Opiate, Antiepileptika und Antidepressiva als Schmerztherapeutika – Update für die Praxis

Adrian Forster

schulthess klinik

1

Pharmakotherapeutische Reflexe

2

Pharmakotherapeutische Reflexe in der Medizin

- Arterielle Hypertonie → Antihypertensivum
- Hyperlipidämie → Lipidsenker
- Diabetes mellitus → Antidiabetikum
- Dyspepsie → PPI
- Bakterieller Infekt → Antibiotikum
- etc.

3

Pharmakotherapeutische Reflexe in der Medizin

- Arterielle Hypertonie → Antihypertensivum
- Hyperlipidämie → Lipidsenker
- Diabetes mellitus → Antidiabetikum
- Dyspepsie → PPI
- Bakterieller Infekt → Antibiotikum
- etc.

- Leichter Schmerz → Paracetamol, NSAR

4

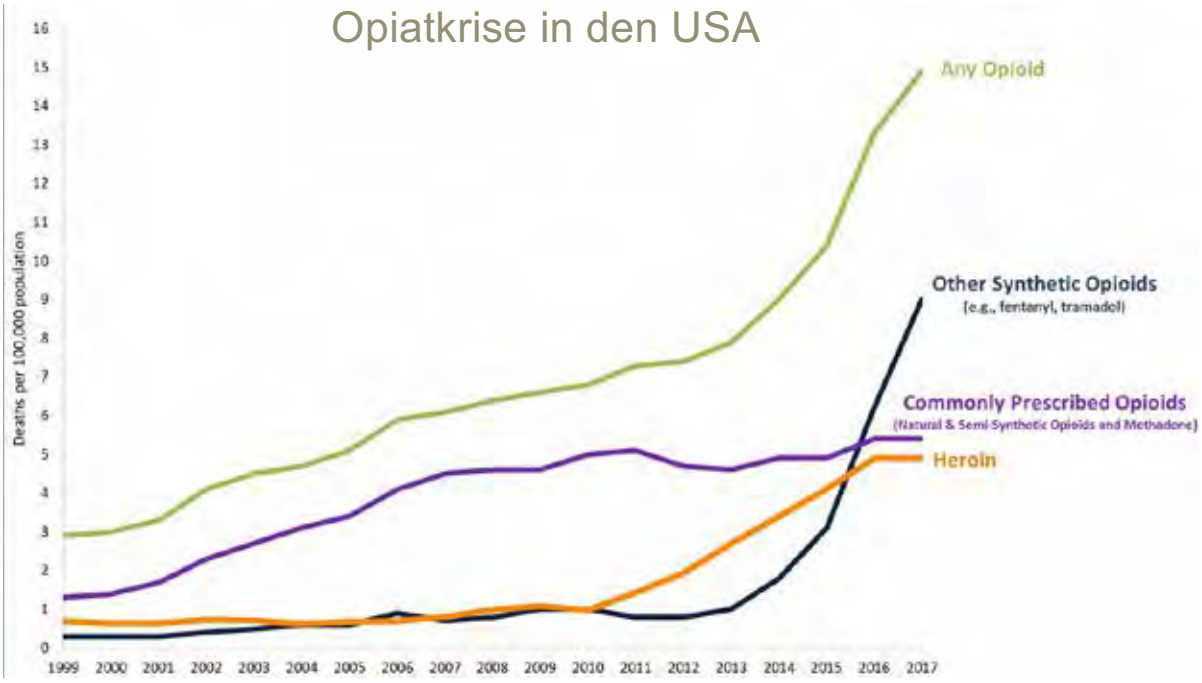
Pharmakotherapeutische Reflexe in der Medizin

- Arterielle Hypertonie → Antihypertensivum
- Hyperlipidämie → Lipidsenker
- Diabetes mellitus → Antidiabetikum
- Dyspepsie → PPI
- Bakterieller Infekt → Antibiotikum
- etc.

