Ağrılı hastada farmakoloji tedavi: NSAİDs

Dr. F. Gonca Şaşal
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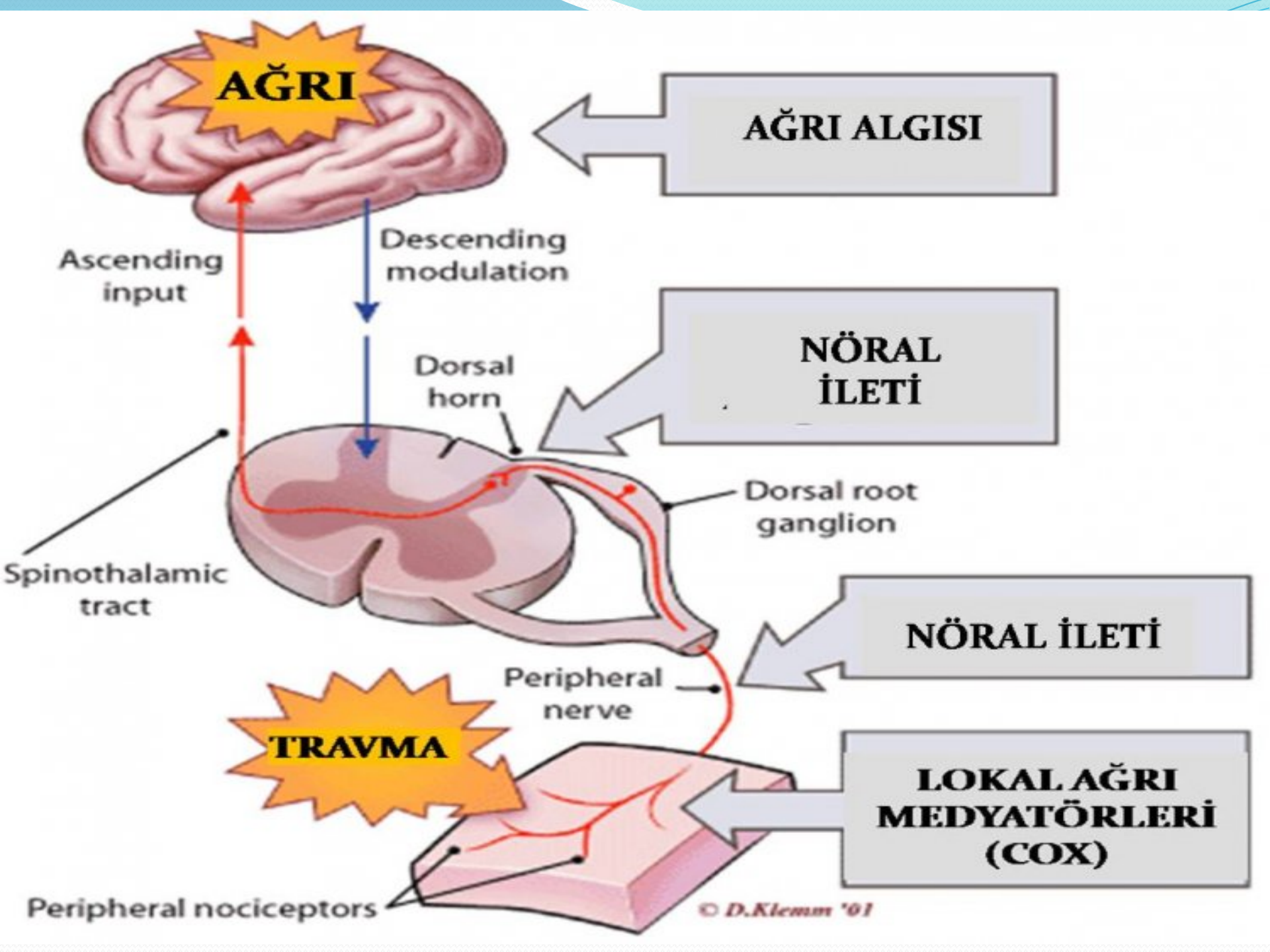
Var olan veya olası doku hasarına eşlik eden bu hasar ile tanımlanabilen,hoşa gitmeyen duyusal ve emosyonel deneyim


AĞRI
AĞRI ALGISI
Ascending input
Descending modulation
Dorsal horn
NÖRAL İLETİ
Dorsal root ganglion
Spinothalamic tract
NÖRAL İLETİ
Peripheral nerve
TRAVMA
LOKAL AĞRI MEDYATÖRLERİ (COX)
Peripheral nociceptors
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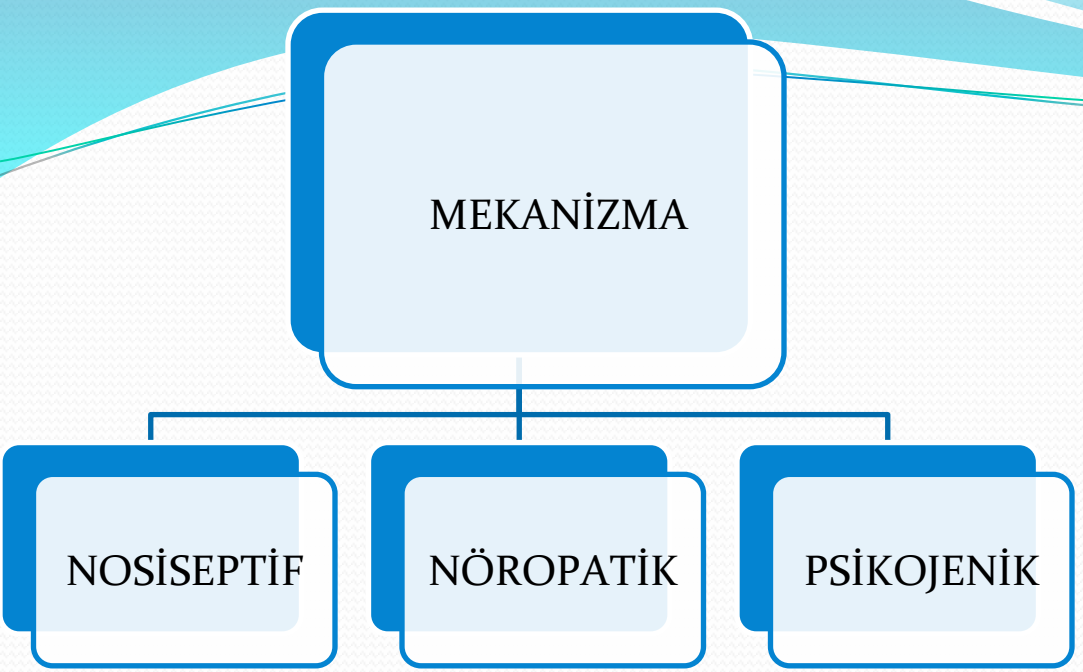
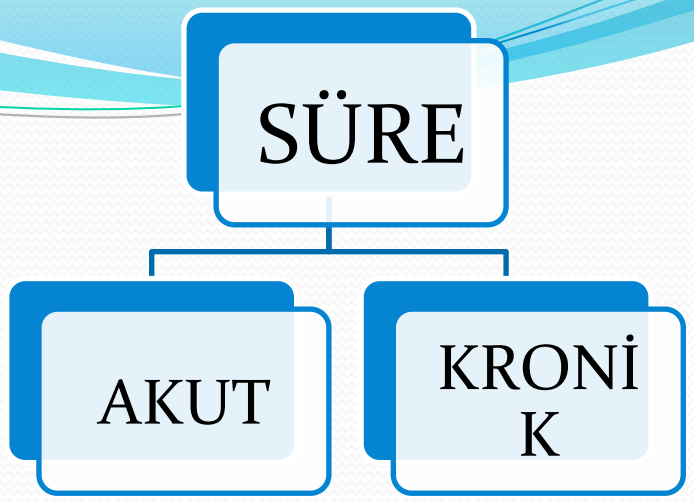
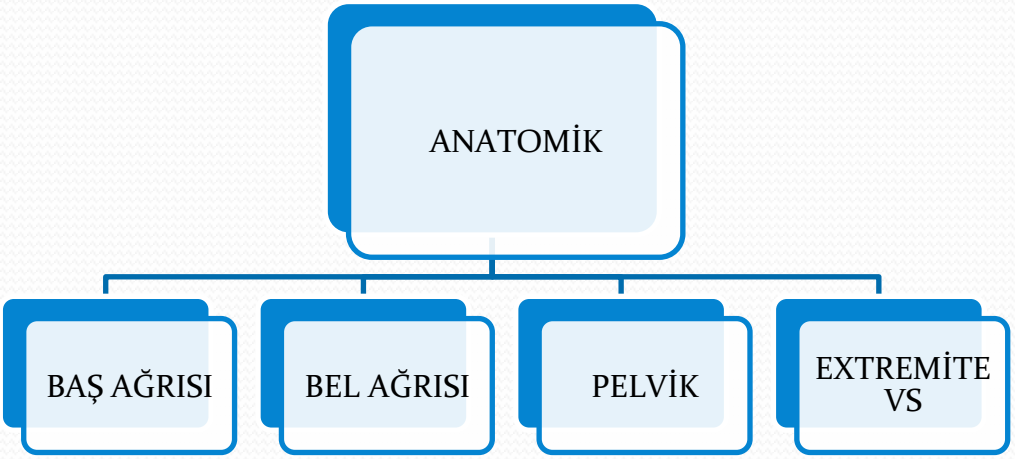
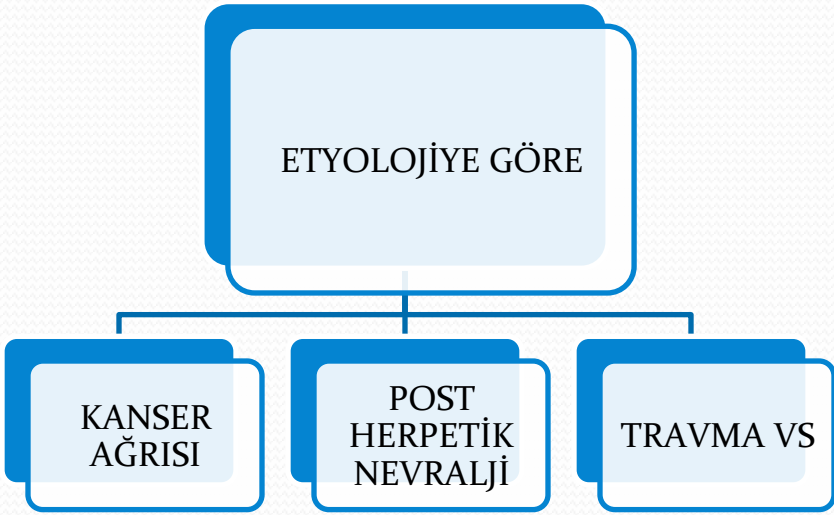

