BEHANDELINGSOPTIES

- acupunctuur/electroacupunctuur

Comparison of decompressive surgery, electroacupuncture, and decompressive surgery followed by electroacupuncture for the treatment of dogs with intervertebral disk disease with long-standing severe neurologic deficits.

RESULTS: The proportion of dogs with clinical success was significantly higher for dogs that underwent EAP (15/19) than for dogs that underwent DSX (4/10); the proportion of dogs with clinical success for dogs that underwent DSX + EAP was intermediate (8/11).

J Am Vet Med Assoc. 2010 Jun 1;236(11):1225-9.

Electroacupuncture analgesia in dogs: is there a difference between uni- and bi-lateral stimulation?

RESULTS: There were no cardiorespiratory differences among the treatments. The cutaneous pain threshold was higher after EA, compared with false points. The latency period was shorter and analgesia was more intense in T-EA/bil than T-EA/uni, when both were compared with T-false and T-control. Six out of eight animals treated with EA were calm during treatment, and 5/8 and 4/8 of the T-false and T-control animals, respectively, were restless. Latency to interdigital thermal stimulation increased in T-EA/bil compared with the others. There was no difference in plasma cortisol concentrations among the treatments.

CONCLUSIONS: Bilateral EA produced a shorter latency period, a greater intensity, and longer duration of analgesia than unilateral stimulation, without stimulating a stress response.

CLINICAL RELEVANCE: Bilateral EA produces a better analgesic effect than unilateral EA.

Vet Anaesth Analg. 2008 Jan;35(1):52-61

BIJKOMENDE BEHANDELINGSOPTIES

- gewichtscontrole!
- gecontroleerde beweging/rehabilitatie
- fysiotherapie:
  - mobilisatie gewrichten
  - hydrotherapie, laser, ultrason
  - doel is behoud en herstel van een normale functie
  - multidisciplinair

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BIJKOMENDE BEHANDELINGSOPTIES

- voedingssupplementen
  - doel: elementaire elementen voor gezonde structuren en normale functie aanbieden
  - in Europa is er geen bewijs van efficiëntie nodig om dergelijke produkten te commercialiseren
  - uitgebreide trials daardoor weinig waarschijnlijk

BIJKOMENDE BEHANDELINGSOPTIES

- voedingssupplementen
  - Vandeweerd et al. (2012) systematische review naar de efficiëntie van nutraceuticals (22 studies)
    - omega 3 vetzuren gesupplementeerde hondenvoeding – highest strength of evidence
    - “symptomatic treatment”, vooral ontstekingsremmend
    - katten – slechts 1 studie, geen huidige aanbeveling

BIJKOMENDE BEHANDELINGSOPTIES

- voedingssupplementen
  - werkingsmechanisme van omega 3 vetzuren
    - verlagen arachidonzuur concentraties
    - veranderen de productie van eicosanoiden naar minder inflammatoire vormen
    - verminderen de expressie van kraakbeen degraderende enzymes

BIJKOMENDE BEHANDELINGSOPTIES

J Vet Intern Med. 2012 May-Jun;26(3):448-56. doi: 10.1111/j.1939-1676.2012.00901.x. Epub 2012 Mar 9.

Systematic review of efficacy of nutraceuticals to alleviate clinical signs of osteoarthritis.

Vandeweerd JM[1], Coisnon C, Clegg P, Cambier C, Pierson A, Hontoir F, Saegerman C, Gustin P, Buczinski S.

Author information

Abstract

BACKGROUND: Various treatments of osteoarthritis (OA) have been described, including use of nutraceuticals.

OBJECTIVES: To review systematically the literature about the effects of nutraceuticals on clinical signs of pain or abnormal locomotion in horses, dogs, and cats, and to discuss methodological aspects of trials and systematic reviews.

METHODS: A systematic search of controlled trials evaluating the impact of nutraceuticals on OA in horses, dogs, and cats was performed, using Medline, CAB Abstracts, and Google Scholar. Scientific evidence was evaluated by means of criteria proposed by the Food and Drug Administration (FDA), and a scoring system adapted from both the CONsolidated Standards of Reporting Trials (CONSORT) statement and recommendations for assessing trials by the Center of Evidence Based Medicine of Oxford.

RESULTS: Twenty-two papers were selected and reviewed, with 5 studies performed in horses, 16 in dogs, and 1 in cats. The strength of evidence was low for all nutraceuticals except for omega-3 fatty acid in dogs. There were limited numbers of rigorous randomized controlled trials and of participants in clinical trials.