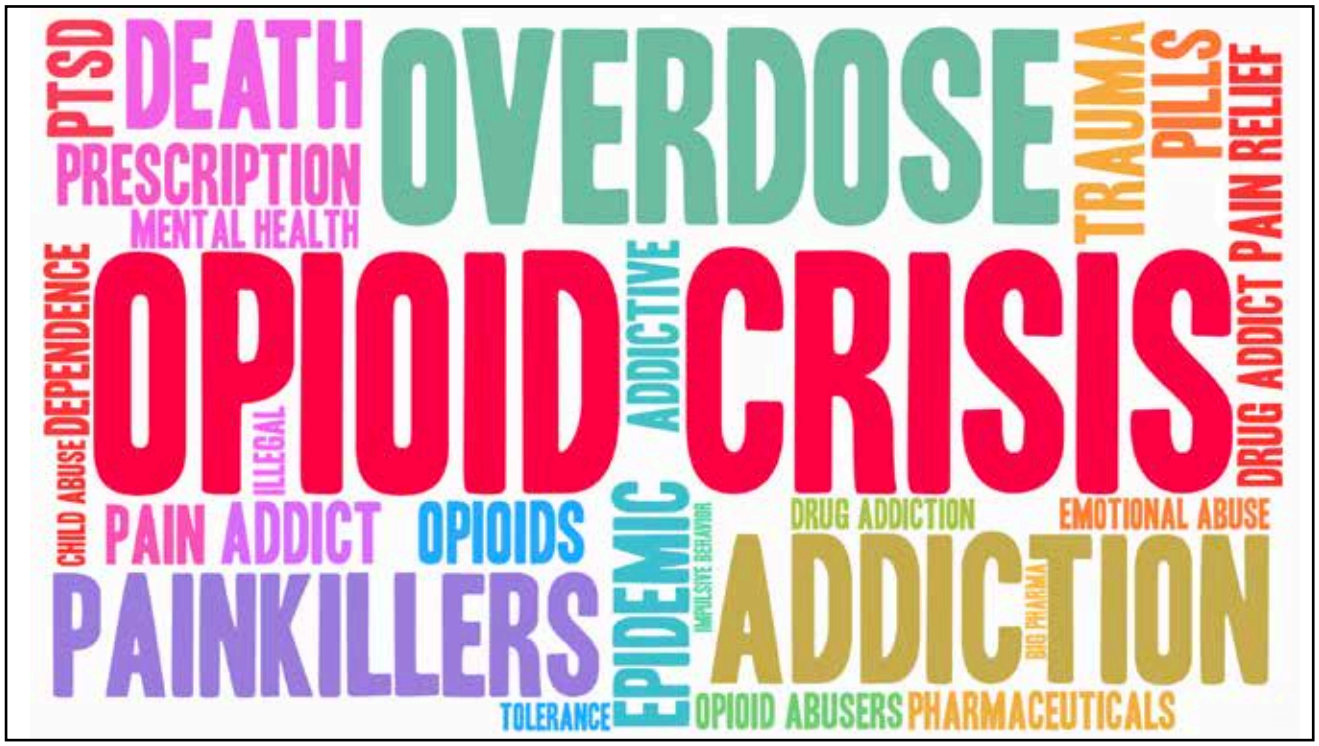
- Leichter Schmerz → Paracetamol, NSAR
- Starker Schmerz → Opiat, Antiepileptikum und Antidepressivum

5

Opiatkrise in den USA



6


PTSD
DEATH
OVERDOSE
TRAUMA
PILLS
PRESCRIPTION
MENTAL HEALTH
PAIN RELIEF
DEPENDENCE
OPIOID
CRISIS
ADDICTIVE
DRUG ADDICT
CHILD ABUSE
ILLEGAL
PAIN ADDICT
OPIOIDS
DRUG ADDICTION
EMOTIONAL ABUSE
PAINKILLERS
EPIDEMIC
IMPULSIVE BEHAVIOR
ADDICTION
BIG PHARMA
TOLERANCE
OPIOID ABUSERS
PHARMACEUTICALS

7


Support The Guardian
Available for everyone, funded by readers
Contribute
Subscribe
Search jobs
Sign in
Search
The Guardian
International edition
News
Opinion
Sport
Culture
Lifestyle
More
US Elections 2020 World Environment Soccer US Politics Business Tech Science
Opioids crisis
Opioids emerge as key sticking point for US-China trade deal
A joint operation that led to the conviction of three Chinese nationals for smuggling fentanyl is a hopeful sign for Trump as he faces election year
Edward Helmore
The seemingly never-ending trade dispute between China and the US often seems like a game of snakes and ladders. Last week China

8

Einsatz beim Nicht-Tumor-Schmerz in Anlehnung an das WHO-Stufenschema der Schmerztherapie

9

Fehlindikationen

(Kissel W, Jeger J. Forum Med Suisse 2012; 12: 149-52)

10

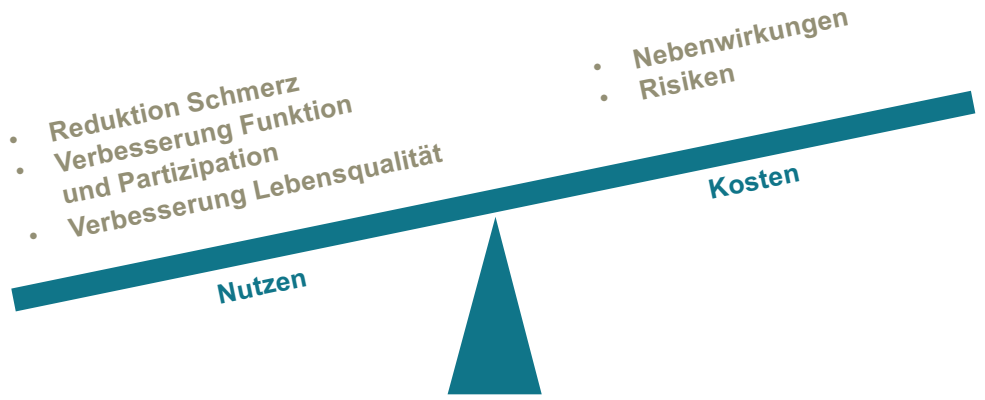

CNN health
For doctors, more opioid prescriptions bring more money
CNN Exclusive: The more opioids doctors prescribe, the more money they make