MEKANİZMA
NOSİSEPTİF
NÖROPATİK
PSİKOJENİK


SÜRE
AKUT
KRONİK


ANATOMİK
BAŞ AĞRISI
BEL AĞRISI
PELVİK
EXTREMİTE VS


ETYOLOJİYE GÖRE
KANSER AĞRISI
POST HERPETİK NEVRALJİ
TRAVMA VS

NOSİSEPTİF AĞRI

SOMATİK

- DUYUSAL
- İYİ LOKALİZE
- KESKİN, BATICI

VİSSERAL

- YAYGIN
- ZOR LOKALİZE
- ZOR TANIMLANAN

NÖROPATİK AĞRI

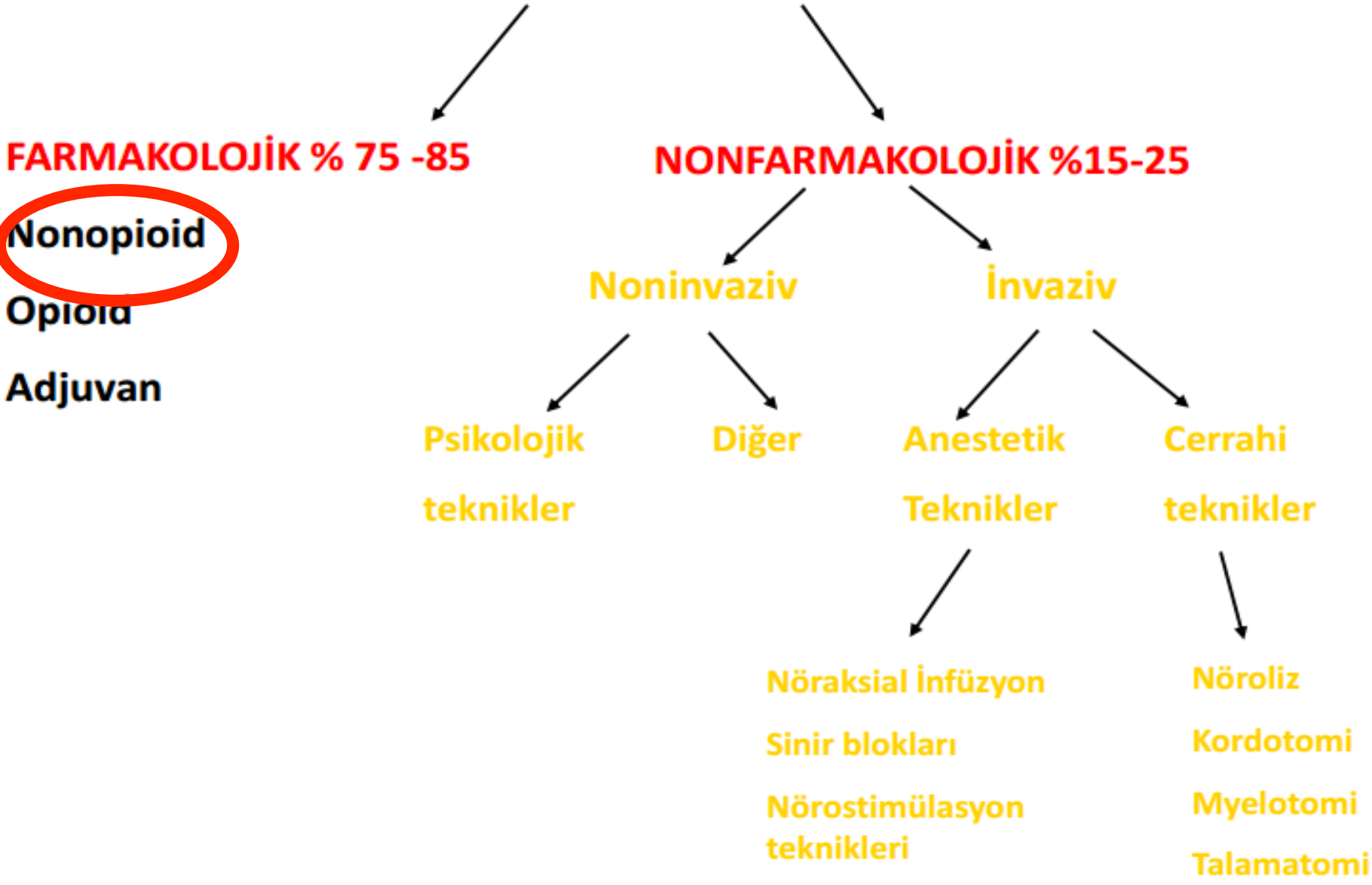
SANTRAL

- POST-HERPETİK NEVRALJİ
- DM NÖROPATİ
- PSS'DE LEZYON

PERİFERİK

- TALAMİK LEZYON
- POST-STROKE AĞRI
- SSS'DE LEZYON

AĞRI TEDAVİSİ

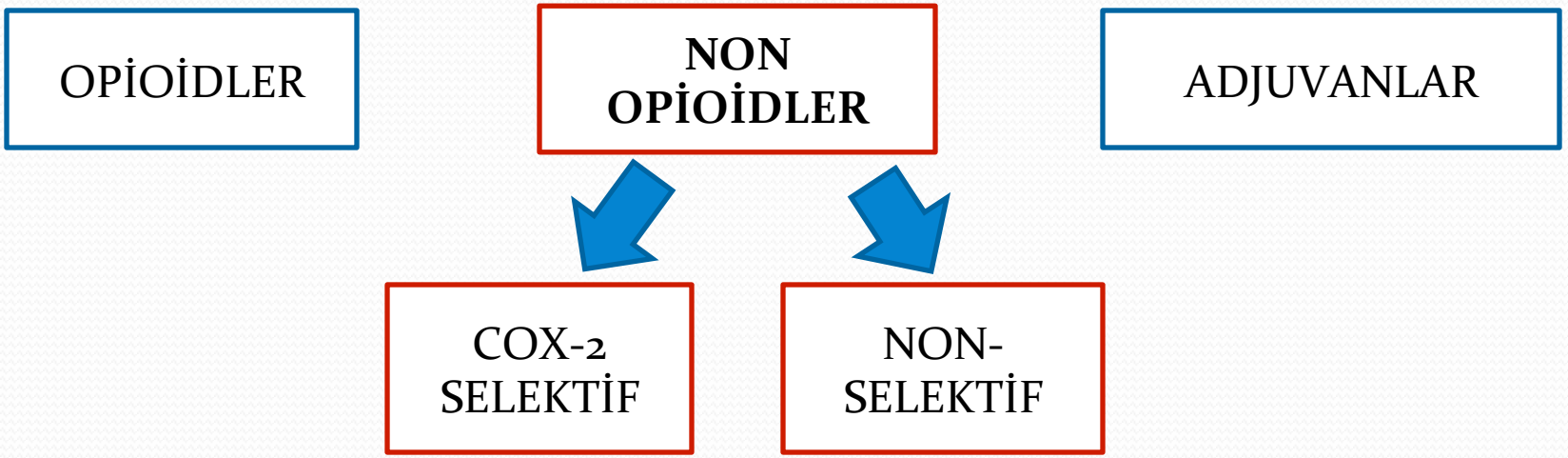


AĞRI TEDAVİSİ AMAÇLARI

- Hastanın fonsiyonel durumunu korumak
- Yaşam kalitesini arttırmak
- Minimal yan etki
- Psikolojik iyileşme

