Author(s): Jana Lass
Question: Kas kasutada mittefarmakoloogilisi võtteid või farmakoloogilist ravi või mõlemaid koos palliatiivravi patsientide kurnatuse sümptomite leevendamiseks?
Setting: Palliatiivset ravi vajavad täiskasvanud, ambulatoorset ja statsionaarset ravi saavad patsiendid, erinevad haigusseisundid
Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mittefarmakoloogilisi	farmakoloogilisi meetodeid	Relative (95% CI)	Absolute (95% CI)		
Psühhosotsiaalsed sekkumised vs mittesekkumine (Poort, mixed cancer patients) (follow up: 3-12 months; assessed with: General Fatigue Scale, Edmonton Symptom Assessment Scale (ESAS), Multidisciplinary Fatigue Inventory, Functional Assessment of Cancer Treatment (FACT) Fatigue, fatigue subscale of the Profiles ofMood States (POMS), fatigue scale of the EORTC QLQ-C30, Functional Assessment of Chronic IllnessTherapy (FACIT) Fatigue Scale, Revised Piper Fatigue Scale, subscale intensity)												
1 [1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16]	randomised trials	not serious	serious [a]	not serious	not serious	none	Psühhosotsiaalsetel sekkumistel ei olnud mõju kurnatusele võrreldes kontrollrühmaga, kui kasutati erinevaid skaalasid (standardiseeritud kesmine erinevus(SMD) -0.25, 95% (CI) -0.50 to 0.00; P = 0.05; osalejaid = 535, uuringuid = 12; I2 = 43%. Väga madala tõenduspõhisusega mõningane positiivne mõju, kui kurnatus oli teisene uuringueesmärk (SMD - 0.66, 95%CI -1.00 to -0.32; P = 0.0001; osalejaid = 147, uuringuid= 4; I2 = 0%). Psühhosotsiaalsed ei mõjuta kurnatust kui teist uuringueesmärki, pikemaajalisel jälgimisel (SMD -0.41, 95% CI -1.12 to 0.30; P = 0.26; osalejaid= 91, uuringuid = 2; I2 = 29%;				⨁⨁⨁◯ MODERATE	
Kognitiiv-käitumuslik teraapia (KKT) vs mingid muud tegevused (Cobenau 2018) (assessed with: EORTC QLQ-C30), PFS, SFI, VAS)												
1 [17,18,19,20,21,22,23]	randomised trials	not serious	serious [a]	serious [b]	serious [c]	none	KKT mõju vähihaigete kurnatusele põhineb 6 uuringul (831 patsienti) KKT mõju kurnatusele oli väheoluline (Cohen's d=0.34, p=.063, 95% CI = [−0.019; 0.710]. Uuringutulemused olid heterogeensed Vaid 2 uuringut (Berger et al., 2009 ja Cohen & Fried, 2007) kirjeldasid mõju kurnatusele teatud aja möödudes (324 patsienti) – mõju oli väheoluline (Cohen's d=0.35, p=.209, 95% CI = [−0.196; 0.896])				⨁◯◯◯ VERY LOW	
Tai chi vs mingi muu liigutamine (Xiang 2017 ja Song 2018) Erinevate diagnoosidega patsiendid (vähk, hulgiskleroos, reuma, KOK jne) (follow up: 3-16 months; assessed with: BFI, SRSS, MFSI-SF, MFSI-SF vigor subscale,FSS, VAS,FSMC, FSI,)												
2 [24,25,26,27,28,29,30,31,32,33,34,35,36]	randomised trials	very serious [d]	serious [a]	not serious	not serious	none	Xiang: 10 uuringut (n = 689) suur pimendamise risk (võlts-tai-chi) Tai-chi vähendas kurnatuse sümptomeid võrreldes muu liigutamisega (standardiseeritud keskmiste vahe (SMD): -0.45, 95% (CI): -0.70, -0.20) ja sellel oli poisitiivne mõju vähihaigete kurnatusele (SMD:-0.38, 95% CI: -0.65, -0.11). Hulgiskleroosiga patsientidel kurnatus ei vähenenud oluliselt (SMD: -0.77, 95% CI: -1.76, 0.22) Song: Metaanalüüsis 6 RCTd (373 patsienti) 2 uuringut 6st kaasasid lõppstaadiumis vähipatsiendid Tai Chil oli oluline positiivne mõju lühiajalisele vähiga seotud kurnatusele (i.e., SCRF; SMD = − 0.54; p < 0.0001), kuid pikaajaline mõju jäi ebaselgeks. Alarühma analüüs näitas positiivset mõju rinnavähi patsientidel (SMD = − 0.81; p < 0.00001) ja kopsuvähi patsientidel (SMD = − 0.50; p = 0.002), kuid mitte eesnäärmevähiga patsientidel (p = 0.98). Tai Chi mõju oli suurem kui psühholoogilisel toetusel ja võimlemisel (SMD = − 0.49 and − 0.84, respectively; both p < 0.05).				⨁◯◯◯ VERY LOW	
Võimlemine vs muu (Kessels 2018) vähihaiged (follow up: 4-24 weeks; assessed with: CRF, cancer-related fatigue; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; PFS, Piper Fatigue Scale; MFSI-SF, Multidimensional Fatigue Symptom Inventory-Short Form;)												
1 [37,38,39,40,41,42,43]	randomised trials	serious	not serious	very serious [e,f]	serious [a]	none	11 uuringut, neist 6 madala kallutatuse riskiga - need kaasati meta-analüüsi Füüsilised harjutused parandasid vähihaigetel kurnatuse sümptomeid olulisel määral (Cohen's d 0.605, 95% CI 0.235–0.975) olenemata vähitüübist. Aeroobsed harjutused (Δ=1.009, CI 0.222–1.797) olid parema mõjuga kui kombinatsioon aeroobsetest ja vastupanu (resistance) harjutustest (Δ=0.341, CI 0.129–0.552).				⨁◯◯◯ VERY LOW	