11


Chronische Rückenschmerzen – Schweizer immer noch unterversorgt

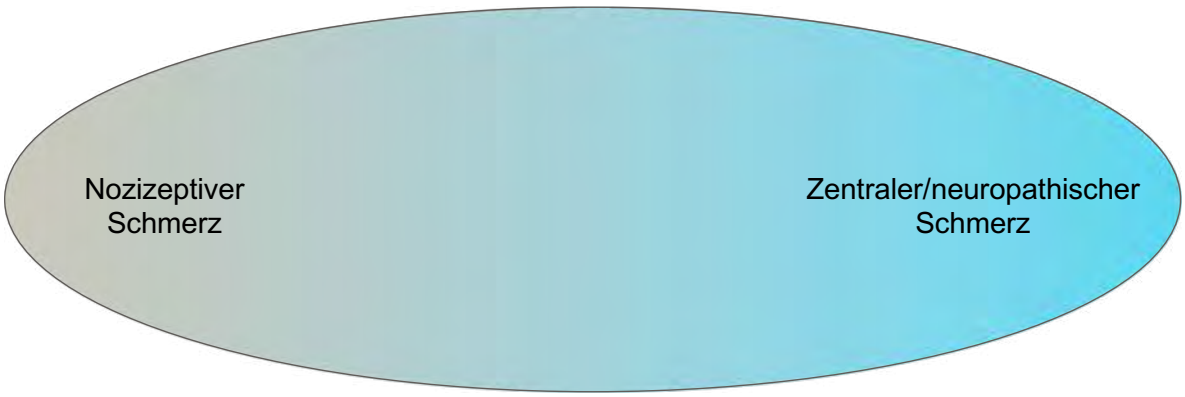
12

Opiate, Antiepileptika und Antidepressiva für chronischen «muskuloskelettalen» Schmerz: Abwägung