SİSTEMİK FARMAKOLOJİK TEDAVİ

ANALJEZİKLER



NON-SELEKTİF NSAİDs

- Salisilatlar- aspirin
- Propriyonik asit deriveleri- ibuprofen, ketoprofen, naproksen
- Anthralinic asit deriveleri- mefenamik asit
- Aril asetik asit deriveleri-diklofenac, aseklofenac
- Oksikam deriveleri-piroksikam, tenoksikam
- Pirol deriveleri- ketorolac
- Indol deriveleri-indometazin
- Pirazolon deriveleri- fenilbutazon

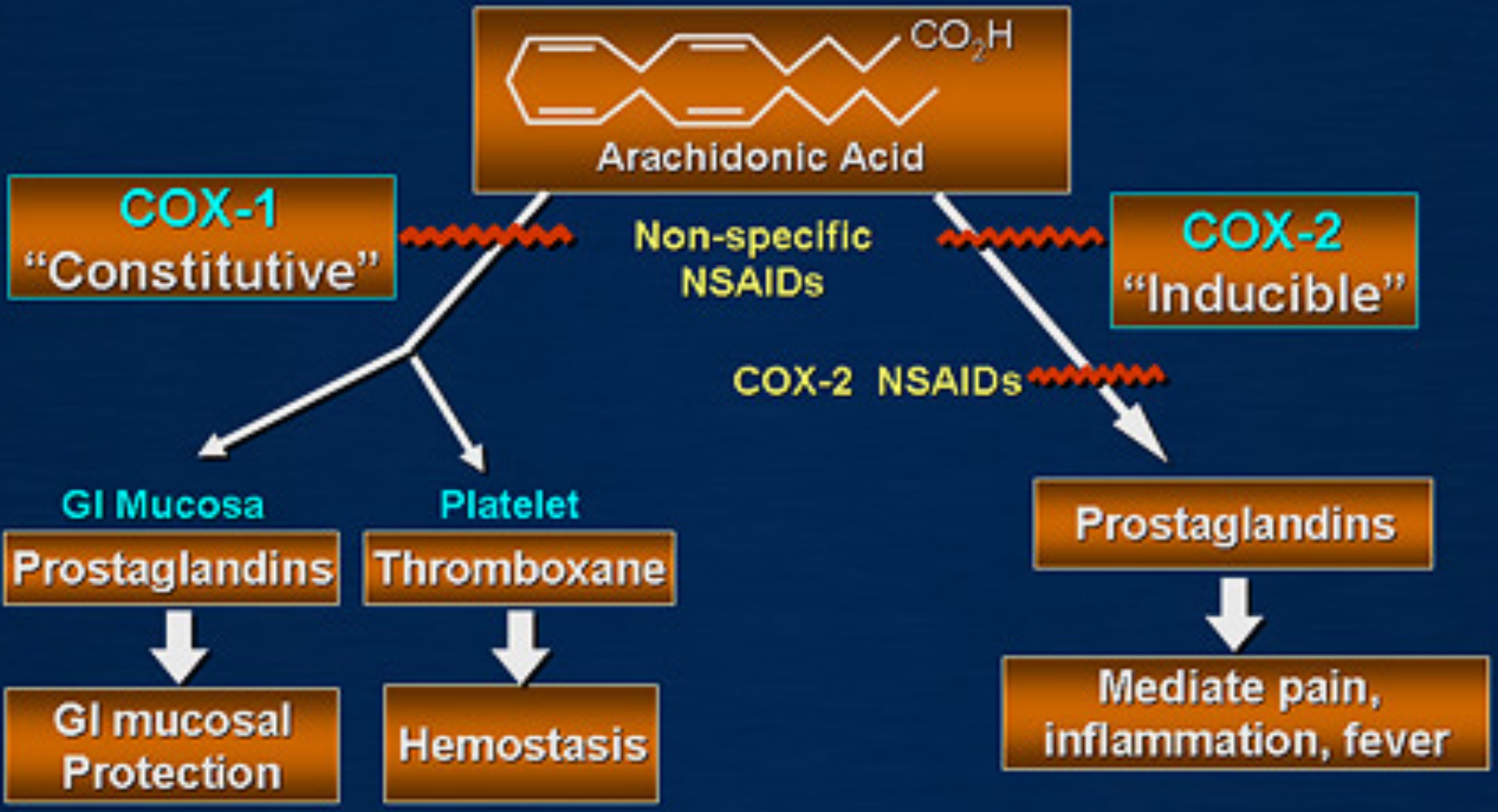
COX-2 SELEKTİF NSAİDs

- Meloksikam
- Nimesulid
- Nabumeton
- Celecoxib
- Etoricoxib
- Parecoxib

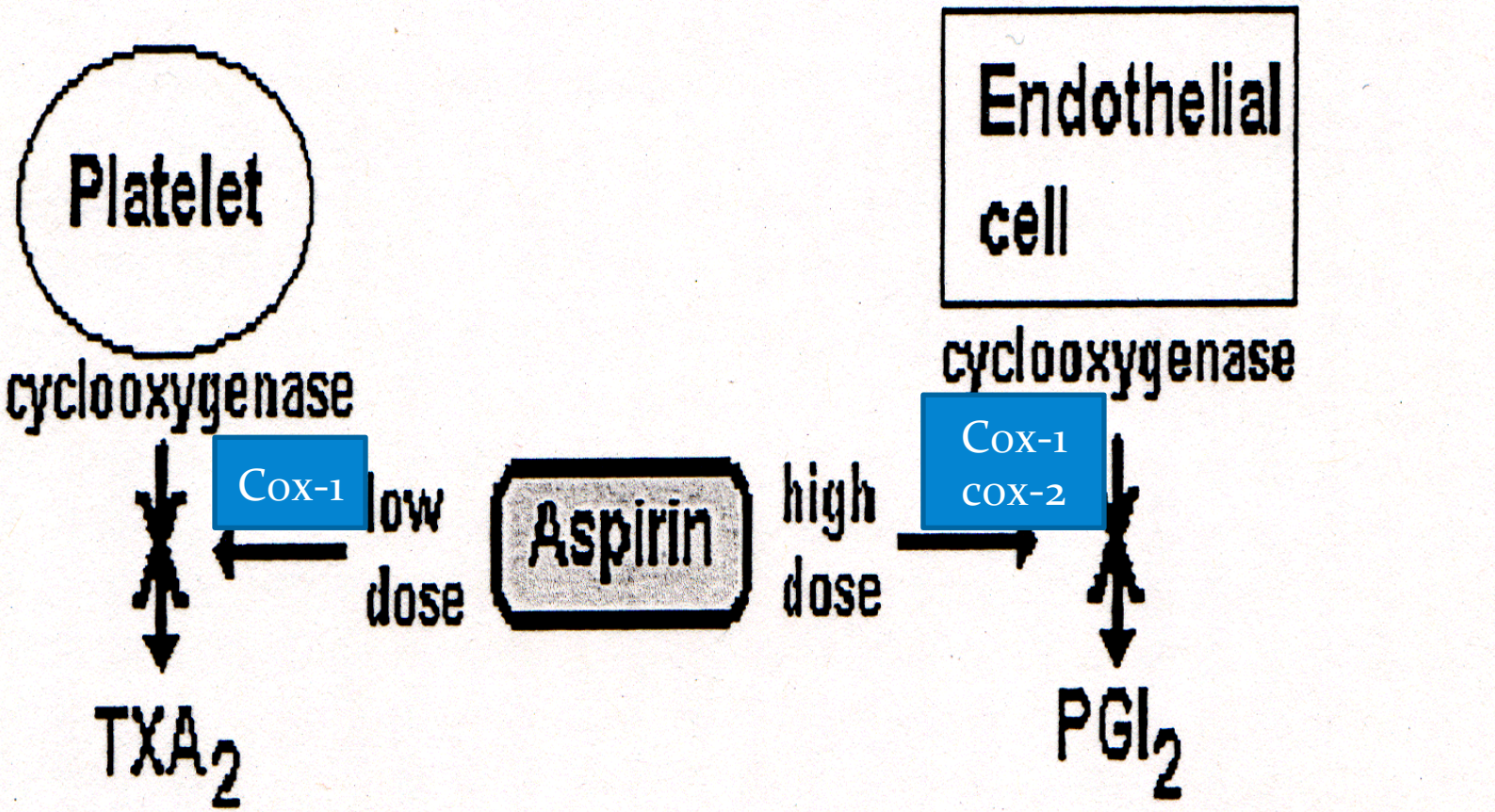
ANTİ-ENF. ETKİNLİĞİ DÜŞÜK NSAİDs

- Paresetamol
- Metamizol
- Propifenazon
- Nefopam

Mechanism of Action of NSAIDs



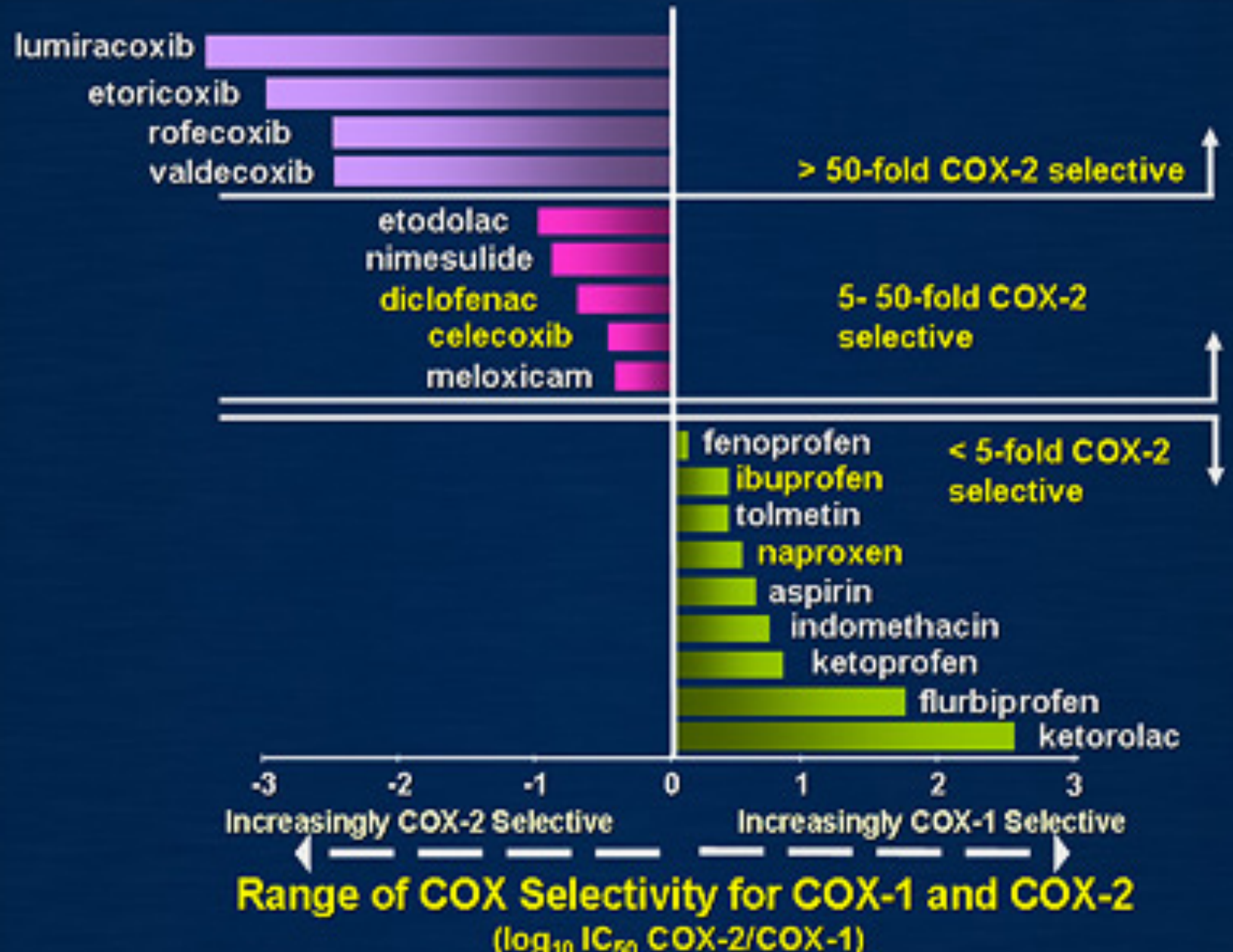
Vane JR, Botting RM. *Inflamm Res.* 1995;44(1):1-10.



+++platelet aggregation
+++platelet shape change
+++platelet granule release
+++vasoconstriction

inhibits platelet aggregation
inhibits platelet secretion
+++vasodilation

In Vitro Selectivity: COX-2/COX-1 Ratio



Ne zaman NSAİDs?

Hafif ağrı

-nsai/asetominofen
asetominofen

Orta şiddette ağrı

-nsai +/-

KE YOKSA NSAİ İLE BAŞLA

Orta-şiddetli ağrı

-nsai+asetominofen

tedavi?

Şiddetli ağrı

-nsai+asetominofen+
opioid? Non-farmakolojik

Eşit analjezik dozlamları

analgesic	PO doz (mg)
Asetominofen	650
Aspirin	650
Choline saliclate	870
İbuprofen	200-400
İndometazin	25
Ketoprofen	**25 (650mg aspirinden daha etkin)**
Naproksen sodyum	275
