

# ANALGETICI U TERAPIJI HRONIČNOG KANCERSKOG BOLA

Project number: 585927-EPP-1-2017-1-RS-EPPKA2-CBHE-JP (2017 – 3109 / 001 – 001)

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*Bol se definiše kao neprijatan osećaj i emocionalno iskustvo, izazvano stvarnim ili potencijalnim oštećenjem tkiva.*

(IASP – International Association for Study od Pain)

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# Hronični bol

- Hronični bol je veliki problem svih sistema zdravstvenog osiguranja
- Samo u SAD oko 50 miliona ljudi doživljava hronični bol
- Više od polovine osoba sa hroničnim bolom je djelimično ili potpuno onesposobljeno
  - ◆ Bol je među najčešćim simptomima u ordinaciji ljekara opšte prakse
  - ◆ prevalenca bola < 60 godina = 125 / 1000
  - ◆ prevalenca bola > 60 godina = 250 / 1000

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# Hronični bol

Bol dugog trajanja  
(IASP: bol koji perzistira duže od tri mjeseca)

Često nepoznate etiologije

Nerijetko dovodi do fizičke i  
psihosocijalne deterioracije ličnosti

Zahtijeva kombinaciju terapijskih modaliteta  
(multidisciplinarni i multimodalni pristup)

Kompleksan i specifičan  
zdravstveni problem- bolest *per se*

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# Klasifikacija hroničnog bola

- Bol koji nastaje posle povredjivanja i traje i po zarastanju povrede:

Kompleks regionalnog bolnog sindroma (refleksna simpatetička distrofija-RSD) ili lumbalni bolni sindrom

- Hronični bol kao posledica osnovne bolesti kao što su:
  - 1.karcinom (**“maligni” hronični bol**)
  2. arthritis, lumboishialgija, fibromyalgia, dijabetička neuropatija... (**“nemaligni” hronični bol**)
- Hronični bol nepoznatog porijekla

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# Organski bol

- Organski bol se definiše kao bol sa utvrđenim organskim uzrokom
- Organski bol može biti

**Nocioceptivni**  
**Neuropatski**  
**Kombinovani**

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# Nocioceptivni bol

- Nastaje kada na slobodne periferne nervne završetke - nocioceptore djeluju štetne mehaničke, termičke ili hemijske draži. Služi kao “alarm” sa ulogom protektivnog sistema za očuvanje tjelesnog integriteta.
- Postoje dvije vrste nocioceptora:
  1. Somatski (u koži, mišićima i zglobovima)
  2. Visceralni (u organima)

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# Nocioceptivni bol

- Somatski bol se lako lokalizuje i obično opisuje kao kontinuirani ili isprekidani, “**kljucajući**” bol
- Visceralni bol se teško lokalizuje jer ima osobinu da se “prenese” na drugi, zdravi region tijela. Fenomen “prenesenog” bola nastaje zbog multiplih senzornih ulaza u jedan isti neuron spinalnih ganglija - iz kože, iz unutrašnjih organa i mišića i zglobova (bol iz pankreasa se širi u ledja a patološke promene centralnog dijela dijafragme upućuju bol koji se doživljava u ramenu)

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# Neuropatski bol

- Neuropatski bol je uzrokovan primarnom lezijom ili disfunkcijom samog nervnog sistema
  1. PNS - periferni neuropatski bol
  2. CNS - centralni neuropatski bol
- Uzrokuju ga: direktna trauma, ishemija, infekcija, metabolički poremećaji i tumori.
- Doživljava se kao konstantan i trajan ili kao intermitentni, **ubodni** bol.

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# Simptomi neuropatskog bola

- **“Dizestezija”**: spontana ili izazvana neprijatna abnormalna senzacija
- **“Parestezija”**: spontana ili evocirana abnormalna senzacija
- **“Hiperalghezija”**: pojačan odgovor na stimulus koji je inače normalno bolan
- **“Alodinija”**: doživljaj bola na dejstvo stimulusa koji normalno ne izaziva bol