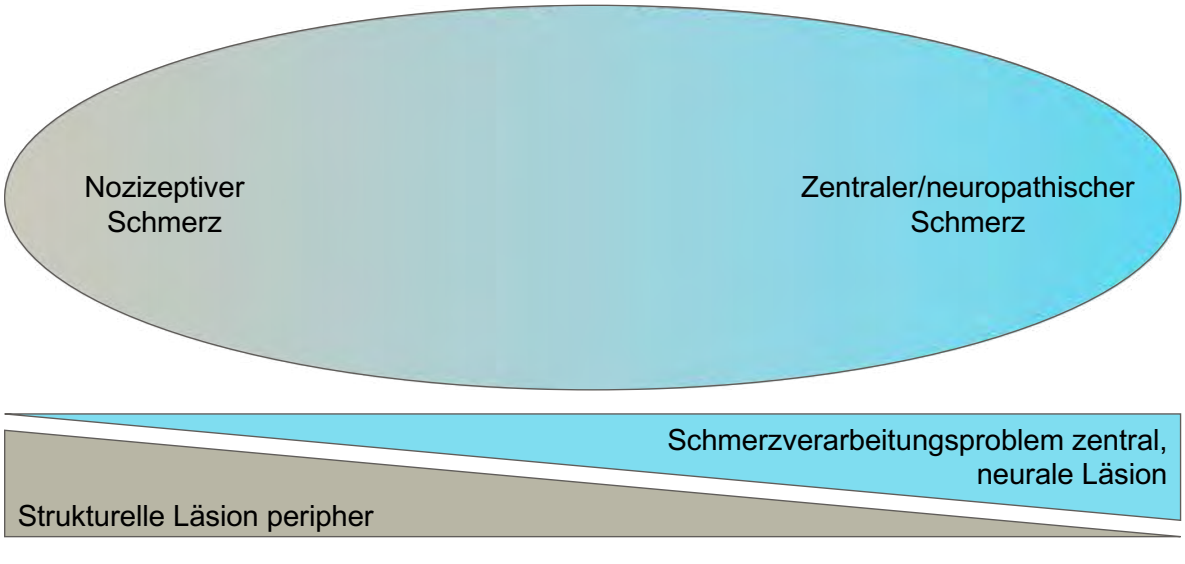
13

Wirkung der Schmerztherapeutika in Abhängigkeit von der Art des Schmerzes



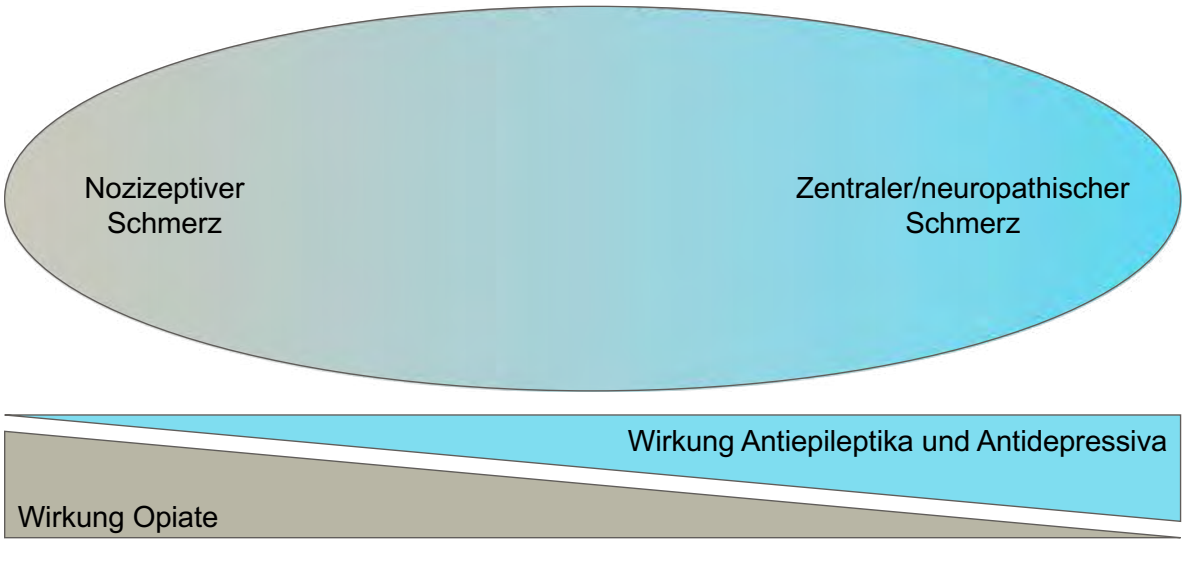
14

Wirkung der Schmerztherapeutika in Abhängigkeit von der Art des Schmerzes



15

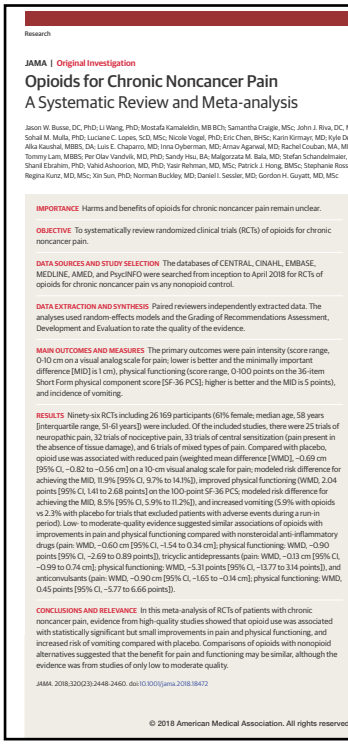
Wirkung der Schmerztherapeutika in Abhängigkeit von der Art des Schmerzes



16

Opiate

17



Research

JAMA | Original Investigation

Opioids for Chronic Noncancer Pain
A Systematic Review and Meta-analysis

Jason W. Busse, DC, PhD; Li Wang, PhD; Mostafa Kamaleldin, MB BCh; Samantha Craigie, MSc; John J. Riva, DC, MSc; Luis Montoya, DDS, MSc; Sohail M. Mulla, PhD; Luciana C. Lopes, ScD, MSc; Nicole Vogel, PhD; Eric Chen, BHSc; Karin Kirmayr, MD; Kyle De Oliveira, MD; Lori Olivieri, MD; Alka Kaushal, MBBS, DA; Luis E. Chaparro, MD; Inna Cyberman, MD; Arnav Agarwal, MD; Rachel Couban, MA, MIST; Ludwig Tsoi, MBChB; Tommy Lam, MBBS; Per Olav Vandvik, MD, PhD; Sandy Hsu, BA; Małgorzata M. Bała, MD; Stefan Schandelmaier, MD; Anne Scheidecker, MD; Shanil Ebrahim, PhD; Vahid Ashoorion, MD, PhD; Yasir Rehman, MD, MSc; Patrick J. Hong, BMSc; Stephanie Ross, PhD; Bradley C. Johnston, PhD; Regina Kunz, MD, MSc; Xin Sun, PhD; Norman Buckley, MD; Daniel I. Sessler, MD; Gordon H. Guyatt, MD, MSc

IMPORTANCE Harms and benefits of opioids for chronic noncancer pain remain unclear.

OBJECTIVE To systematically review randomized clinical trials (RCTs) of opioids for chronic noncancer pain.

DATA SOURCES AND STUDY SELECTION The databases of CENTRAL, CINAHL, EMBASE, MEDLINE, AMED, and PsycINFO were searched from inception to April 2018 for RCTs of opioids for chronic noncancer pain vs any nonopioid control.

DATA EXTRACTION AND SYNTHESIS Paired reviewers independently extracted data. The analyses used random-effects models and the Grading of Recommendations Assessment, Development and Evaluation to rate the quality of the evidence.

MAIN OUTCOMES AND MEASURES The primary outcomes were pain intensity (score range, 0-10 cm on a visual analog scale for pain, lower is better and the minimally important difference [MID] is 1 cm), physical functioning (score range, 0-100 points on the 36-item Short Form physical component score [SF-36 PCS]; higher is better and the MID is 5 points), and incidence of vomiting.

RESULTS Ninety-six RCTs including 26 169 participants (61% female; median age, 58 years [interquartile range, 51-61 years]) were included. Of the included studies, there were 25 trials of neuropathic pain, 32 trials of nociceptive pain, 33 trials of central sensitization (pain present in the absence of tissue damage), and 6 trials of mixed types of pain. Compared with placebo, opioid use was associated with reduced pain (weighted mean difference [WMD], −0.69 cm [95% CI, −0.82 to −0.56 cm] on a 10-cm visual analog scale for pain; modeled risk difference for achieving the MID, 11.9% [95% CI, 9.7% to 14.1%]), improved physical functioning (WMD, 2.04 points [95% CI, 1.41 to 2.68 points] on the 100-point SF-36 PCS; modeled risk difference for achieving the MID, 8.5% [95% CI, 5.9% to 11.2%]), and increased vomiting (5.9% with opioids vs 2.3% with placebo for trials that excluded patients with adverse events during a run-in period). Low- to moderate-quality evidence suggested similar associations of opioids with improvements in pain and physical functioning compared with nonsteroidal anti-inflammatory drugs (pain: WMD, −0.60 cm [95% CI, −1.54 to 0.34 cm]; physical functioning: WMD, −0.90 points [95% CI, −2.69 to 0.89 points]), tricyclic antidepressants (pain: WMD, −0.13 cm [95% CI, −0.99 to 0.74 cm]; physical functioning: WMD, −5.31 points [95% CI, −13.77 to 3.14 points]), and anticonvulsants (pain: WMD, −0.90 cm [95% CI, −1.65 to −0.14 cm]; physical functioning: WMD, 0.45 points [95% CI, −5.77 to 6.66 points]).