CONCLUSIONS AND CLINICAL IMPORTANCE: The evidence of efficacy of nutraceuticals is poor, with the exception of diets supplemented with omega-3 fatty acids in dogs. Greater access to systematic reviews must be part of the objectives of the veterinary science in the future. Their reporting would be improved by internationally agreed-upon criteria for standards and guidelines.

BIJKOMENDE BEHANDELINGSOPTIES

- voedingssupplementen
  - glucosamine en chondroitine sulfaat
    - bouwstenen kraakbeen aanreiken
    - beschermend tegen synovitis
    - modulatie van gewrichtskraakbeen
    - “Disease modifying supplements”

    - strength of evidence is zwak
    - studies zijn variabel in lengte, bevatten verschillende doseringen en actieve bestanddelen

BIJKOMENDE BEHANDELINGSOPTIES

Vet Comp Orthop Traumatol. 2017 Sep 12;30(5):318-323. doi: 10.3415/VCOT-17-02-0020. Epub 2017 Aug 1.

Efficacy of an oral nutraceutical for the treatment of canine osteoarthritis. A double-blind, randomized, placebo-controlled prospective clinical trial.

Scott RM[1], Evans R, Conzemius MG.

Author information

Abstract

OBJECTIVES: To assess the safety and efficacy of an orally administered nutraceutical (Glu/CS+; + for additional ingredient) for the treatment of clinical osteoarthritis (OA) in dogs.

METHODS: In this double-blind, randomized, placebo-controlled clinical trial, client-owned dogs with clinical signs of OA in one or more joints were assigned to a Glu/CS+ (n = 30) or placebo (n = 30) group. Dogs were administered Glu/CS+ or placebo orally and wore an activity monitor (AM) continuously throughout a 97 day study period. Prior to the initiation of the treatment, seven days of baseline activity was collected. On days -7, 30, 60 and 90 of the study, owners completed a patient assessment form (Canine Brief Pain Inventory). Data between groups were compared.

RESULTS: No serious adverse events were reported. No difference was found between groups when evaluating daily activity counts during the seven-day pre-treatment period and the 90-day treatment period. Owner assessment (pain interference and pain severity scores) improved over the 90-day treatment period for both groups, however no difference was found between treatment groups.

CONCLUSIONS: Treatment with oral Glu/CS+ for a 90 day treatment period when compared to placebo treatment did not result in a significant increase in activity counts in dogs with clinical OA. However, owner assessment scores similarly improved throughout the study period for dogs in both groups, suggesting a caregiver placebo effect in this outcome measure.

BIJKOMENDE BEHANDELINGSOPTIES

Top Companion Anim Med. 2017 Dec;32(4):126-129. doi: 10.1053/j.tcam.2017.10.003. Epub 2017 Nov 2.

Effect of an Oral Joint Supplement When Compared to Carprofen in the Management of Hip Osteoarthritis in Working Dogs.

Alves JC[1], Santos AM[2], Jorge PI[2].

Author information

Abstract

The goal of this study was to evaluate the effectiveness of an oral joint supplement in working dogs with hip osteoarthritis compared with a positive control group (CG). Fifteen animals were divided in treatment group (TG, n = 10) and CG (n = 5). To TG a commercially available joint supplement, containing glucosamine HCl, chondroitin sulphate, and hyaluronic acid was given for 40 days and a 70-day course of a placebo, to be administered as if it was carprofen. The CG received carprofen for 70 days, and a placebo to be administered as the joint supplement. Response to treatment, measured by the canine brief pain inventory (CBPI) and the Hudson visual analog scale, was evaluated before treatment (T0), after 15 days (T1) and 1 (T2), 2 (T3), 3 (T4), 4 (T5), and 5 (T6) months. With CBPI, no differences were found in pain interference score and pain severity score between TG and CG throughout or when comparing results within groups. Individual results were considered successful in a maximal of three dogs of the TG by T3 (30%) and 1 in CG (25%). With Hudson visual analog scale, improvements where registered with individual results, for 40%-50% of the animals in TG and 60%-80% of cases in CG. The oral joint supplement and carprofen produced some improvements in individual scores but where unable to do so when overall results were considered. Each of these options may not be able, by itself, to fully address the demands of a working dog with joint disease and related pain.

BIJKOMENDE BEHANDELINGSOPTIES

BMC Vet Res. 2017 Dec 20;13(1):395. doi: 10.1186/s12917-017-1317-8.