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# Hijerarhijski nivoi bola

**Senzorno-Diskriminatorna  
Komponenta**

**lokacija, intenzitet, kvalitet**

**Motivaciono-Afektivna  
Komponenta**

**depresija, strah**

**Kognitivno-Evaluativna  
Komponenta**

**misli preokupirane uzrokom i značajem bola**

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# KLINIČKA PROCJENA BOLA

**Vjerovati pacijentu !!!**

**Anamneza**

**Fizikalni pregled**

**Psihosocijalni status**

**Ostali pregledi: RTG, scintigrafija skeleta, UZ, CT, MRI**

**Dokumentacija**

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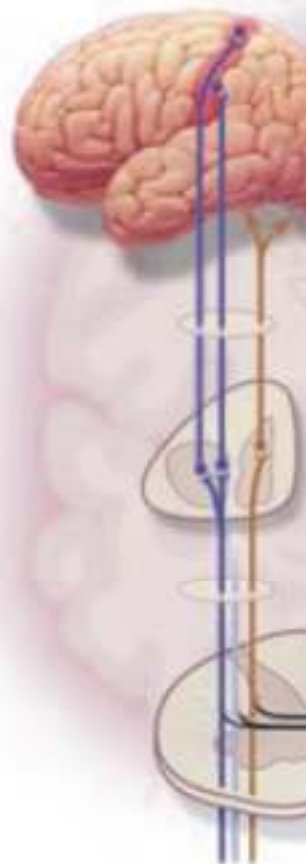
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# Kritični elementi istorije bola

- Kako se razvio bol
- Opis bola
- Lokacija bola i eventualno širenje
- Učestalost bola tokom vremena
- Pred-patološko i trenutno funkcionisanje i nivoi oštećenja
- Prethodni pokušaji liječenja

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**Kvantifikacija  
intenziteta bola čini  
osnovu inicijalne i  
trajne procjene.**

**Postoje razne  
odobrene skale bola  
koje pomažu da se  
izmjeri intenzitet.**

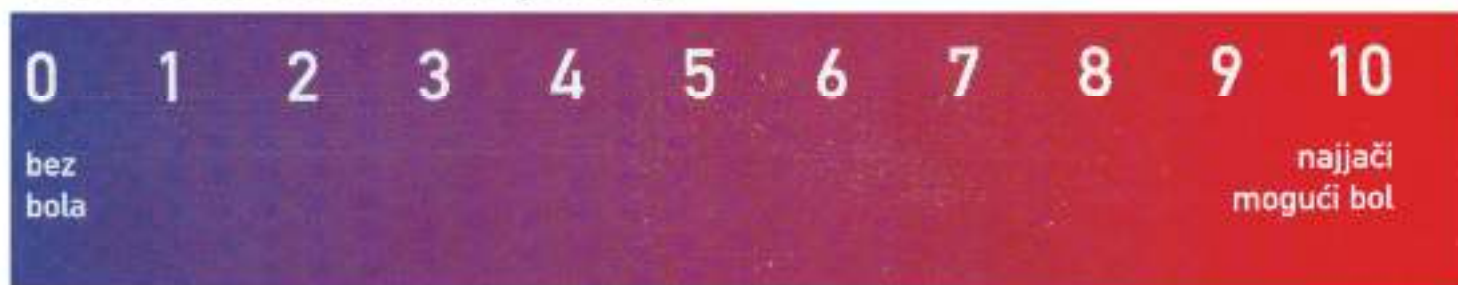
**One uključuju  
unidimenzionalne i  
multidimenzionalne  
mjerne instrumente i  
upitnike.**

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# Unidimenzionalne skale bola