Mefanamik asit	50-100
Etodolak	100
Sulindak	150-200
Mg saliklat	1000

- Eklem ağrılarılarında şiddetli ağrı → NSAİ ile başla
- NSAİ+asetominofen → etki ↑
- NSAİD'leri kendi içinde kombinleme → Y.E ↑

"Formerly, 'Regular' and 'Extra-Strength'."

Akut ağrı

- Asetominofen/NSAİD ilk tercih
- Hafif/orta şiddetteki ağrılarda tek başına yeterli
- Diş ağrısı, bağ ağrısı, travma/cerrahi, dismenore de tek başına oldukça etkili
- Şiddetli ağrıda ketorolac düşün

Kronik ağrı

- Kas-iskelet sistemi ağrılarında ilk tercih asetominofen düşün
- Asetominofen etkisiz kaldığında NSAİD
- NSAİD+asetominofen
- NSAİD+asetominofen+opioid
- Non-opioid+opioid ⟶ etkinlik ↑ Y.E.↓

YAN ETKİLER

ASETOMİNOFEN

- Günlük max. doz 4g

Hepatotoksisite!

- Tekralandıkça hepatotoksisite riski ↑
- Tek bir doz ile fulminan hepatit riski!!!!
- Amerika'da yapılmış 662 akut kc yetmezliği hastasının üzerinde yapılmış prospektif bir çalışmada %42 sinin asetominofen toksisitesi olduğu görülmüş
- 1990-2002 arası organ tx merkezinden alınan datalarda kc tx hastalarının %49- asetominofen toksisitesi

altta yatan kc hastalığı
+alınan hepatotoksik ilaç
malnutrisyon
kronik alkol kullanımı

YÜKSEK RİSK

- FDA → 2-3içki/gün alkol kull. → risk ↑
- AGS (American geriatrics society)

kronik alkol kullanımı → relatif kontraendikasyon

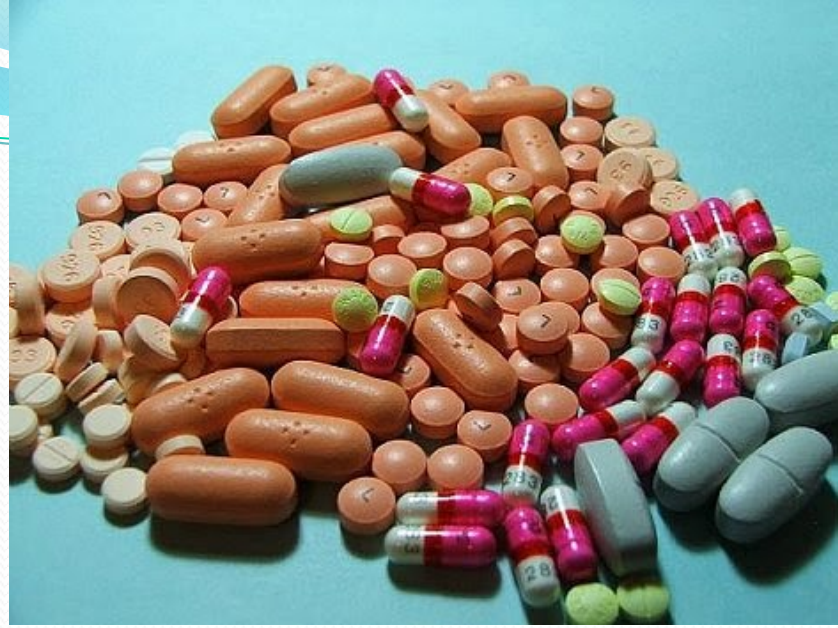
- Renal etkisi?- Nsaid lere göre çok daha az.
- Renal yetmezlik var ise Nsaid lere tercih edilir.