Jooga vs muu (Sadja 2013) (assessed with: Brief Fatigue Inventory, the Functional Assessment of Chronic Illness Therapy–Fatigue, Cella's Functional Assessment of CancerTherapy- Breast (FACT-B),30 European Organization for Research and Treatment of Cancer Quality of Life Questionnaire(EORTC QLQ)-C30,31 FACT-Fatigue,32 the Fatigue Symptom Inventory (FSI), the Rotterdam Symptom Checklist(RSCL), a telephone reported 0–9 scale in which higher scores reflected greater fatigueu)

10 [44]	randomised trials	very serious [g]	serious [a]	serious [f,h]	serious [f]	publication bias strongly suspected [i]	10 uuringut, 583 patsienti, enamasti rinnavähiga naised 4 uuringut leidis, et jooga vähendas oluliselt kurnatust (Banasik, 2011; Bower 2012; Carson 2009; Chandwani 2010; Cohen 2004; Culos-Reed 2006; Danhauer 2009; Littman 2011; Moadel 2007; Vadiraja 2009)	⨁◯◯◯ VERY LOW	

Atsetüül-L-karnitiin vs platseebo (Mücke 2015) vähipatsiendid, lõppstaadiumis neeruhaigusega patsiendid (follow up: kuni 12 weeks; assessed with: FACT-f, BFI, Kidney Disease Questionnaire (KDQ) kurnatuse lõik)

3 [45,46,47,48]	randomised trials	serious [g]	serious [a]	serious [f]	serious [f]	none	1. (Cruciani 2009) 29 kurnatusega vähipatsienti, FACT-f kurnatuse keskmised skoorid olid 15.7 (SD 10.6) ravi alguses ja 22.2 (10.4) teisel nädalal (P value = 0.97). 2. (Cruciani 2012) 209 patsienti, kurnatuse skoor (BFI) paranes mõlemas ravirühmas (L-karnitiiniga: -0.96, 95% (CI) -1.32 to -0.60; platseeboga: -1.11, 95%CI -1.44 to -0.78). Gruppide vahel ei olnud stat erinevust (P väärtus = 0.57) 3. (Brass 2001) Kidney Disease Questionnaire (KDQ) kurnatuse lõik paranes 12 ja 24 nädalase karnitiinravi järgselt võrreldes platseeboga 56-l lõppstaadiumis neeruhaigusega patsiendil, kuid kogu skoor ei muutnud oluliselt	⨁◯◯◯ VERY LOW	

Amantadiin vs platseebo (Mücke 2015) hulgiskleroosiga patsiendid (follow up: kuni 12 weeks)