## Numerička skala (NRS)

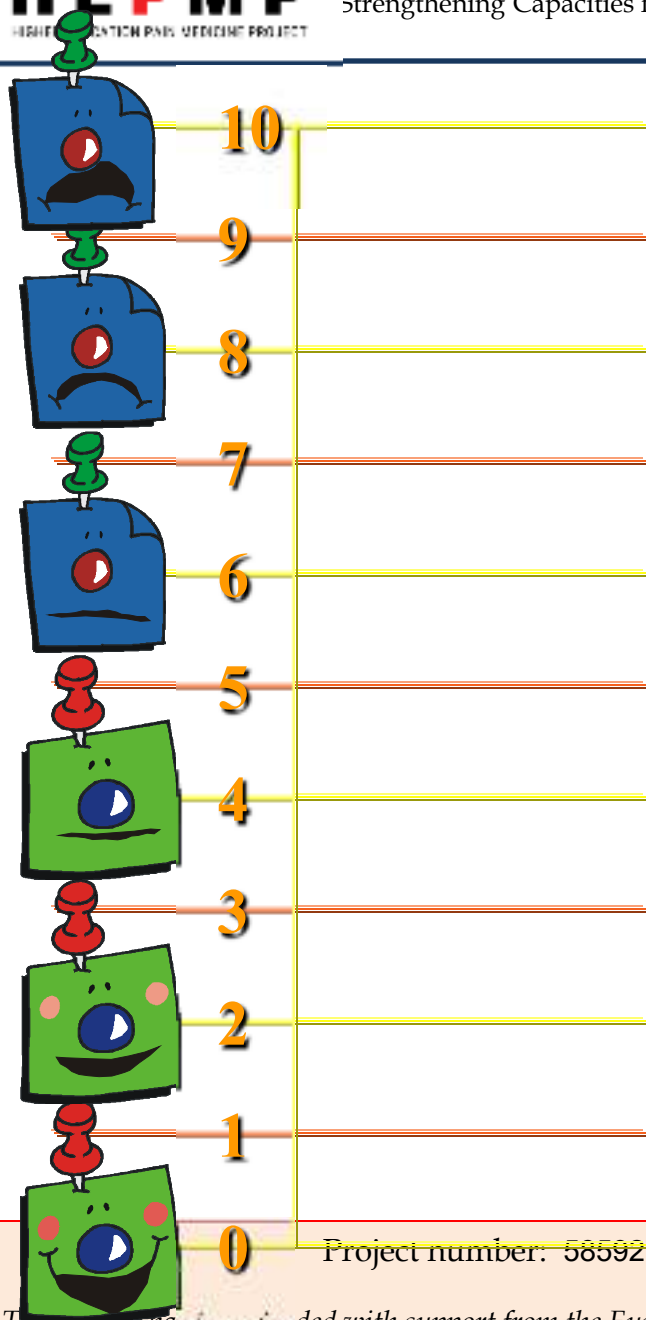


## Verbalno opisna skala (SDS)



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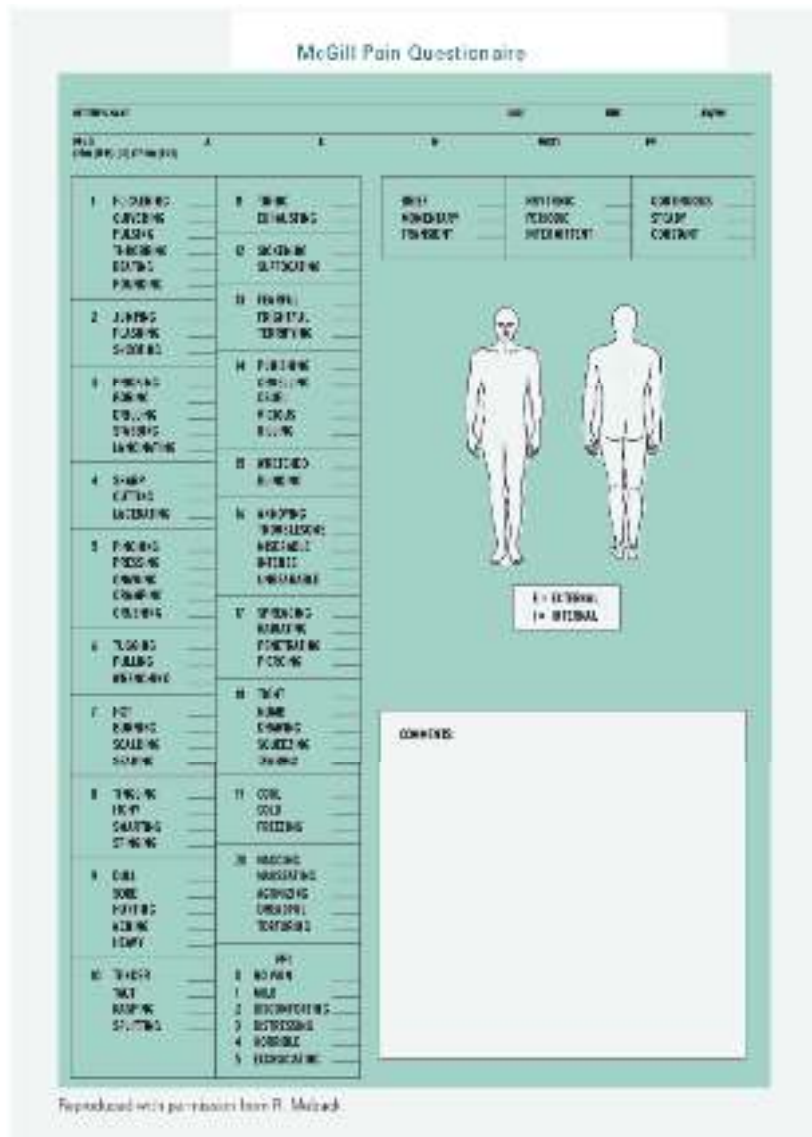
# Unidimensionalne skale bola