CONCLUSIONS AND RELEVANCE In this meta-analysis of RCTs of patients with chronic noncancer pain, evidence from high-quality studies showed that opioid use was associated with statistically significant but small improvements in pain and physical functioning, and increased risk of vomiting compared with placebo. Comparisons of opioids with nonopioid alternatives suggested that the benefit for pain and functioning may be similar, although the evidence was from studies of only low to moderate quality.

JAMA. 2018;320(23):2448-2460. doi:10.1001/jama.2018.18472

Editorial page 2427

Video and Supplemental content

CME Quiz at jamanetwork.com/learning

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Jason W. Busse, DC, PhD, Department of Anesthesia, Michael G. DeGroote School of Medicine, McMaster University, HSC 2V9, 1280 Main St W, Hamilton, ON L8S 4K1, Canada (bussejw@mcmaster.ca).

Geringe Wirkung der Opiate bei chronischem Schmerz

Conclusion and relevance:

…statistically significant but small improvements in pain an physical functioning…

Comparison of opioids with nonopioid alternatives suggested that the benefit for pain an functioning may be similar…

(Busse JW et al. JAMA 2018; 320: 2448-60)

18

Opiate vs. Nichtopiate
bei chronischem Rückenschmerz und Cox-/Gonarthrose

Effect of opioid vs. nonopioid medications on pain-related function in patients with chronic back pain or hip or knee osteoarthritis pain over 12 months (The SPACE Randomized Clinical Trial)

240 patients, mean age 58.3 y

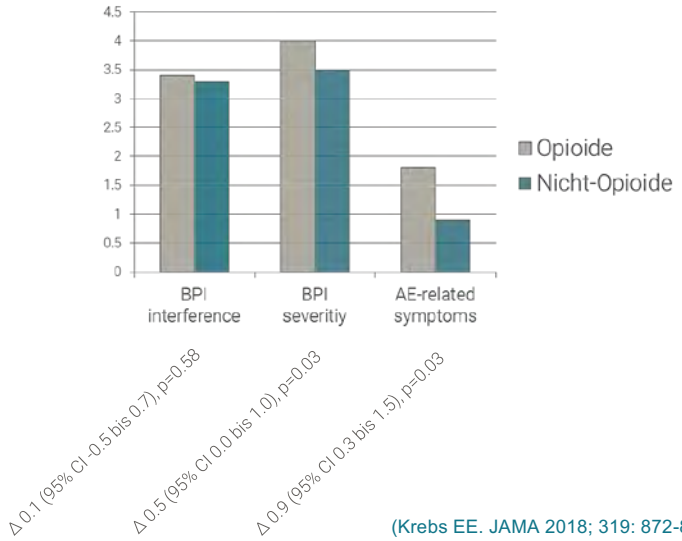
Treat to target strategy

- Pain-related function (BPI interference scale)
- Pain intensitiy (BPI severety scale)
- AE-related symptoms

(Krebs EE. JAMA 2018; 319: 872-82)

19

Opiate vs. Nichtopiate
bei chronischem Rückenschmerz und Cox-/Gonarthrose



(Krebs EE. JAMA 2018; 319: 872-82)

20

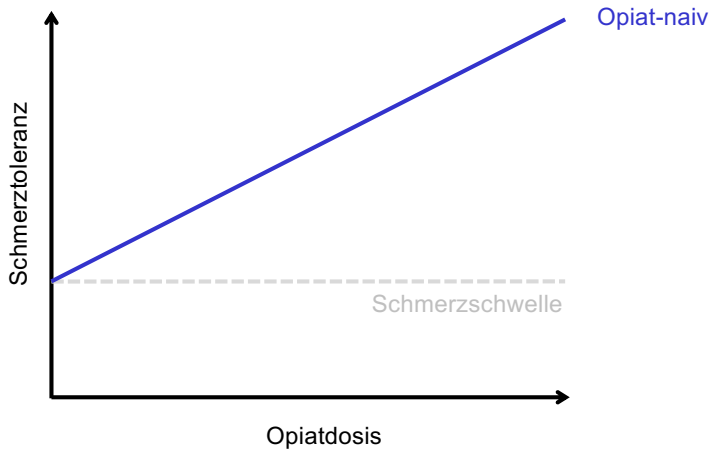
Probleme der Opiate bei chronischem Schmerz (Langzeittherapie)

- Abnahme der Partizipation
  (Soziale Kontaktpflege, Rückkehr zur Arbeit)
- Verschlechterung der Lebensqualität
- Wirkungsabnahme/-verlust (Toleranzentwicklung)
- Opioid-induzierte Hyperalgesie
- Abhängigkeitsentwicklung

(Crofford LJ. J Nat Rev Rheumatol 2010; 6: 191-7,
Hooten WM et al. Pain 2015; 156: 1145–52)