A randomized, double-blind, prospective, placebo-controlled study of the efficacy of a diet supplemented with curcuminoids extract, hydrolyzed collagen and green tea extract in owner's dogs with osteoarthritis.

Comblain F[1], Barthélémy N[2], Lefèbvre M[2], Schwartz C[3], Lesponne I[4], Serisier S[4], Feugier A[4], Balligand M[2], Henrotin Y[5,6].

Author information

Abstract

BACKGROUND: We have previously demonstrated that a mixture of Curcuminoids extract, hydrolyzed COllagen and green Tea extract (CCOT) inhibited inflammatory and catabolic mediator's synthesis by bovine and human chondrocytes. A randomly allocated, double-blind, prospective, placebo-controlled study was performed to evaluate the efficacy of a diet containing this CCOT mixture on dogs with naturally occurring osteoarthritis (OA). Therefore, 42 owner's dogs with OA were randomly assigned to receive for 3 months an experimental diet (control) or the same diet supplemented with CCOT.

RESULTS: Ground reaction forces did not show statistical differences between groups. After 3 months of feeding, there was a significant reduction of pain at manipulation in the CCOT group, but not in the control group. The evolution for pain at manipulation depended on the diet. The three other parameters evaluated by veterinary subjective assessment (lameness, pain at palpation and joint mobility) did not show statistical differences. Concerning owner subjective assessment, pain severity score worsened in the control group but remained stable in CCOT group. The evolution for pain severity depended on the diet. No statistical difference was found for pain interference, except for the ability to rise to standing from lying down, which was significantly improved in the CCOT compared to the control group. Serum OA biomarkers did not show statistical differences.

CONCLUSIONS: Objective variables measured, such as ground reaction forces and OA biomarkers, did not show statistical differences. However, indicators of pain appeared reduced in dogs receiving CCOT mixture for 3 months. The difference of evolution between groups suggests that a greater number of dogs may be necessary to reach a stronger effect on other parameters.

BIJKOMENDE BEHANDELINGSOPTIES

- Cannabinoïden CBD verkregen uit Hennep (>60 # cannabinoïden)
  - Tetrahydrocannabinol (THC) max. 0.2%
    - Psychotroop effect (hersenen)
    - CB1-receptor (centraal zenuwstelsel)
    - Marihuana

  - Cannabidiol (CBD)
    - Therapeutische effecten via Endogeen Cannabinoïd Systeem (ECS)
    - Geen psychotroop effect
    - CB2-receptor (perifeer zenuwstelsel & synovia)
    - “PAINS”
      - Pain (anti-hyperalgesie)
      - Anti-inflammatoir
      - Immunologisch
      - Nociceptief (anti-nociceptie)
      - Seizures

BIJKOMENDE BEHANDELINGSOPTIES

- Cannabidiol CBD
  - niet geregistreerd als geneesmiddel
  - supplement & vrij verkrijgbaar:
    - olie
    - tabletten of capsules
    - poeder
  - dosering:
    - gebruik best een product met meerdere cannabinoïden
    - titreren (laag beginnen tot effect)

BIJKOMENDE BEHANDELINGSOPTIES

- Cannabidiol CBD
  - Veilig?
    - geen langetermijn veiligheidsstudies
    - stijging ALP: inductie CYP450 oxydatief metabolisme
    - geneesmiddelinteracties: CYP450 metabolisme
    - invloed op # orgaansystemen: opletten bij cardiologische aandoeningen

frontiers in Veterinary Science

ORIGINAL RESEARCH
published: 23 July 2018
doi: 10.3389/fvets.2018.00165

Pharmacokinetics, Safety, and Clinical Efficacy of Cannabidiol Treatment in Osteoarthritic Dogs

*Lauri-Jo Gamble[1], Jordyn M. Boesch[1], Christopher W. Frye[1], Wayne S. Schwark[2], Sabine Mann[3], Lisa Wolfe[4], Holly Brown[5], Erin S. Berthelsen[1] and Joseph J. Wakshlag[1]**

HHS Public Access
Author manuscript
Pain. Author manuscript; available in PMC 2021 September 01.

Published in final edited form as:
Pain. 2020 September 01; 161(9): 2191–2202. doi:10.1097/j.pain.0000000000001896.