## Pain faces scale

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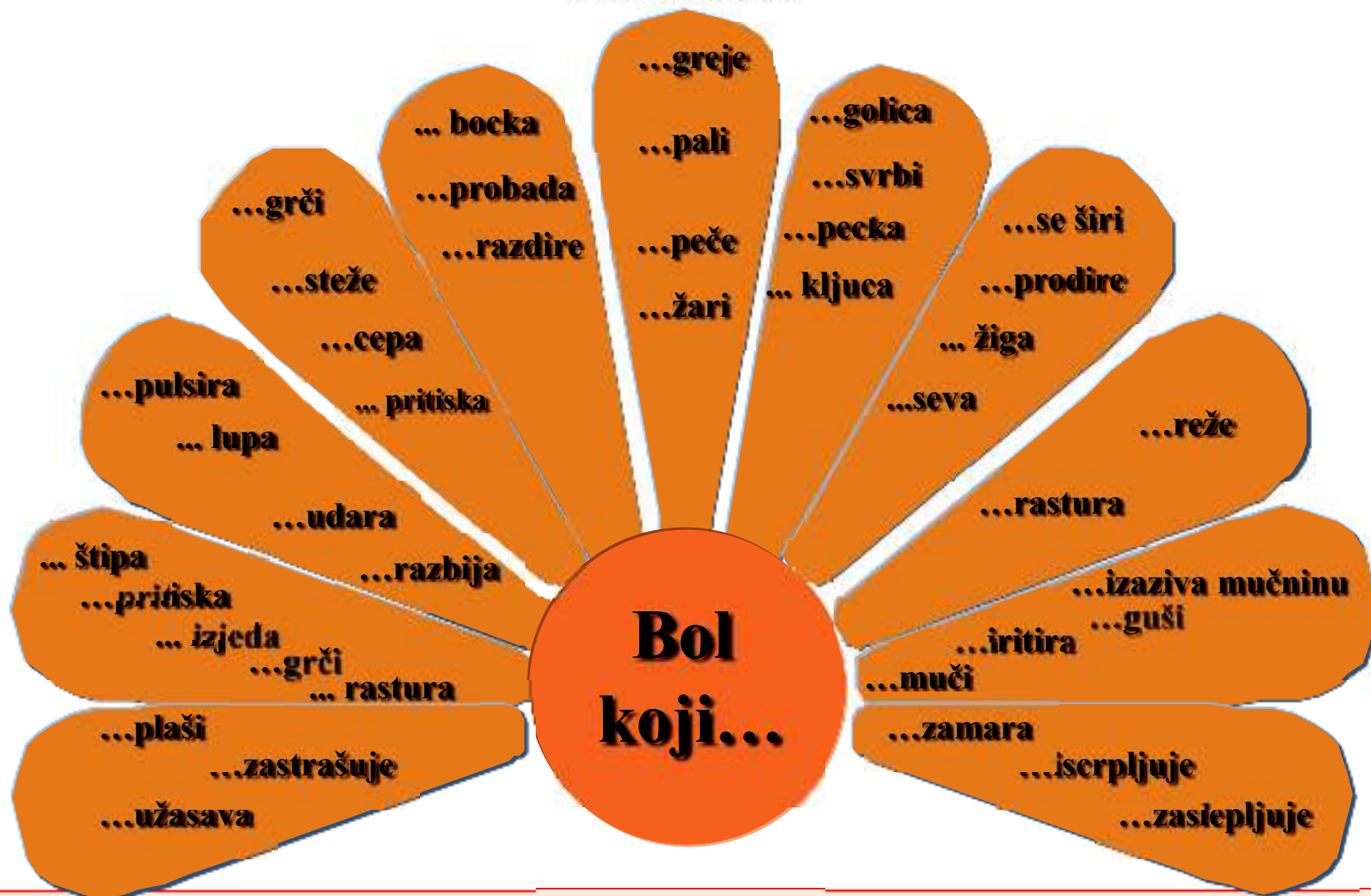
# Multidimensionalna skala bola

**“McGill-ova skala”**

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# Multidimenzionalna skala bola