21

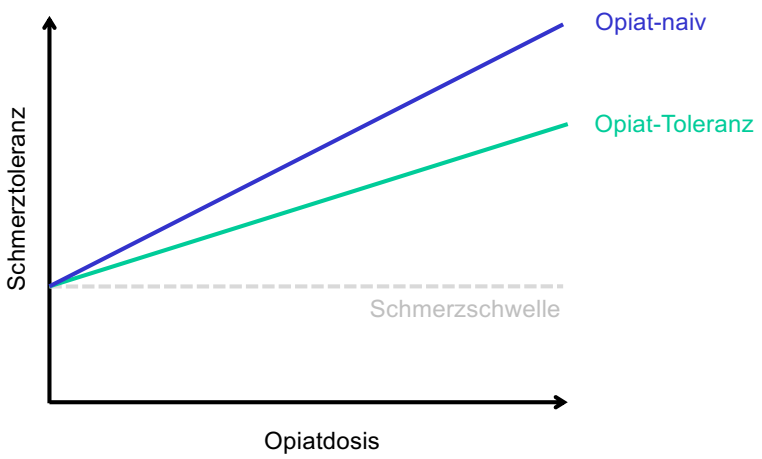
Toleranz- und Hyperalgesie-Entwicklung unter Opiattherapie



(Crofford LJ. J Nat Rev Rheumatol 2010; 6: 191-7)

22

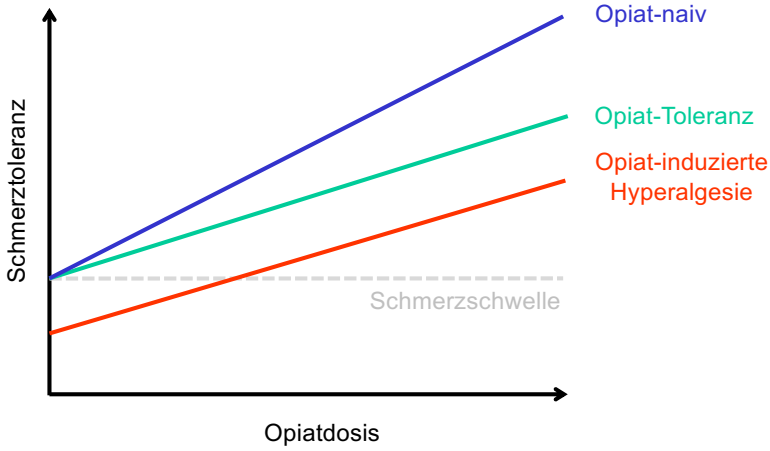
Toleranz- und Hyperalgesie-Entwicklung unter Opiattherapie



(Crofford LJ. J Nat Rev Rheumatol 2010; 6: 191-7)

23

Toleranz- und Hyperalgesie-Entwicklung unter Opiattherapie



(Crofford LJ. J Nat Rev Rheumatol 2010; 6: 191-7)

24

Klinische Hinweise auf Opiat-induzierte Hyperalgesie

- Schmerzzunahme bei konstanter Opiat-Dosierung
- Schmerz stärker als vor der Opiat-Therapie
- Schmerz diffuser und schlechter charakterisierbar im Therapieverlauf
- Schmerzpersistenz/-zunahme bei Steigerung der Opiat-Dosierung

(Crofford LJ. J Nat Rev Rheumatol 2010; 6: 191-7,
Hooten WM et al. Pain 2015; 156: 1145–52)

25

Opiate vs. Nichtopiate
bei Fibromyalgie

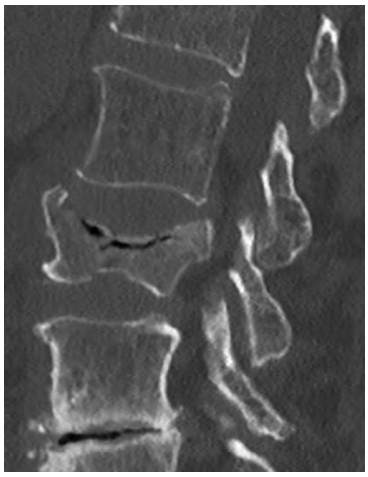
Schlechteres Outcome unter Opiaten:

- Geringere Schmerzabnahme
- Geringere Funktionsverbesserung
- Geringere Besserung der Schlafstörung, Angst und Depression
- Geringere Zunahme der Arbeitsfähigkeit

(Goldenberg DL et al. Mayo Clin Proc 2016; 91: 640-8,
Fitzcharles MA et al. Pain Res Treat 2013; 898493,
Peng X et al. Clin J Pain 2015; 31: 7-13)

26

Empfehlungen zur Therapie des msk. Schmerzes mit Opiaten



Indikation umso besser, je akuter und nozizeptiver der Schmerz

27

Empfehlungen zur Therapie des msk. Schmerzes mit Opiaten

- Immer zuerst **Klärung der Ursache**
  → **Spezifische Therapie** soweit möglich
- Nur im Rahmen eines multimodalen Therapiekonzepts
- Kontraindikationen:
  - Myofasziales Schmerzsyndrom («zentrale Sensibilisierung») dominierend
  - Psychiatrische Erkrankung dominierend: Somatoforme Schmerzstörung, Depression mit somatischem Syndrom usw.
  - Abhängigkeitsanamnese