A randomized, double-blind, placebo-controlled study of daily cannabidiol for the treatment of canine osteoarthritis pain

Chris D. Verrico[1,2,+], Shonda Wesson[3,+], Vanaja Konduri[4], Colby J. Hofferek[4], Jonathan Vazquez-Perez[4], Emek Blair[5], Kenneth Dunner Jr[6], Pedram Salimpour[7], William K. Decker[4,8,9,+,*], Matthew M. Halpert[4,+]

Scientific Report

The Use of Cannabidiol-Rich Hemp Oil Extract to Treat Canine Osteoarthritis-Related Pain: A Pilot Study

Lori Kogan, PhD, Peter Hellyer, DVM, Robin Downing, DVM, MS

GHENT UNIVERSITY

•Gamble LJ, Boesch JM, Frye CW, et al. Pharmacokinetics, safety, and clinical efficacy of cannabidiol treatment in osteoarthritic dogs. *Front Vet Sci.* 2018;5:165. doi:10.3389/fvets.2018.00165
•Verrico CD, Wesson S, Konduri V, et al. A randomized, double-blind, placebo-controlled study of daily cannabidiol for the treatment of canine osteoarthritis pain. *Pain.* 2020;161(9):2191-2202. doi:10.1097/j.pain.0000000000001896
•Kogan L, Hellyer P, Downing R. The use of cannabidiol-rich hemp oil extract to treat canine osteoarthritis-related pain: a pilot study. *J Am Holistic Vet Med Assoc.* 2020;58:35-43.

BIJKOMENDE BEHANDELINGSOPTIES

- Intra-articulaire injecties:
  - Hyaluronzuur (HA):
    - component gewrichtsvocht
      - smering gewricht & captatie vrije radicalen
    - OA: depolarisatie HA, waardoor gedaalde elasticiteit

    - Intra-articulaire injectie bootst effect na, maar herstelt niet de volledige functie:
      - analgetisch effect
      - humane placebo gecontroleerde studies met + effect

GHENT UNIVERSITY

Recent advances in hyaluronic acid based therapy for osteoarthritis. Bosnan S. et al. (2018) Clinical and Translational Medicine volume 7.