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# HRONIČNI BOL JE BOLEST

## SAMA PO SEBI I

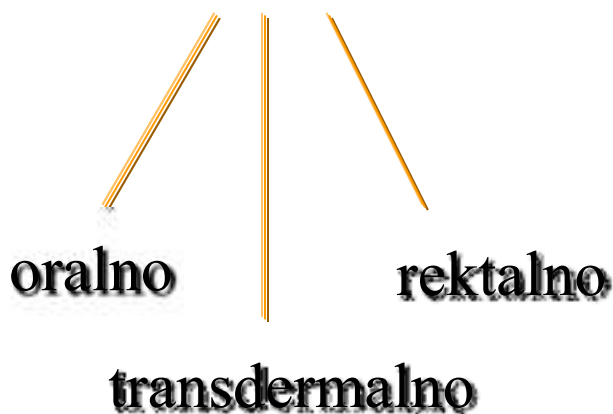
## TREBA GA LIJEČITI !!!

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# Terapija hroničnog bola

## neinvazivna



- jednostavno
- pogodno
- omogućava adekvatno trajanje dejstva lijeka

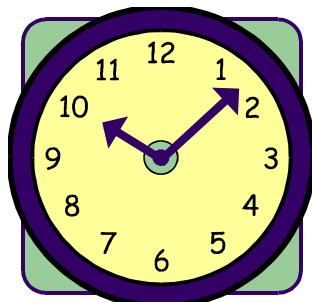
## invazivna



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**Kontinuirana farmakoterapija  
osnova je liječenja hroničnog  
bola**



*oralno*  
*“po satu”*  
*“princip stepenica”*  
Individualni pristup  
Obraćanje pažnje na detalje

## Farmakoterapija hroničnog kancerskog bola- principi SZO

Jaki opioidi  
+/- koanalgetici

**Jak bol  
(7-10)**

Slabi opioidi  
+/- koanalgetici

**Umjeren bol  
(4-6)**

Neopioidi  
+/- koanalgetici

**Blag bol (0-3)**

*Bol perzistira ili se pojačava*



### **SZO Princip stepenica**

# procjenjena jačina bola

# odredjuje izbor analgetika

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# Stepenasta farmakoterapija WHO



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# Adjuvanti



1. Antidepresivi
2. Antikonvulzivi
3. Lokalni antestetici
4. Neuroleptici
5. Kortikosteroidi
6. Mišićni relaksanti
7. Bisfosfonati

- koanalgetici
- za tretman neželjenih dejstava
- ne daju se rutinski
- indikovani kod specifičnih potreba pacijenata

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# Adjuvanti

## 1. Antidepresivi

- hronični **žareći** neuropatski bol
- poremećen san
- depresija

### triciklični antidepresivi:

- amitriptilin
- nortriptilin

## MAO inhibitori

## 2. Antikonvulzivi

- hronični **probadajući** neuropatski bol
- suzbija klonično-tonične grčeve

- karbamazepin
- gabapentin

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# Stepenasta farmakoterapija



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# Farmakoterapija bola prema WHO

## 1. Neopioidni analgetici

(NSAID-diklofenak, indometacin; ibuprofen, ketoprofen, naproksen, piroksikam...)

- ## 2. Opioidi
- slabi - tramadol, kodein, dihidrokodein
  - jaki - agonisti
    - parcijalni agonisti
    - agonist-antagonist

## 3. Adjuvanti

*Potrošnja opioida je mjera standarda liječenja hroničnog bola!*

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# NEOPIOIDNI ANALGETICI

-za blage bolove

**OPREZ !**

-nekritička upotreba

-neopravdano visoke doze

-neželjena dejstva (GIT tegobe)

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# Kada opiodi?

- **nezadovoljavajući efekat neopioidnih analgetika**



## OPIOIDNA TERAPIJA

- smanjenje bola u 80% slučajeva
- treba da spriječi napad bola
- jednostavno doziranje
- terapija se određuje za svakog pacijenta ponaosob

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# OPIOIDI PROTIV BLAGIH I UMERENIH BOLOVA

“slabi opioidi”

lijek	pojedinačne doze (mg/p.o.)	interval doziranja (h)
<b>kodein</b> (lek izbora SZO)	<b>30 - 60</b>	<b>4</b>
<b>tramadol</b>	<b>50 - 100*</b>	<b>4 – 6, 12*</b>

\*odnosi se na formulacije sa produženim dejstvom

## Ljekovi “2. stepenice” nisu farmakološki neophodni

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# JAKI OPIOIDI

## AGONISTI

**Morfin,**

**Transdermalni fentanil**

**Metadon**

**Oksikodon**

**Hidromorfon**

## PARCIJALNI AGONISTI

**Buprenorfin**

## MJEŠOVITI AGONISTI/ANTAGONISTI

**Pentazocin**

**Butorfanol**



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# JAKI OPIOIDNI ANALGETICI

## Osnova liječenja hroničnog kancerskog bola!

**Ostvaruju dejstva preko opioidnih receptora**

(mozak, kičmena moždina)

mu ( $\mu_1$   $\mu_2$ ), delta ( $\delta$ ), kappa ( $\kappa$ )

