

PEARL - Tincture of opium

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Palliative Medicine
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Tincture of opium

- Indication symptomatic treatment of severe diarrhea, not responsive to standard therapy
 diarrhea caused by cytostatic drugs, radiation, or neuroendocrine tumors
- No indication Treatment of pain, (irritant) cough
- Mechanism Activation of peripheral μ -opioid receptors: slowing of intestinal activity and prolongation of
 intestinal transit time, increase spincter tone
- Route oral intake, gastrointestinal absorption, liver metabolization, renal clearance
- Dosing multiple regimes 2-20 drops 2-4 times daily. Single dose max. 1ml, total daily dose max. 6ml.

Tincture of opium

- **Formula** Standardized formula (European Pharmacopoeia)
alcoholic plant extract, all alkaloids from opium poppy
adjusted to morphine content of 10mg/ml (1%), other active substances: codeine, thebaine, noscapine, papaverine, narceine, etc.
finished pharmaceutical: Dropizol, no longer available
- **Variation** denarcotized or deodorized tincture of opium (DTO): noscapine removed
- **Legal status** Switzerland: pharmacopoeial preparation, no swissmedic approval

Tincture of opium

- Literature Uptodate: widely used, despite the absence of literature supporting efficacy
recent systematic review (Graven-Nielsen et al, 2023): no clinical studies on efficacy
- Limitations might be considered if no response to standard therapy

No additional benefit when added to ongoing opioid treatment
- Pitfalls Codeine: cytochrome metabolizer-subtypes (ultra rapid to poor)

Noscipine: strong emetic

Narcotic prescription required

No Driving ability

Management of (chemotherapy-related) diarrhea

- Cause of diarrhea (causal treatment)
- Grade severity
- Dietary interventions, rehydration and electrolytes
- Pharmacological: stop prokinetics, laxatives, naloxone
- Reevaluation of reexposition of triggers

Standard care (uptodate)

- Line Loperamide (Grade 1A)
 - Mechanism Activation of peripheral μ -opioid receptor, hardly any central effects
 - Limitation No additional benefit when added to ongoing opioid treatment
 - Dosing initial 4mg dose, followed by 2-4mg every four hours or after every loose stool, max. 16mg daily
 - Effect diarrhea resolution within 48h: 84% in grade 1-2, 52% in grade 3-4

NCI CTCAE v5.0 diarrhea

Adverse event	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Diarrhea	Increase of <4 stools per day over baseline; mild increase in ostomy output compared with baseline	Increase of four to six stools per day over baseline; moderate increase in ostomy output compared with baseline; limiting instrumental ADL*	Increase of seven or more stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared with baseline; limiting self-care ADL*	Life-threatening consequences; urgent intervention indicated	Death

Standard care (uptodate)

2. Line Octreotide (Grade 1B)

- Indication If refractory to Loperamide (after 24-48h)
- Mechanism reduce secretion, prolongs intestinal transit time, promotes intestinal absorption
- Limitation multiple daily doses, expensive
- Dosing initial 100 or 150 mcg sc TID, max. 500 mcg sc TID
- Effect complete resolution of loperamide-refractory diarrhea in 94% after 72h (≈50% after 48h)

Make use of drug side-effects

- Scopolamine antisecretory, prolongs intestinal transit time, Indication esp. when associated with cramping
- Ondansetron antisecretory, prolongs intestinal transit time
- Clonidine increases negative feedback on release of neurotransmitters, reduces peristaltic movement
- GLP1-Analoga reduces gastrointestinal motility and secretion
- GLP2-Analoga promotes water/ electrolyte absorption through mucosal growth

Take home messages



1. Line
Loperamide

2. Line
Octreotide

3. Line
combined
therapy



Klinik kompakt ▶

Patienten und Angehörige ▶

Fach- und Arztinfo ▶

Fort- und Weiterbildung ▶

Forschung und Lehre ▶

Palliativpharmazie ▼

Arzneimittelinformation

Zentralstelle Off-Label-Use ▶

Mischinfusionen pall-iv

Aktuelles

Kompetenzzentrum Palliativpharmazie



Informieren. Beraten. Helfen.

Unser Kompetenzzentrum Palliativpharmazie hat es sich zum Ziel gesetzt ärztliches Personal, Pflegekräfte, Apotheker:innen bei der anspruchsvollen Aufgabe der medikamentösen Therapie innerhalb der Palliativmedizin zu unterstützen und zu entlasten.

Unser Anliegen +

Unser Expert:innen-Team +

Wen beraten wir? +

Unser Beratungsangebot +

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CHARTA-FUER-
STERBENDE.DE

Wir unterstützen die Charta

Literature

- https://www.uptodate.com/contents/management-of-acute-chemotherapy-related-diarrhea?search=diarrhoe%20opium&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1
- https://www.uptodate.com/contents/image?imageKey=ONC%2F65649&topicKey=HEME%2F90856&search=nci+ctcae+diarrhea&rank=1%7E150&source=see_link
- S3-Leitlinie Supportive Therapie bei onkologischen PatientInnen, 2020
(https://www.leitlinienprogrammonkologie.de/fileadmin/user_upload/Downloads/Leitlinien/Supportivtherapie/LL_Supportiv_Langversion_1.3.pdf)
- Graven-Nielsen CS et al. Opioids in the Treatment of Chronic Idiopathic Diarrhea in Humans-A Systematic Review and Treatment Guideline. J Clin Med. 2023;12(7):2488
- Fachinformation Dropizol[®], Stand 07/2021
- Arzneimittelinformation Palliativmedizin. Kompetenzzentrum Palliativpharmazie mit Zentralstelle. LMU Klinikum München
- Information Spitalapotheke Stadtspital Zürich