7 [49]	randomised trials	serious [g]	serious [a]	serious [j,k]	not serious	none	Ashtari 2009; Canadian MSRG 1987; Krupp 1995;Murray 1985; Rosenberg 1988; Shaygannejad 2012; Tomassini 2004. Kokku 7 uuringut, 370 hulgiskeroosiga patsienti, heterogeensed tulemused, suund amantadiini positiivsele mõjule . YAng 2017 meta-analüüsis 5 uuringut (Canadian MSRG 1987; Ashtari 2009; Gisler 1996; Krupp 1995; Ledinek 2013): amantadiin oli kurnatuse ravis tõhus (SMD ja CI olid −1.09(−1.30 to −0.87), z-skoor 9.75 (P = 0.00001). Varieeruva uuritavate arvuga uuringud.	⨁◯◯◯ VERY LOW	

Amantadiin vs platseebo (Yang 2017) hulgiskleroosiga patsiendid (assessed with: MS-specific fatigue scale, Modified Fatigue Impact Scale, Fatigue Severity Scale, Visual Analogue Scale)

5 [50]	randomised trials	serious [g]	serious [a]	serious [j]	not serious	none	5 uuringut (Canadian MSRG 1987; Ashtari 2009; Gisler 1996; Krupp 1995; Ledinek 2013): patsiente n=313. amantadiin oli kurnatuse ravis tõhus (SMD ja CI olid −1.09(−1.30 to −0.87), z-skoor 9.75 (P = 0.00001). Varieeruva uuritavate arvuga uuringud.	⨁◯◯◯ VERY LOW	

Metüülfenidaat vs platseebo (Mücke 2015) vähipatsiendid (assessed with: FACIT-F, the Brief Fatigue Inventory (BFI))

5 [49]	randomised trials	serious [j]	serious [a]	not serious	not serious	none	318 vähipatsienti (Bruera 2006; Butler 2007; Escalante 2014; Moraska 2010; Roth 2010). Meta-analüüsi sai teha vaid 2 uuringuga (Bruera 2006; Butler 2007), kasutasid FACIT-F skaalat kurnatuse hindamiseks. Metüülfenidaat oli veidi tõhusam kui paltseebo (standardiseeritud kesmine erinevus (SMD) 0.49, 95% CI 0.15 - 0.83. Ülejäänud kolm uuringut: Moraska 2010: metüülfenidaat (18 mg - 54 mg) ei olnud oluliselt parem kui platseebo Escalante 2014: metüülfenidaat (18mg) 2 nädalat, BFI skoor paranes ravimiga Roth 2010: metüülfenidaat (5 mg - 30 mg). BFI skoor paranes kliiniliselt oluliselt Kerr et al. uuringus oli 30 hospiitsi patsienti erinevate diagnoosidega. Metüülfenidaat toimis neil paremini kui platseebo, toime sõltus annusest	⨁⨁◯◯ LOW	

Modafiniil vs platseebo (Mücke 2015) vähihaiged (assessed with: FACIT-F scores)

2 [49]	randomised trials	not serious	not serious	serious [l]	not serious	none	704 vähipatsienti: 1. Jean-Pierre 2010: modafiniil 200mg/päevas – raskema kurnatusega patsiendid said kasu, kergemaga mitte 2. Spathis 2014: modafiniil (100 - 200 mg/päevas) ja platseebo mõjutasid FACIT-F skoori positiivses suunas, vahe platseeboga puudus.	⨁⨁⨁◯ MODERATE	

Metüülfenidaat vs platseebo (Mücke 2015 analüüsist Breitbart 2001) HIV patsiendid (assessed with: Piper Fatigue Scale (PFS) and the Visual Analogue Scale for Fatigue (VAS-F))

1 [49,51]	randomised trials	serious [j]	not serious	not serious	serious [g]	none	109 HIV patsienti: lõptas uuringu (metüülfenidaat n=15), pemoliin, platseebo – VAS-F skoor ei erinenud gruppide vahel (F = 1.61 [P = .21]; effect size, 0.17; 95% CI, −0.02 to 0.36) ega kurnatuse alaskaalal (F = 0.77 [P = .47]; effect size, 0.12; 95% CI, −0.07 to 0.31).	⨁⨁◯◯ LOW	