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# Opioidi

Podjela: • na osnovu vezivanja za receptore u CNS  
• na osnovu jačine opioida

- na osnovu - dejstva na nastanak bola
  - dužine dejstva
  - profila neželjenih dejstava

Utiče na

primjenljivost u specifičnim kliničkim situacijama

Opioid sa kratkim dejstvom - iznenadni bol

Opioid sa dugim dejstvom - hronični bol

npr. slow-release morphine  
transdermalni fentanil

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# MORFIN

## DOBAR ANALGETSKI EFEKAT

## FARMAKOLOŠKE OSOBINE

- brza resorpcija bez obzira na način primjene (oralno, rektalno, sc, im, iv, spinalno)
- brzo razlaganje i eliminacija

## OBLICI:

Morfinski sirup (10mg/5ml) (rijetko dostupan)

Tablete (10,20,50 mg) (IR) (neregistrovane)

“Slow-release” tablete ili kapsule (10,30,60 mg)

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# OGRANIČENJA MORFINA

Opioid	Bio-raspoloživost (%)	Analgezija (h)	Aktivni metaboliti	Korekcija doze (HI)	Korekcija doze (BI)
Morfin	20-30	4-6 (IR) 8-12 (SR)	M6G*	Da	Da
Metadon	60-90	8-12	Ne	Ne	Ne
TD fentanil	90 / TD	48-72	Ne	Ne	Ne

Neophodna korekcija doze kod bubrežne insuficijencije

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# METADON

- Agonista  $\mu$  i  $\delta$  receptora
  - Blokator NMDA rec. kanala, presinaptičkog preuzimanja serotonina
  - Niska cijena, više formulacija
- kod odvikavanja od narkomanije,  
neuropatskog bola, bubrežne insuf., neželjenih dejstava morfina

## NEDOSTACI:

- Akumulacija – neželjeni efekti
- Komplikovana rotacija (posebno sa viših doza morfina)
- Zahtijeva dugogodišnje iskustvo

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# TRANSDERMALNI FENTANIL

## Indikacije:

- **Jak, stabilan hronični bol (NRS > 5)**
- **Poremećaji gutanja**
- **Nekomplijantni pacijenti**
- **Bubrežna insuficijencija**

## Kontraindikacije:

- **Jak bol koji zahteva brzu titraciju doze (akutni bol)**
- **Alergija na fentanil**

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# TRANSDERMALNI FENTANIL

## Prednosti:

- **Komforan za primjenu (“flasteri”)**
- **Trodnevna kontrola bola – bolja saradljivost sa bolesnikom**
- **Manje neželjenih dejstava**
- **Prihvatljiv za pacijente – “patient friendly”**

## Nedostaci:

- **Nepodesan za brzo titriranje (deluje nakon 12h)**

## Oprez:

**Vlažna koža, povišena temperatura, spoljašnje zagrijavanje**

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# KOLIKO BOLA TOLIKO ANALGETIKA !!!

BOL JE GLAVNI ANTIDOT LIJEKU

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# JAKI OPIJATI NEMAJU MAKSIMALNU TERAPIJSKU DOZU !!!

ZA RAZLIKU OD **NSAIL I SLABIH OPIJATA**  
KOJI IMAJU  
“**EFEKAT PLAFONA**”

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# Podešavanje terapije

## 1. uvođenje novog opioida

- izbor opioida i načina doziranja (individualno)
- titracija opioidom kratkog dejstva
- konverzija u željeni lijek

## 2. povećanje doze da bi se postigla bolja kontrola bola

- 50% - 100%
- adjuvantna terapija
- optimalizacija terapije prije prelaska na drugi opioid