- Hematolojik etkileri?
- Varfarin etkisini ↑ INR ↑ doz bağımlı

asetominofen

TxA2 ⟶✖⟶ TxB2 (ancak min. etki)

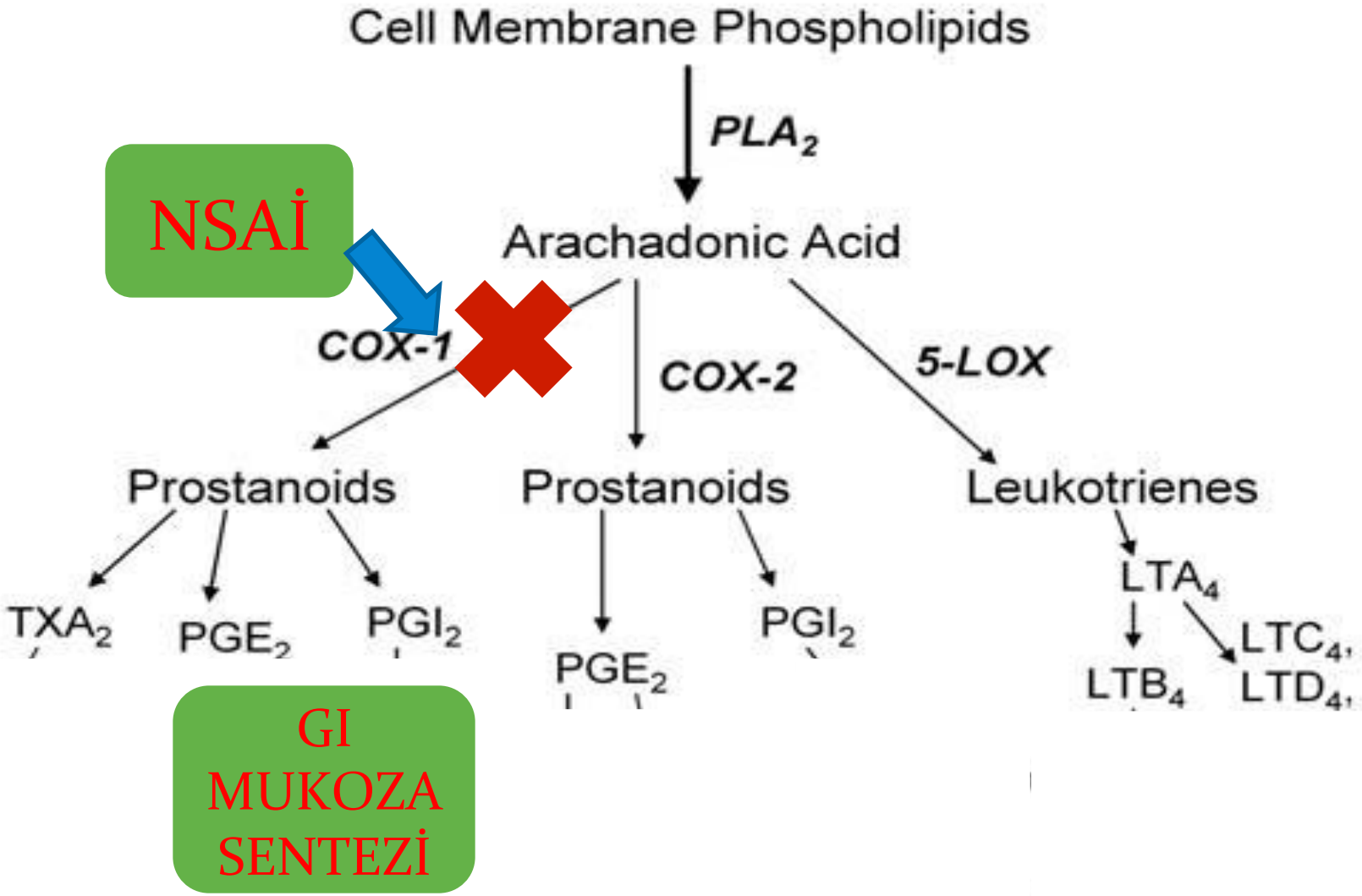
- Gastrointestinal etkileri?
- 500mg/gün kronik kullanımı gastrik mukozayı ↓
- Nsaid lere göre etkisi çok daha az



NSAİDs

Gastrointestinal yan etkiler!

- En sık yan etkisi
- Gastritten GI kanama, GI perforasyona kadar ilerleyebilen şiddette
- Doz ve kullanım süresi bağımlı
- Non-selektif Nsaid lerin kronik kullanımında %15-30 GI ülser.
- Cox-2 selektif nsai lerin GI yan etkisi çok daha az
- Oral alımında lokal irritasyon var ama esas mekanizma PG sentez inhibisyonu


Cell Membrane Phospholipids
PLA2
NSAİ
Arachadonic Acid
COX-1
COX-2
5-LOX
Prostanoids
Prostanoids
Leukotrienes
TXA2
PGE2
PGI2
PGE2
PGI2
LTA4
LTB4
LTC4,
LTD4,
GI
MUKOZA
SENTEZİ

Risk Faktörleri

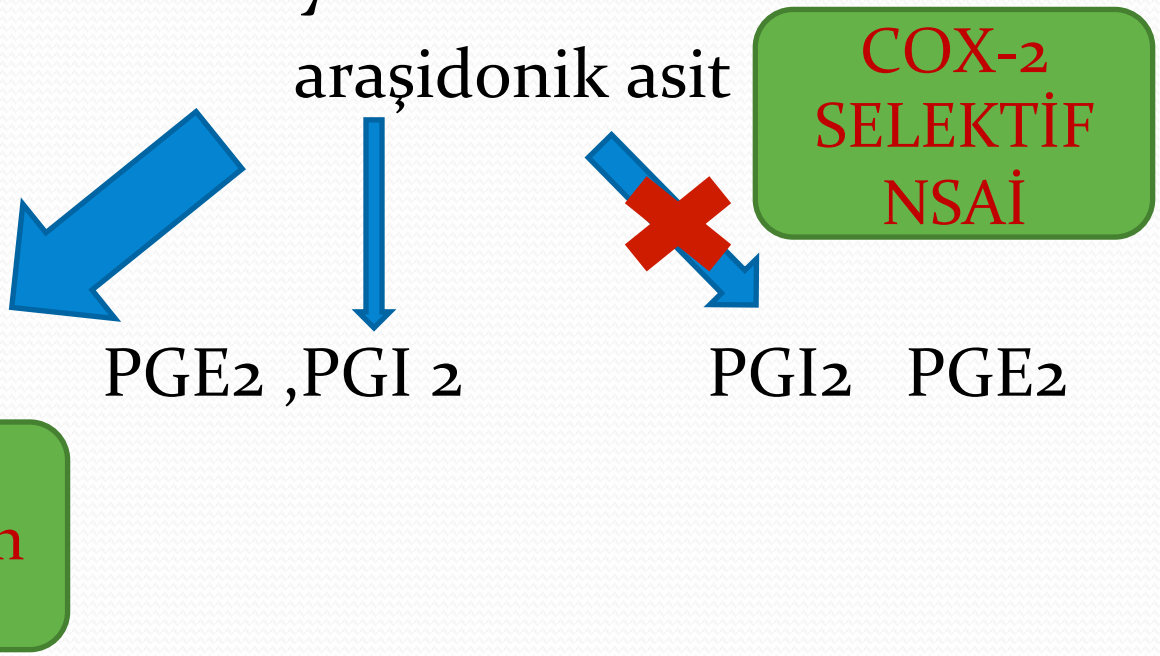
- Önceden var olan GI ülser (en önemli risk faktörü!)
- 65 üstü yaş
- Kardiyovasküler hastalık olması
- Şiddetli romatoid artrit varlığı
- Steroid kullanımı
- Antikoagülan/antiagregan tedavi almak
- H. Pilori enfeksiyonu
- Sigara kullanmak
- Aşırı alkol kullanımı (risk boyutu net değil)

GI risk faktörü olanlarda analjezik seçimi

- Cox-2 selektif bir ajan (kvs risk faktörlerini araştır)
- Non-selektif nsai+ gastroprotektif ajan (H2 res. blokerleri, misoprostol, ppi)
- Hafif-orta şiddette ağrı- asetominofen düşün
- Şiddetli ağrı+ GI ciddi risk- opioid düşün?

COX-2 SELEKTİF NSAİLERİN DE GI YAN ETKİSİ!