Modafiniil vs platseebo (Mücke 2015) hulgiskleroosiga patsiendid

2 [49]	randomised trials	serious [j]	not serious	not serious	serious [l]	none	1. Stankoff 2005 (n = 115), Modafiniil ei olnud parem kui platseebo 2. Lange 2009 (n=21) modanifiil vähendas kurnatust Nende uuringute metaanalüüs ei näidanud olulist efekti (SMD of -0.14)	⨁⨁◯◯ LOW	

Modafiniil vs platseebo (Mücke 2015 ülevaatest Vasconselos 2007) polümüeliidijärgsed patsiendid (assessed with: Fatigue Severity Scale)

1 [49]	randomised trials	serious [j]	not serious	serious [l]	not serious [l]	none	n=33 patsienti, modafinil ei erinenud platseebost	⨁⨁◯◯ LOW	

Modafiniil vs platseebo (Mücke uuringust Rabkin) HIV patsientidel

1	randomised trials	serious [j]	not serious	serious [l]	not serious	none	1 uuring HIV patsientidel (Rabkin 2010): 105HIV/AIDSi patsienti, kurnatus vähenes modafiniili grupis 73% ja platseebo grupis 28%;	⨁⨁◯◯ LOW	

Modafiniil vs platseebo (Yang 2013) hulgiskleroosiga patsiendid (assessed with: MFIS, FSS)

3 [50]	randomised trials	serious [g]	serious [a]	serious [l]	not serious	none	(Ledinek 2013; Möller 2011; Stankoff 2005): patsiente 285. MD ja CI olid −3.93 (−12.38 kuni 4.51); Iruut oli 81%, ja z-score 0.91 (P = 0.36). Kahes uuringus mõõdeti kurnatust FSS skaalaga; MDja CI olid −6.56 (−19.97 to 6.55), Iruut oli 92%, ja z-score 0.98 (P = 0.33). Seega modafiniil ei olnud hulgiskleroosiga patsientidel kurnatuse vähendamises tõhus	⨁◯◯◯ VERY LOW	

Modafiniil vs platseebo (Shangyan 2018) hulgiskleroos (follow up: 30-56 days; assessed with: MFIS, FSS)

5 [52]	randomised trials	serious [j]	serious [a]	serious [l]	not serious	publication bias strongly suspected dose response gradient [m]	patsiente n=303 (Ford-Johnson et al., 2016; Lange et al., 2009; Ledinek et al., 2013; Moller et al., 2011; Stankoff, 2005). Modafinilil oli parema toimega kui platseebo MFIS skoori alusel (MD = −5.27, 95% CI:−8.51 to −2.03, P = 0.001). FSS, ei erinenud gruppide vahel (MD =2.50, 95%CI: −0.70 to 5.70, P = 0.13).	⨁◯◯◯ VERY LOW	

Platseebo vs ravi (Pedro Nazareth Aguiar 2019) vähipatsiendid (assessed with: Functional Assessment of Chronic Illness (FACIT-F) and Brief Fatigue Inventory (BFI) scales)

29 [53]							29 uuringut, n=3758 patsienti PPlatseebo kesmine mõju oli + 4.88 (95%CI + 2.45 to + 7.29) FACIT-F skaalal, mõju väiksem kui võrdlusravimitel (p = 0.005). BFI skaalat kasutades oli platseebo keskmine mõju + 0.64 (95%CI + 0.02 to + 1.30), kuid mõju oli väiksem kui võrdlusravimitel (p = 0.002).29% (95%CI 25–32%) patsientidest, kes tarvitasid platseebot, teatas olulisest vähiga seotud kurnatuse sümptomite paranemisest võrreldes 36% patsientidega võrdlusrühmas (p = 0.030).	-	

CI: Confidence interval

Explanations

a. Uuringutulemused olid heterogeensed
b. ainult rinnavähi patsiendid
c. ravi pikkus ei olenud enamasti kirjas, muu ravi ei olnud kirjas
d. suur pimendamise risk
e. palliatiivravi patsiendid jäeti välja
f. ainult vähipatsiendid
g. uuritavate valiku kallutatus
h. <3% uuritavatest olid mehed
i. There was evidence of mixed high and low risk of reporting bias across studies
j. väike uuritavate arv
k. ainult hulgiskleroosiga patsiendid
l. ei olnud ainult palliatiivravi patsiendid
m. some smaller, negative studies might be present but not published

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