Summary of Findings – May 25, 2011 – Duloxetine

Duloxetine

Is Duloxetine effective in reducing pain and improving function in patients with symptomatic OA knee pain compared to placebo? Is duloxetine well tolerated by these patients?

Step 1: Search results

We found the most recent randomized placebo-controlled trial (Chappell, 2011) which assessed the efficacy and safety of duloxetine in patients with OA knee pain.

Intervention description: This was a 13-week, randomized, double-blind, placebo-controlled trial in patients meeting American College of Rheumatology clinical and radiographic criteria for osteoarthritis of the knee. Patients were randomized to either duloxetine 60 mg once daily (QD) or placebo. At week 7, the duloxetine dosage was increased, in a blinded fashion, to 120-mg QD in patients reporting < 30% pain reduction.

Step 2: GRADE Summary of findings table

Duloxetine compared to placebo for Knee OA

Patient or population: patients with Knee OA
Intervention: Duloxetine
Comparison: placebo

Outcomes	Illustrative comparative risks* (95% CI)		Absolute Difference	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	NNT
	Assumed risk **Placebo**	Corresponding risk **Duloxetine**					
Benefits							
Pain Brief Pain Inventory (BPI) average pain subscale. Scale from: 0 to 10. (follow-up: 13 weeks)	36%	51%[1] (41% to 60%)	15%	1.42	256 (1[2])	⊕⊕⊕O **moderate**[3]	6 (4 to 18)
Physical function WOMAC function subscale. Scale from: 0 to 68 (follow-up 13 weeks)	34%	44% (35% to 54%)	10%	1.29	256 (1[2])	⊕⊕⊕O **moderate**[3]	9 (5 to 208)
Harms							
Serious adverse events[4] Number of patients Follow-up: 13 weeks	1.6%	2.3%	0.7%	**RR 1.50** (0.25 to 8.83)	256 (1 study)	⊕⊕⊕O **moderate**[3]	Not statistically significant

[1] The authors note that results for the WOMAC pain and stiffness scales were not statistically significant but did not report those results numerically.
[2] The included study was the RCT by Chappell (2011).
[3] The quality of the study was downgraded because of imprecision. The effect size ranges from clinically non significant to clinically significant. The authors do not clearly state on which scale physical function is rated. We assumed they used the WOMAC rated on a 68 point scale to make the calculations. We did not downgrade the quality of the study for this.
[4] Serious adverse events include atrial fibrillation and acute pyelonephritis in the placebo group and drug intolerance, memory impairment, and supraventricular tachycardia in the duloxetine group.

Note: A total of 107 (41.8%) patients reported one or more treatment-emergent adverse events (TEAEs) during the treatment phase. As illustrated by the authors, significantly more duloxetine-treated patients experienced TEAEs than patients in the placebo group ($P = 0.005$). Compared with placebo, significantly more duloxetine-treated patients experienced nausea ($P = 0.018$), constipation ($P = 0.034$), and hyperhidrosis ($P = 0.014$). However, the authors did not report the number of participants who presented those symptoms in the placebo and treatment groups, precluding the use of statistics.

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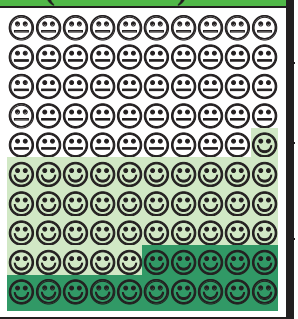
Visual Summary of findings figure: Duloxetine compared to placebo

Issue **Evidence from SRs and trials** **Judgment** (panel)
1. Balance between desirable and undesirable effects

Chance: Improving pain (13 weeks)

NNT: 6		
49%	😐	Don't improve
36%	☺	Improve with or without Rx
15%	☺	Benefit with Rx



Chance: Improving physical function (13 weeks)

NNT: 9		
56%	😐	Don't improve
34%	☺	Improve with or without Rx
10%	☺	Benefit with Rx

Chance: Serious adverse events (13 weeks)

NNH			
97.7%	😐	Avoid bad outcome	**Not statistically significant**
1.6%	☹	Bad outcome with or without Rx	
0.7%	☹	Harmed by Rx	

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Step 3: GRADE Evidence profile:

Author(s): Karine Toupin April
Date: 2011-05-24
Question: Should Duloxetine versus placebo be used for OA Knee pain?
Bibliography: Chappell, 2011

Quality assessment							Summary of findings					Import-ance
							No of patients		Effect			
No of studies	Design	Limit-ations	Inconsis-tency	Indirect-ness	Impre-cision	Other consider-ations	Duloxetine	placebo	Relative (95% CI)	Absolute	Quality	
Pain (follow-up 13 weeks; measured with: Brief Pain Inventory (BPI) average pain subscale; range of scores: 0-10; Better indicated by less)												
1[1]	random-ised trial	no serious limit-ations	no serious inconsis-tency	no serious indirect-ness	Serious impre-cision[2]	None	128	128	1.42	SMD -0.37 (-0.61 to -0.12)[3]	⊕⊕⊕O MODERATE	CRITICAL
Physical function (follow-up 13 weeks; measured with: WOMAC; range of scores: 0-68; Better indicated by less)												
1[1]	random-ised trial	no serious limit-ations	no serious inconsis-tency	no serious indirect-ness	Serious impre-cision[2]	None	128	128	1.29	SMD -0.26 (-0.5 to -0.01)	⊕⊕⊕O MODERATE	CRITICAL
Serious adverse events (follow-up mean 13 weeks; number of patients with event)												
1[1]	random-ised trial	no serious limit-ations	no serious inconsis-tency	no serious indirect-ness	Serious impre-cision[2]	none	3/128 (2.3%)	2/128 (1.6%)	RR 1.50 (0.25 to 8.83)[4]	0.7% more	⊕⊕⊕O MODERATE	CRITICAL

[1] The included study was the RCT by Chappell (2011).
[2] The quality of the study was downgraded because of imprecision. The effect size ranges from clinically non significant to clinically significant. The authors do not clearly state on which scale physical function is rated. We assumed they used the WOMAC rated on a 68 point scale to make the calculations. We did not downgrade the quality of the study for this.
[3] The authors note that results for the WOMAC pain and stiffness scales were not statistically significant but did not report those results numerically.
[4] Serious adverse events include atrial fibrillation and acute pyelonephritis in the placebo group and drug intolerance, memory impairment, and supraventricular tachycardia in the duloxetine group.

Step 4: Other recommendations

Group	Recommendation
EULAR	No recommendation
OARSI	No recommendation

References

Chappell AS, Desaiah D, Liu-Seifert H, Zhang S, Skljarevski V, Belenkov Y *et al.* A double-blind, randomized, placebo-controlled study of the efficacy and safety of duloxetine for the treatment of chronic pain due to osteoarthritis of the knee. Pain pract 2011;11:33-41.