Kardiyovasküler yan etkileri



Hem selektif hem non-selektif nsai ler için de PGI azalması epitel hücre azalması ve sonucunda ateroskleroz, HT yatkınlık

Modifiye edilemez risk faktörleri	• İleri yaş • Erkek cinsiyet • Genetik faktörler
Modifiye edilebilir risk faktörleri	• Aterosklerotik damar hastalığı(ASKH,periferik arter hast) • Valvuler kapak hast, kardiyomyopati • HT, DM, AF, obezite, sigara kull, dislipidemi, fiziksel inaktivite, post-menopozal hormon terapisi
Potansiyel olarak modifiye edilebilir risk faktörleri	• Metabolik sendrom, OSAS, migren • Oks kullanımı, alkol/madde bağımlılığı

Curr Cardiol Rep (2016) 18: 25
DOI 10.1007/s11886-016-0702-4

ISCHEMIC HEART DISEASE (D MUKHERJEE, SECTION EDITOR)

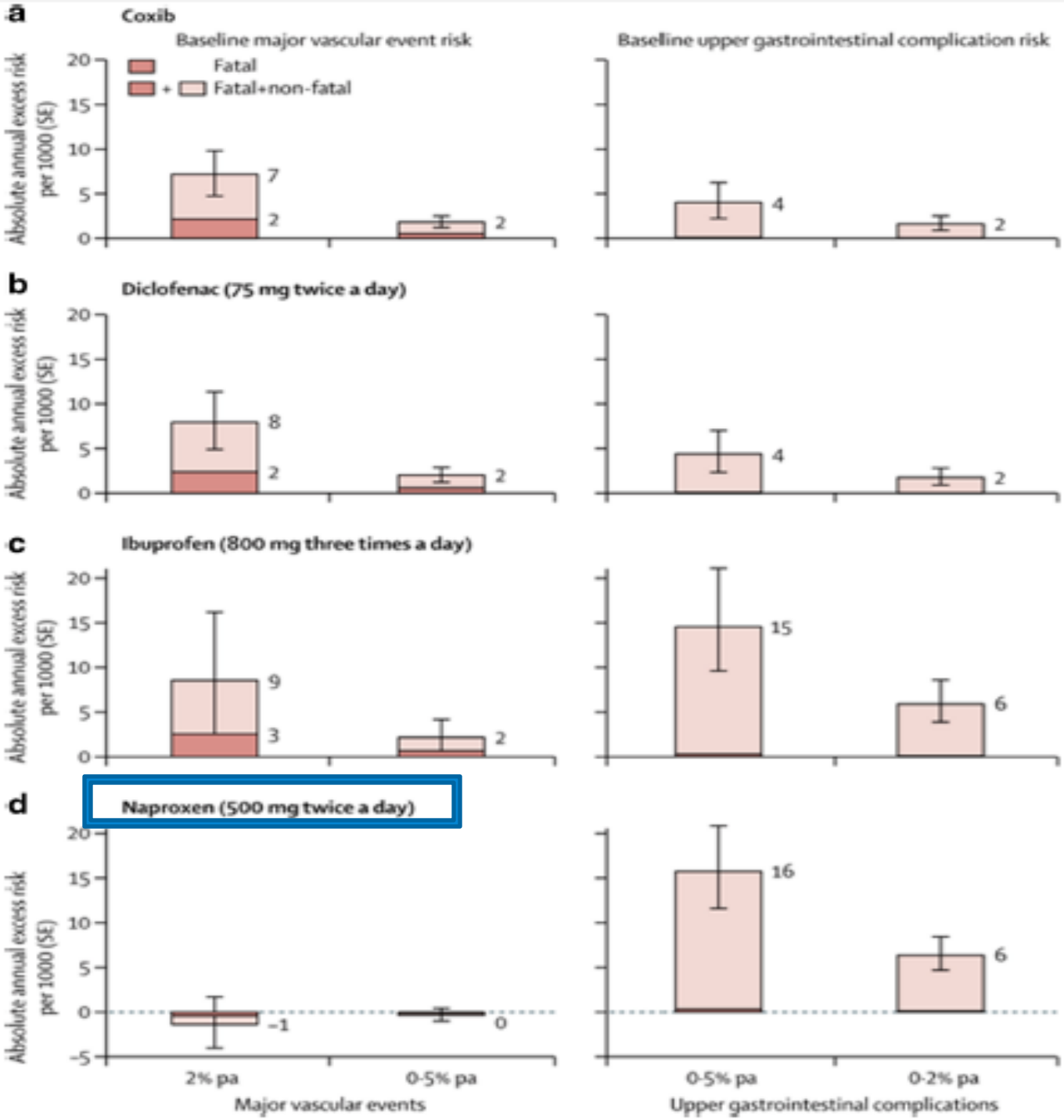
Cardiovascular Effects of Nonsteroidal Anti-inflammatory Drugs

Carlo Patrono[1]

Published online: 3 February 2016

Abstract Nonsteroidal anti-inflammatory drugs (NSAIDs) include aspirin, other traditional NSAIDs, and coxibs. Evidence obtained during the past 10 years has focused attention on the cardiovascular hazard associated with coxibs and some traditional NSAIDs. The large randomized trials of prolonged coxib treatment added importantly to information

relief of chronic pain and inflammation associated with osteoarthritis (OA) and rheumatoid arthritis (RA) [1]. The NSAID family includes aspirin, other traditional NSAIDs (tNSAIDs) developed to mimic aspirin's pharmacological effects, and a relatively newer class—the coxibs—developed to reduce the gastrointestinal (GI) toxicity of tNSAIDs [2]. NSAIDs share a


a
Coxib
Baseline major vascular event risk
Baseline upper gastrointestinal complication risk
Fatal
+ Fatal+non-fatal
Absolute annual excess risk per 1000 (SE)
20
15
10
5
0
7
2
2
4
2
b
Diclofenac (75 mg twice a day)
8
2
2
4
2
c
Ibuprofen (800 mg three times a day)
9
3
2
15
6
d
Naproxen (500 mg twice a day)
-5
-1
0
16
6
2% pa
0·5% pa
0·5% pa
0·2% pa
Major vascular events
Upper gastrointestinal complications

KVS risk faktörleri olan hastada Nsaid seçimi?

- Naproksen düşünülebilinir
- Cox-2 selektif nsaid en son tercih

KVS+GI risk faktörleri olan hastada Nsai seçimi?

- Naproksen+plavix(aspirin olmamalı) düşük doz?
- Düşük doz cox-2 selektif nsai+ düşük doz aspirin+ ppi ?

Opioid düşün!

Hematolojik yan etkileri

- Aspirin geri dönüşümsüz şekilde trombositler üzerinde inhibisyon yapar
- Diğer Nsaid lerin de trombositler üzerinde etkisi vardır ancak geri dönüşümlüdür.
- Ibuprofen trombositlerin üzerindeki aspirinin bağlanma yerine bağlandığı için aspirinin etkisini azaltır. Aspirinden 30dk-2saat önce alınmalı ya da 8saat sonrasında
- Diğer Nsaidlerin de cox-1 inhibisyonu var ancak aspirin gibi geri dönüşümsüz olmadığı için kardiyoprotektif etki yok. Yine de kanama zamanını uzatabilirler

Renal yan etkileri

- **COX-2**--- henle, makula densa, afferent arteriol de PG sentezini sağlar. Diüretik etki gösterir
- COX-1--- glomerul ve afferent arteriolde PG sentezini sağlar. Renal homeostazise yardımcı olur
- **COX** inhibisyonu ile ödem, HT, hiperkalemi görülebilir.

★ Yeterli volum sağlanıyorsa böbrekteki PG lerin etkileri minimaldir.

- Nsaid ilişkili renal yan etki olasılığı genel populasyonda- %1-5

Risk faktörleri

- erkek cinsiyet
- Komorbid hastalıklar: HT, DM
- **Yeterli volum sağlanamaması**

KKY
KBY
SİROZ

KONTRAENDİKE

Hepatotoksik yan etkileri

- 1/100000 den daha az
- Siroz varsa uzak durulabilir
- Diflofenac, rofecoxib transaminazları biraz yükseltebilir

Kognitif fonksiyonlara olan etkileri

- Baş dönmesi, sersemlik hali, dikkat azalması
- Duygu durum değişiklikleri

Alerjik yan etkileri

- Kendileri arasında çapraz reaksiyon gözlenebilinir
- COX-2 selektif Nsai lerde daha az alerjik reaksiyonlar gözlemlenmiş
- Astım, kronik ürtiker öyküsü olanlarda dikkatli kullanılmalı

★celecoxib ve valdecoxib preparatlarında sulfon bileşiği bulunduğu için sulfonamid alerjisi olanlarda dikkat

Özel durumlarda kullanım

GEBELİKTE KULLANIM

- FDA-- non-selektif nsaid ⟹ kategori B
  cox-2 selektif nsaid ⟹ kategori C
- Fetusa geçerler
- ibuprofen- duktal kapanma, oligohidroamnioz
  indometazin- duktal konstriksiyon
  aspirin- duktus arteriosusun erken kapanması, gastroşizis, son trimesterda kanama riski artışı, plasenta dekolmanı

- PG sentez inhibisyonundan dolayı kontraksiyonları arttırabilirler
- Acetominofen güvenle kullanılabilinir. Yeni doğanda wheezing?

EMZİRME DÖNEMİNDE KULLANIM

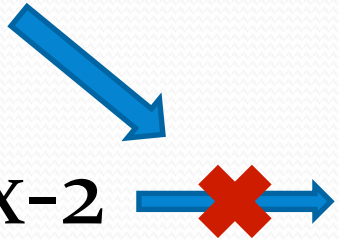
- Süte geçebilir. Ciddi yan etki görülmemiş
- Yeni doğan bebekte sarılık riski artışı?
- Kısa yarı ömürlü olan nsaileri seçmek mantıklı
- Asetominofen, ibuprofen tercih edilebilinir
- topikal kullanım?