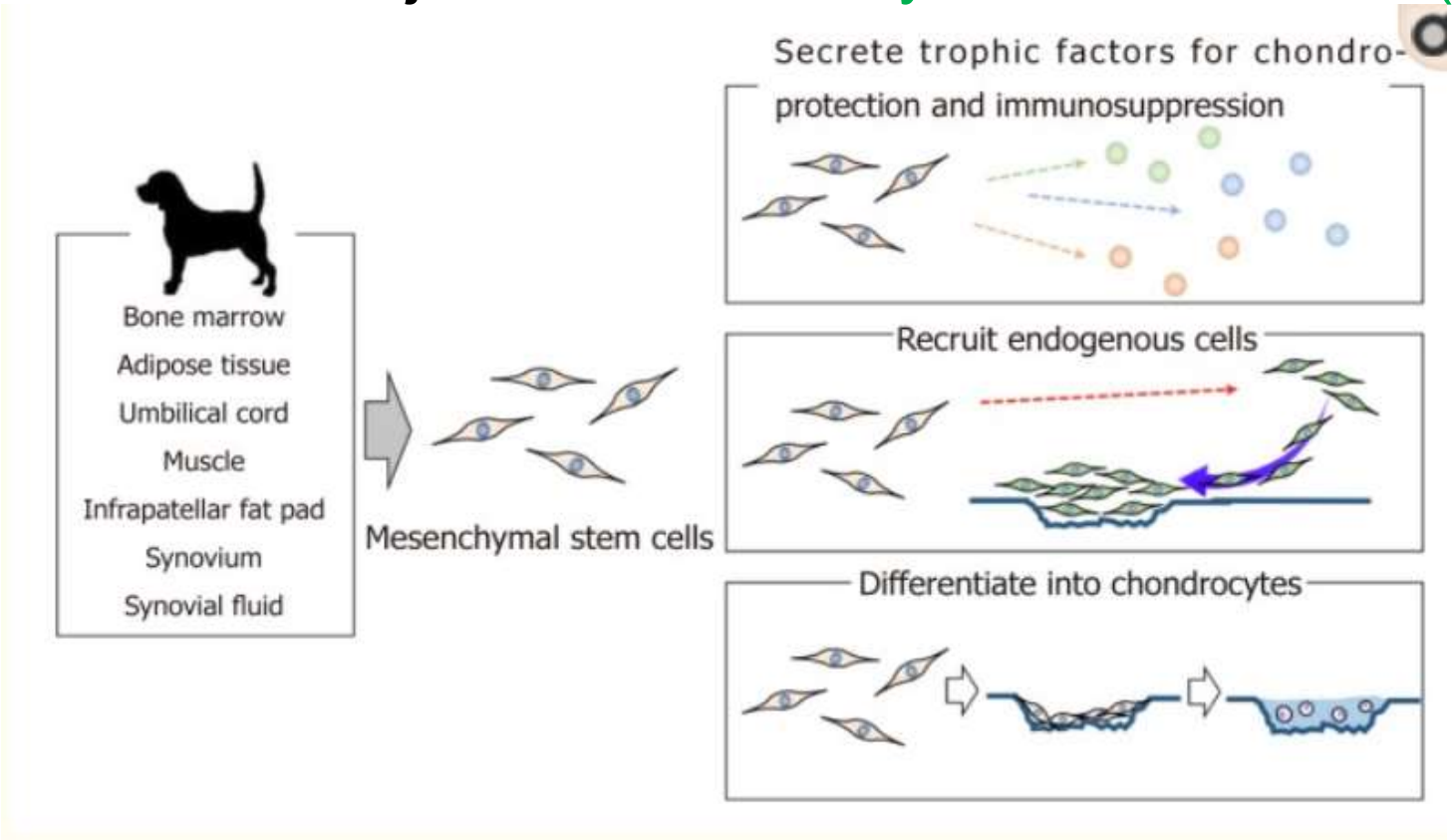
BIJKOMENDE BEHANDELINGSOPTIES

- Intra-articulaire injecties:
  - Platelet Rich Plasma (PRP):
    - autologe aangerijkte bloedplaatjes (3-8x plasmaconc)
    - bevat alpha granules & PDGF's
    - effecten:
      - angiogenese
      - aantrekken progenitor cellen
      - weefselgroei
      - aanvullen extracellulaire matrix
      - fundering voor aanhechten van mesenchymale stamcellen bij gezamenlijke therapie

Platelet rich plasma therapy in dogs with bilateral hiposteoarthritis.
Alves et al. 2021. BMC Vet Res, 17: 207.

BIJKOMENDE BEHANDELINGSOPTIES

- Intra-articulaire injecties: Mesenchymale Stamcellen (MSM):



- Mesenchymal Stem Cells for cartilage regeneration in dogs. Sasaki et al. (2019) World J Stem Cells 11, 254-269.
- Clinical application of mesenchymal stem cells therapy in musculoskeletal injuries in dogs – a review of the scientific literature. Dias et al. (2021). Open Vet J 11, 188-202.

BIJKOMENDE BEHANDELINGSOPTIES

Effects of administration of adipose-derived stromal vascular fraction and platelet-rich plasma to dogs with osteoarthritis of the hip joints
Upchurch DA et al. (2016), AVMA
DOI: https://doi.org/10.2460/ajvr.77.9.940

OBJECTIVE To evaluate effects of simultaneous intra-articular and IV injection of autologous adipose-derived stromal vascular fraction (SVF) and platelet-rich plasma (PRP) to dogs with osteoarthritis of the hip joints.

ANIMALS 22 client-owned dogs (12 placebo-treated [control] dogs and 10 treated dogs).

PROCEDURES Dogs with osteoarthritis of the hip joints that caused signs of lameness or discomfort were characterized on the basis of results of orthopedic examination, goniometry, lameness score, the Canine Brief Pain Inventory (CBPI), a visual analogue scale, and results obtained by use of a pressure-sensing walkway at week 0 (baseline). Dogs received a simultaneous intraarticular and IV injection of SVF and PRP or a placebo. Dogs were examined again 4, 8, 12, and 24 weeks after injection.

RESULTS CBPI scores were significantly lower for the treatment group at week 24, compared with scores for the control group. Mean visual analogue scale score for the treatment group was significantly higher at week 0 than at weeks 4, 8, or 24. Dogs with baseline peak vertical force (PVF) in the lowest 25th percentile were compared, and the treatment group had a significantly higher PVF than did the control group. After the SVF-PRP injection, fewer dogs in the treated group than in the control group had lameness confirmed during examination.

CONCLUSIONS AND CLINICAL RELEVANCE For dogs with osteoarthritis of the hip joints treated with SVF and PRP, improvements in CBPI and PVF were evident at some time points, compared with results for the control group.

CONCLUSIE BEHANDELINGSOPTIES

- multimodale aanpak is nodig, niet alleen medicamenteus
- scoor pijn & progressie OA
- ‘trial and error’
- goede samenwerking met de eigenaar is nodig
  - wijs de eigenaar op de subtiliteiten van pijn

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