28

Empfehlungen zur Therapie des msk. Schmerzes mit Opiaten

- Fixe Dosierung (retardiertes Präparat); Rescue-Medikation (kurzwirksames Präparat; 5-15% der Tagesdosis)
- Berücksichtigung der Tagesrhythmik
- Engmaschiges Monitoring:
  - Wirkungen: Schmerz, Funktion, Partizipation
  - Nebenwirkungen

29

Empfehlungen zur Therapie des msk. Schmerzes mit Opiaten

- Therapieabbruch bei ungenügendem Nutzen
- Starke interindividuelle Variabilität von Wirkung und Nebenwirkungen
  → Opioidwechsel (mit reduzierter äquianalgetischer Dosis)
- Therapie von Nebenwirkungen

30

Antiepileptika und Antidepressiva

31

32

GOV.UK

Search

Home > Drug Safety Update

Pregabalin (Lyrica), gabapentin (Neurontin) and risk of abuse and dependence: new scheduling requirements from 1 April

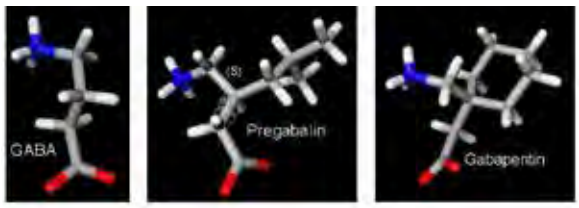
As of 1 April 2019, pregabalin and gabapentin are controlled under the Misuse of Drugs Act 1971 as Class C substances and scheduled under the Misuse of Drugs Regulations 2001 as Schedule 3. Evaluate patients carefully for a history of drug abuse before prescribing pregabalin and gabapentin and observe patients for development of signs of abuse and dependence.

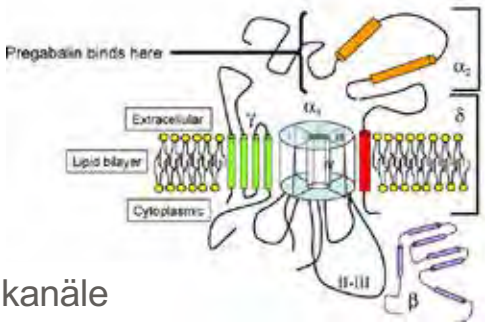
Published 16 April 2019
From: Medicines and Healthcare products Regulatory Agency

33

Antiepileptika

- Pregabalin und Gabapentin (Gabapentinoide)





- Binden an spannungsabhängige Kalziumkanäle und hemmen die Neurotransmitterfreisetzung

(Taylor CP et al. Epilepsy Res 2007; 73: 137-50,
Azmi S et al. Diabetes Ther 2019; 10: 35-56)

34

Pregabalin

- Indikationen: Postherpetischer Schmerz, diabetische Polyneuropathie, Fibromyalgie und Angsttstörungen
- Maximale Serumkonzentration 1 h nach Einnahme
- Kurze Serumhalbwertszeit (5-6 h)
- Bis 600 mg pro Tag
- Renale Elimination: Dosisanpassung bei Nierenfunktionseinschränkung

(Taylor CP et al. Epilepsy Res 2007; 73: 137-50,
Azmi S et al. Diabetes Ther 2019; 10: 35-56)

35

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 MARCH 23, 2017 VOL. 376 NO. 12

Trial of Pregabalin for Acute and Chronic Sciatica

Stephanie Mathieson, M.Chiro., Christopher G. Maher, Ph.D., Andrew J. McLachlan, Ph.D., Jane Latimer, Ph.D., Bart W. Koes, Ph.D., Mark J. Hancock, Ph.D., Ian Harris, Ph.D., Richard O. Day, M.B., B.S., M.D., Laurent Billot, M.Sc., M.Res., Justin Pik, M.B., B.S., Stephen Jan, Ph.D., and C.-W. Christine Lin, Ph.D.

ABSTRACT

BACKGROUND
Sciatica can be disabling, and evidence regarding medical treatments is limited. Pregabalin is effective in the treatment of some types of neuropathic pain. This study examined whether pregabalin may reduce the intensity of sciatica.

METHODS
We conducted a randomized, double-blind, placebo-controlled trial of pregabalin in patients with sciatica. Patients were randomly assigned to receive either pregabalin at a dose of 150 mg per day that was adjusted to a maximum dose of 600 mg per day or matching placebo for up to 8 weeks. The primary outcome was the leg-pain intensity score on a 10-point scale (with 0 indicating no pain and 10 the worst possible pain) at week 8; the leg-pain intensity score was also evaluated at week 52, a secondary time point for the primary outcome. Secondary outcomes included the extent of disability, back-pain intensity, and quality-of-life measures at prespecified time points over the course of 1 year.