## 3. smanjenje doze

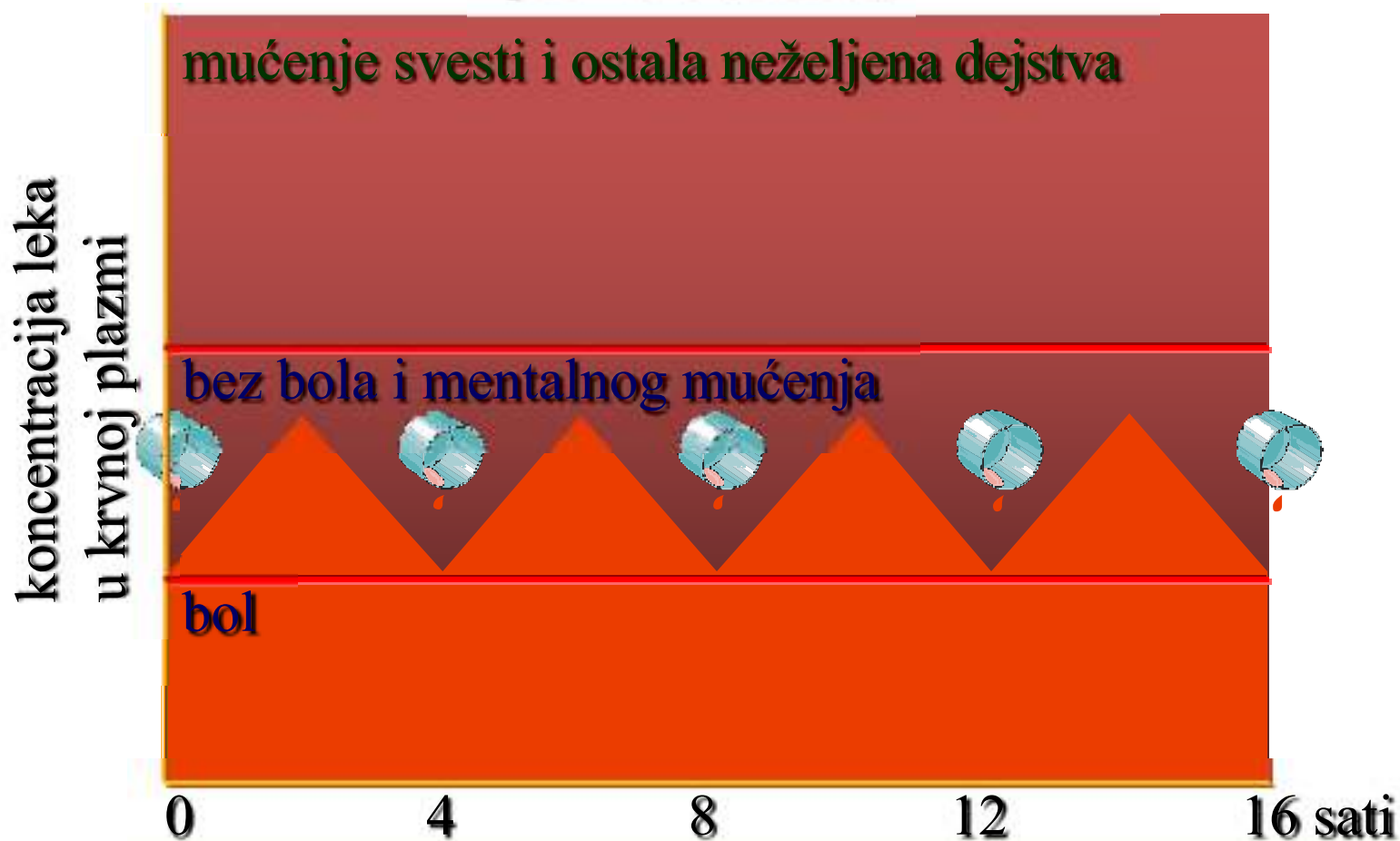
- postepeno
- nepostojanje bola nije razlog za smanjenje doze već potvrđuje da terapija odgovara