PEDİATRİK KULLANIM

- En güvenli analjezikler asetominofen, ibuprofen
- indometazin, ketorolac, naproxen de pediatrik kullanım için onay alınmış

Anti kanserojen etkileri

NSAİ



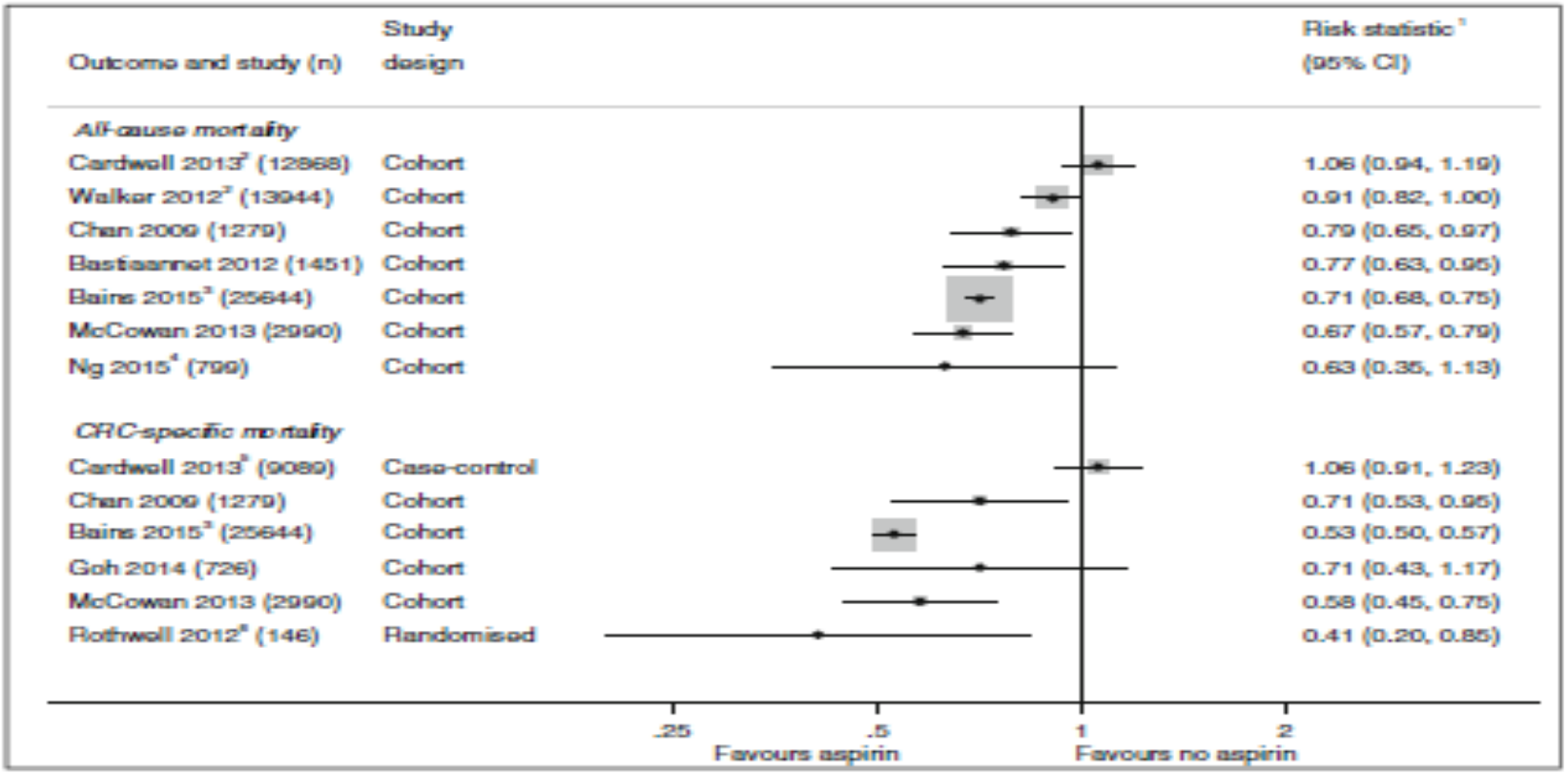
COX-2 hücre çoğalması, antiapoptotik etki

- Özellikle kolon kanseri üzerine olumlu etkisi görülmüş.

Curr Colorectal Cancer Rep (2016) 12:27–34
DOI 10.1007/s11888-016-0306-9

Aspirin and Colorectal Cancer Prevention and Treatment: Is It for Everyone?

Christopher Coyle[1] · Fay Helen Cafferty[1] · Ruth Elizabeth Langley[1]



Chemoprevention of colorectal neoplasia

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Key words
adenoma, aspirin, chemoprophylaxis, colon cancer, prevention.

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Abstract

Background: Colorectal cancer is a common and often fatal malignancy. Currently, the modifications that alter disease outcome include early symptom recognition, population screening as well as improved surgical and adjuvant treatments. Preventative strategies have been limited with little evidence that lifestyle changes significantly alter risk. There is however a growing awareness of a potential role for chemoprevention in some patient groups. This study aimed to review the literature associated with chemoprevention in colorectal cancer.

Methods: An electronic literature search of MEDLINE and Embase databases was performed on PubMed for studies detailing the use of chemoprevention agents in colon and rectal cancer. The search was limited to clinical trials on adult humans (>16 years of age) published in English since 1990.

Results: The strongest evidence is for non-steroidal anti-inflammatory drugs slowing polyp progression, notably sulindac and aspirin in patients with familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer, respectively. There is also increasing evidence that continuing use of low-dose aspirin reduces long-term incidence of colorectal cancers. Cyclooxygenase 2 inhibitors also have a potential role but cardiac toxicity currently limits their use. Folic acid, statins, antioxidants, calcium and 5-aminosalicylic acid lack evidence to support their use at present.

Conclusions: Currently, there is not enough evidence to support the implementation of a chemopreventative agent for general use. However, there appears to be a role for aspirin in selected subgroups.

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Review Article

Non-steroidal anti-inflammatory drug use and risk of endometrial cancer: A systematic review and meta-analysis of observational studies

Freija Verdoodt [a], Søren Friis [b,c], Christian Dehlendorff [b], Vanna Albieri [b], Susanne K. Kjaer [a,d,*]

[a] Unit of Virus, Lifestyle and Genes, Danish Cancer Society Research Center, Copenhagen, Denmark
[b] Unit of Statistics, Bioinformatics and Registry, Danish Cancer Society Research Center, Copenhagen, Denmark
[c] Department of Public Health, University of Copenhagen, Copenhagen, and Department of Clinical Epidemiology, Faculty of Health, Aarhus University Hospital, Aarhus, Denmark
[d] Department of Gynecology, Rigshospitalet, University of Copenhagen, Denmark

HIGHLIGHTS

- Regular aspirin or NA-NSAID use was associated with a reduced risk of endometrial cancer.
- The reduction in endometrial cancer risk was consistent, albeit small.
- The reduction in endometrial cancer risk increased with frequency of NSAID use.

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Endometrial cancer
Non-steroidal anti-inflammatory drugs
Aspirin
Cancer prevention

ABSTRACT

Objective. Non-steroidal anti-inflammatory drug (NSAID) use has been linked to a reduction in the risk of several cancer types. For endometrial cancer, however, results have been inconsistent. To summarize the available evidence on the risk of endometrial cancer associated with use of aspirin or non-aspirin (NA-) NSAIDs, we performed a systematic review and meta-analysis of observational studies.

Methods. We conducted a bibliographic database search in PubMed, Embase and Cochrane Library. Relative risk estimates were extracted from eligible case–control and cohort studies and pooled using a random effects model.

Results. Six case–control and seven cohort studies were found eligible for our meta-analysis. We observed risk reductions in endometrial cancer associated with regular use of aspirin (case–control: 11%, cohort: 8%) and NA-NSAIDs (case–control: 9%, cohort: 6%), compared to non-use. However, the pooled risk ratios were not statistically significant. Higher risk reductions were seen with high frequency of notably aspirin use (case–control: 37%, cohort: 20%). The inverse association between regular aspirin use and endometrial cancer risk was strongest among women with a body mass index above 30 (case–control: 44%, cohort: 20%).

Conclusions. Regular use of aspirin or NA-NSAIDs was associated with a marginally reduced risk of endometrial cancer. Larger risk reductions were linked with high frequency of NSAID use and high BMI.

Kognitif fonksiyonlara olan etkileri

- Alzheimer hastalığını azaltabilir?