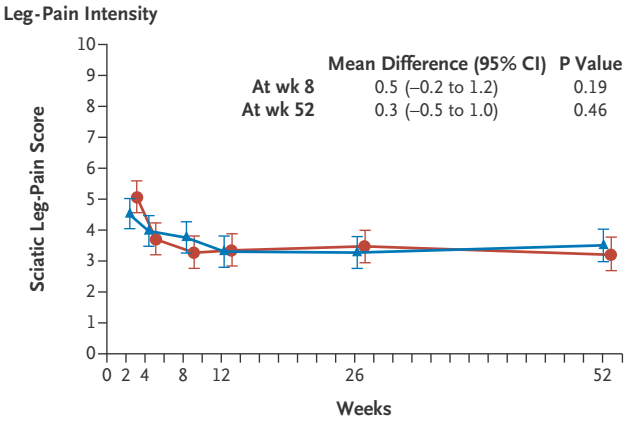
RESULTS
A total of 209 patients underwent randomization, of whom 108 received pregabalin and 101 received placebo; after randomization, 2 patients in the pregabalin group were determined to be ineligible and were excluded from the analyses. At week 8, the mean unadjusted leg-pain intensity score was 3.7 in the pregabalin group and 3.1 in the placebo group (adjusted mean difference, 0.5; 95% confidence interval [CI], −0.2 to 1.2; P=0.19). At week 52, the mean unadjusted leg-pain intensity score was 3.4 in the pregabalin group and 3.0 in the placebo group (adjusted mean difference, 0.3; 95% CI, −0.5 to 1.0; P=0.46). No significant between-group differences were observed with respect to any secondary outcome at either week 8 or week 52. A total of 227 adverse events were reported in the pregabalin group and 124 in the placebo group. Dizziness was more common in the pregabalin group than in the placebo group.

CONCLUSIONS
Treatment with pregabalin did not significantly reduce the intensity of leg pain associated with sciatica and did not significantly improve other outcomes, as compared with placebo, over the course of 8 weeks. The incidence of adverse events was significantly higher in the pregabalin group than in the placebo group. (Funded by the National Health and Medical Research Council of Australia; PRECISE Australian and New Zealand Clinical Trials Registry number, ACTRN12613000530729.)

From the George Institute for Global Health and Sydney Medical School (S.M., C.G.M., J.L., L.B., S.J., C.-W.C.L.) and Faculty of Pharmacy and Centre for Education and Research on Ageing (A.J.M.), University of Sydney, Faculty of Medicine and Health Science, Macquarie University (M.J.H.), the Ingham Institute for Applied Medical Research, South Western Sydney Clinical School (I.H.), and St. Vincent's Clinical School (R.O.D.), Faculty of Medicine, University of New South Wales, Sydney, and Australian Capital Territory NeuroSpine Clinic, Deakin, ACT (J.P.) — all in Australia; and the Department of General Practice, Erasmus University Medical Center, Rotterdam, the Netherlands (B.W.K.). Address reprint requests to Dr. Lin at the George Institute for Global Health, 1 King St., Newtown, NSW 2042, Australia, or at clin@georgeinstitute.org.au.

N Engl J Med 2017;376:1111-20.
DOI: 10.1056/NEJMoa1614292

Pregabalin bei lumboradikulärem Schmerz unwirksam



(Mathieson S et al. N Engl J Med 2017; 376: 111-20)

36

Pregabalin

- Indikationen: Postherpetischer Schmerz, diabetische Polyneuropathie, Fibromyalgie und Angsttstörungen
- Maximale Serumkonzentration 1 h nach Einnahme
- Kurze Serumhalbwertszeit (5-6 h)
- Bis 600 mg pro Tag
- Renale Elimination: Dosisanpassung bei Nierenfunktionseinschränkung

(Taylor CP et al. Epilepsy Res 2007; 73: 137-50,
Azmi S et al. Diabetes Ther 2019; 10: 35-56)

37

Pregabalin

- Nebenwirkungen:
  Müdigkeit, Schwindel, Euphorie, Mundtrockenheit, Gewichtszunahme, Oedeme
- Cave Atemdepression bei Älteren/Allgemeinanästhesie
- Vorsicht bei Kombination mit Opiaten (Mortalität erhöht)
- Cave abruptes Absetzen (Entzugssymptomatik)
- Cave Abusus,
  Vorsicht bei Abhängigkeitsanamnese

(Evoy KE et al. Drugs 2017; 77: 403-26)

38

Antidepressiva

- Trizyklische Antidepressiva
  z. B. Amitriptylin, Trimipramin
- Serotonin- und Noradrenalin-Reuptake-Hemmer (duale Reuptake-Hemmer)
  z. B. Duloxetin, Venlafaxin
- Wirken bei neuropathischem und zentralem (myofaszialem) Schmerz

39

Empfehlungen zur Therapie des «msk.» Schmerzes mit Antiepileptika und Antidepressiva

- Indikation umso besser, je zentraler (generalisierter, myofaszialer) bzw. je neuropathischer der Schmerz
- Nur im Rahmen eines multimodalen Therapiekonzepts
- Psychiatrische Komorbidität miteinbeziehen
- Langsames Einschleichen bei zentralem (generalisiertem myofaszialem) Schmerz

40

Empfehlungen zur Therapie der «Fibromyalgie» mit Antiepileptika und Antidepressiva

- Nicht-medikamentöse Behandlungsmöglichkeiten ausschöpfen
- Primär trizyklisches Antidepressivum
- Bei Non-response:
  - Duloxetin morgens, wenn Müdigkeit dominiert
  - Pregabalin vor Zubettgehen, wenn Schlafstörung dominier
- Keine Opiate

41

Zauberlehrling

Die ich rief, die Geister,
werd' ich nun nicht los.

(Johann Wolfgang von Goethe, 1797)

42

HANDS OFF

43

44