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# Terapija i doziranje

## po satnici



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# Terapija i doziranje

po potrebi ili zahtevu



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# Terapija i doziranje

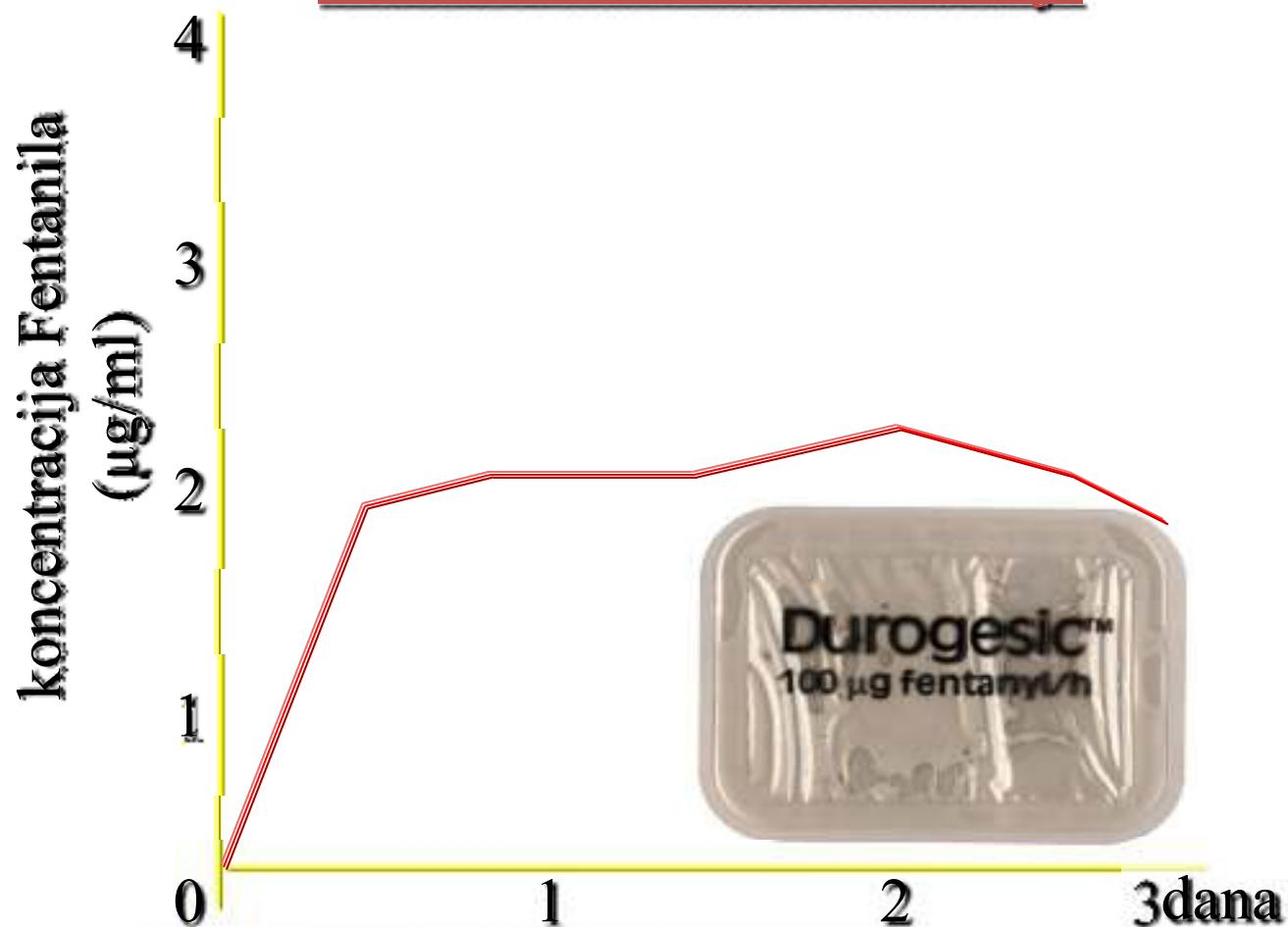
## Prednosti:

“patient friendly”

djeluje 72 sata

bolja saradljivost  
bolesnika

## Transdermalni način doziranja



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# OPIOIDE NE TREBA ČUVATI KAO LJEKOVE “ZA KRAJ” !!!

## TREBA IH UVODITI NA VRIJEME

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# **Osnovni principi uspješne terapije**

## **Zaključak:**

**ANAMNEZA BOLA !**

- pacijenta posmatrati u cjelini
- svaki tip bola ponaosob prepoznati i tretirati
- obratiti pažnju na mentalni sklop i socijalni faktor

**MJERITI INTENZITET BOLA!**

# Osnovni principi uspješne terapije

## Zaključak:

- poznavanje farmakoloških karakteristika analgetika
- vrijeme trajanja dejstva, analgetski efekat farmakokinetike, aktivnih metabolita, ekvianalgetske doze
- uzimanje analgetika po vremenskom intervalu  
**a ne po potrebi**

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# STRAH OD OPIJATA JE POTPUNO NEOPRAVDAN

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# MISLITI NA KVALITET

# ŽIVOTA

# OBOLJELOG

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# UVODITI OPIJATE NA VRIJEME

## I

### DOBRO TITRIRATI

### PREMA INTENZITETU BOLA

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***“SEDARE***

***DOLORUM***

***DIVINUM OPUS EST”***