Non-selective NSAIDs improve the amyloid-β-mediated suppression of memory and synaptic plasticity

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ABSTRACT

Alzheimer's disease (AD) is characterized by the formation of amyloid beta (Aβ) plaques in the brain. Dysfunctional excitatory synaptic transmission and neuronal plasticity are generally accepted as primary events in the development of AD. There is evidence to suggest that both COX-1 expression and COX-2 expression are changed in the brain of AD patients. However, the impact of COX-dependent mechanisms on synaptic dysfunction underlying the memory deficit is not fully elucidated. In the present study effects of non-selective NSAIDs (aspirin and sodium salicylate) on associated memory impairment as well as Aβ-mediated suppression of synaptic plasticity in the hippocampus were examined. Aβ1-42 (5 μg/μl) and ibotenic acid (5 μg/μl) were injected bilaterally into the dorsal hippocampus of rats and the spatial memory and long term potentiation (LTP) were assessed by water maze performance and in vivo field potential recording, respectively. Field excitatory post synaptic potentials (fEPSP) were recorded from stratum radiatum of area CA1 following Schaffer collateral stimulation. Behavioral study revealed that both sub-chronic high dose of sodium salicylate (SS) and chronic low dose of aspirin improved the spatial memory impairment of Aβ treated rats, however the effects of SS were lower than those of aspirin. Animals treated with SS and aspirin showed a significant decrease in escape latency (SS: $F(1, 24) = 15.85$, $p < 0.01$, aspirin: $F(1, 22) = 25.24$, $p < 0.001$, ANOVA). Furthermore, in probe test, animals treated with aspirin ($p < 0.05$) but not SS ($p > 0.05$) spent more time (one-way ANOVA) in target quadrant zone. Both applied drugs restored the suppression of fEPSP slope LTP that was induced by Aβ treatment (unpaired t-test, $p < 0.001$). Aspirin showed a preventative effect also against Aβ-induced changes in LTP and memory task when applied before Aβ administration. Since aspirin and SS improved synaptic dysfunction, we can suggest that COX-dependent mechanisms may play a role in synaptic dysfunction in an experimental model of AD.

Non-Steroidal Anti-Inflammatory Drugs as a Treatment for Alzheimer's Disease: A Systematic Review and Meta-Analysis of Treatment Effect

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Abstract

Introduction Alzheimer's disease (AD) is the cause of more than two-thirds of all dementia cases. Although there is no effective treatment against this disorder, its association with neuroinflammation suggests that non-steroidal anti-inflammatory drugs (NSAIDs) might represent a potential therapeutic option.

Objective The objective of this study was to evaluate the efficacy of NSAIDs in the treatment of AD using a meta-analysis approach.

Methods MEDLINE, Web of Science, Science Direct, and the Cochrane Library were used to search all the randomized controlled trials that have evaluated the efficacy of NSAIDs as a treatment for AD (up to 1 October 2014). The overall effect of NSAIDs versus placebo was determined using a random effects model meta-analysis where we compared changes (i.e., mean differences pre- vs. post-treatment) between the two conditions in test scores indicative of cognition, disease severity, and related outcomes.

Results Seven studies were finally included in the meta-analysis. Diclofenac/misoprostol, nimesulide, naproxen, rofecoxib, ibuprofen, indomethacin, tarenflurbil, and celecoxib were the NSAIDs used in these reports. The results of the AD Assessment Scale–cognitive subscale (ADAS–cog), the Clinical Dementia Rating Scale sum-of-boxes (CDR-SOB), and the Mini-Mental State Examination (MMSE) showed no statistical or clinical significance of NSAIDs treatment compared with placebo, i.e., mean differences of −0.24 (95 % Confidence Interval (CI) −1.04 to 0.57; $P = 0.52$), −0.07 (95 % CI −0.7 to 0.56; $P = 0.82$), and 0.35 (95 % CI −0.34 to 1.04; $P = 0.32$), respectively.

Conclusion Current preliminary evidence suggests no beneficial effect of NSAIDs on cognition or overall AD severity. Thus, although more research is needed in the field, the evidence available does not support the use of NSAIDs for AD treatment.

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Kas-iskelet sistemine olan etkileri

- Heterotopik ossifikasyon tedavisinde ve önlenmesinde kullanılıyor

yara iyileşmesi

- inflamasyon
- proliferasyon
- remodelling

NSAİ → PG sentez inh.

Anlamlı sonuç bulunamamış

Review article

Repercussions of NSAIDS drugs on bone tissue: The osteoblast

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ABSTRACT

Non-steroidal anti-inflammatory drugs (NSAIDs) can act by modulating the behavior of osteoblasts, including their proliferation, differentiation, adhesion, and migration, but not all NSAIDs have these effects. Our objective was to update the information on this issue in a review of the literature in order to offer guidance on the prescription of the appropriate NSAID(s) to patients requiring bone tissue repair.

To review current knowledge of this issue by searching for all relevant publications since 2001 in the MEDLINE, EMBASE and Cochrane Library databases, we used the following descriptors: bone tissue, osteoblast, NSAIDs, Anti-inflammatory drugs.

Published studies show that most NSAIDs have an adverse effect on osteoblast growth by cell cycle arrest and apoptosis induction. The effect on differentiation varies according to the drug, dose, and treatment time. Osteoblast adhesion is increased and migration decreased by some NSAIDs, such as indomethacin and diclofenac. The antigenic profile or phagocytic function can also be modulated by NSAIDs.

In general, NSAIDs have an adverse effect on bone tissue and given the routine administration of NSAIDs to individuals requiring bone repair, in which the osteoblast has an essential role, this effect on bone should be borne in mind.

Comparative clinical study of the prophylaxis of heterotopic ossifications after total hip arthroplasty using etoricoxib or diclofenac

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Abstract

Purpose This study investigated whether etoricoxib (COX-II blocker) has a superior efficacy of preventing heterotopic ossification (HO) after total hip arthroplasty (THA) compared to diclofenac (non-selective NSAID).

Methods One hundred patients were included (50 in each group) in this single centre, prospective, double-blinded, randomized, controlled trial. Etoricoxib (90 mg) was administered once and diclofenac (75 mg) twice per day for a perioperative period of nine days. The incidence of HO was evaluated on radiographs of the pelvis six months after surgery.

Results Eighty nine of 100 (89 %) patients could be analysed. The overall HO incidence was 37.8 %. There was no significant difference between both study groups. Twelve patients (27.3 %) of the DIC group and 13 patients (28.9 %) of the ETO group showed Brooker grade I ossifications. Five patients (11.4 %) of the DIC and four patients of the ETO (8.9 %) group showed grade II HO formations. No class III or IV HO formations occured in both groups. Ad hoc analysis detected a negative correlation between HO incidence and

Conclusions Etoricoxib and diclofenac are equally effective for oral HO prophylaxis after primary cementless THA when given for nine peri-operative days to ensure a full recovery and high patient satisfaction.

✉ Sebastian Winkler
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Perioperatif Nsaid kullanımı

- Perioperatif multimodal analjezi yaklaşımı
- En sık kullanılan ağrı tedavisi rejimi

Non-opioid
Opioid
Lokal anestezik
Anti konvülzan

- Post operatif yoğun analjezik tedavisi doğru mu?

- 18 metaanaliz, 8 randomize kontrollü çalışmayı ele alan bir derlemede post-operatif agresif ağrı tedavisinin komplikasyonu arttırdığı görülmüş.

- Varılan son nokta post-operatif ağrı tedavisinde amaç hastanın rehabilitasyon programlarına uyumunu sağlayacak kadar analjezi.

Ketorolac

- Şiddetli ağrı için çok iyi bir ajan
- 30mg x 4 günlük önerilen doz.
- Yaşlılarda dozun 90mg/g a düşürülmesi önerilir.

Ibuprofen

- 400-800mg x 4 günlük önerilen dozu
- Y.E. Leri diğer nsaid lere benzer

Parecoxib

- 40mg parecoxib=30mg ketorolac
- COX-2 selektif

Asetominofen

- Günlük 4g a kadar çıkılabilinir
- Hafif baş dönmesi, mide bulantısı yapabilir
- 1000mg asetominofen=30mg ketorolac
- İnfüzyon yerinde ağrı (suda çözünürlük az, ph:3.5)

Akut aşırı doz

ASETOMİNOFEN

- Hafif transaminaz yükselmesinden fulminan hepatik nekroza kadar değişen seviyelerde hepatotoksisiteye sebeb olabilir
- Plazma düzeyleri 300mcg/ml-4saat , 45mcg/ml-15saat altındaki değerlerin karaciğer rejenerasyonu ile düzeleceği öngörülür
- Karın ağrısı, mide bulantısı, kusma, kcft yüksekliği ilk belirtiler iken hepatik ensefalopati, koagülopati kötü prognoz kriterleridir.
- İlk 4 saat gastrik lavaj, aktif kömür denenebilinir. Sonrasında N-asetil sistein

ASPİRİN VE DİĞER SALİSİLATLAR

- Kronik fazla doz kullanımda-baş ağrısı, sersemlik hali, kulaklarda zonklama
- Akut kullanımda 150-300mg/kg orta şiddette toksisite 300mg/kg ın üzerinde dozlar şiddetli toksisiteye neden olurlar.
- Letarji, kusma-aspirasyon, hipoventilasyon, taşıkardi
- Beraberinde opioid alımı varsa bulgular maskelenebilir!!!
- Specifik antidotu yok! Aktif kullanımı denenebilinir erken dönemde tespit edilmişse.
- İdrarı alkalileştirmek. $NaHCO_3$+KCL infüzyonu.

DİĞER NSAİD LER

- Toksisiteleri nadir
- Karın ağrısı, mide bulantısı, kusma
- Çok aşırı dozlarda metabolik asidoza neden olabilirler. Hipotansiyon, hipotermi ile birlikte seyredebilir
- Destek tedavisi