

Evidence Tables

NEUR2: Is gabapentin effective for the treatment of painful neuropathy in people with type 2 diabetes?

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Effect size	Source of funding
M. Backonja, A. Beydoun, K. R. Edwards, S. L. Schwartz, V. Fonseca, M. Hes, L. Lamoreaux, and E. Garofalo. Gabapentin for the symptomatic treatment of painful neuropathy in patients with diabetes mellitus: a randomized controlled trial.[see comment]. <i>JAMA</i> 280 (21):1831-1836, 1998.	RCT, double blind, multicentre 1++	N=165 (approximately 75% T2D)	Inclusion criteria: type 1 or 2 diabetes, pain from diabetic neuropathy for 1-5yrs, pain rating of ≥ 40 mm on the VAS of the SF-MPQ, av pain score ≥ 4 on an 11-point Likert scale, ≥ 4 observations in daily pain diaries in a week, HbA1c ≤ 0.11 Exclusion criteria: other severe pain, renal impairment, prohibited medications. Patient demographics at baseline	N=84 gabapentin TID, titrated dose (week 1, 900 mg/d; week 2, 1800 mg/d; week 3, 2400 mg/d; week 4, 3600 mg/d) Medication doses for diabetes remained stable during the study	N=81 matched placebo TID	15 weeks 7 week screening phase, 4-week dose titration and 4-week fixed dose	Pain severity rating (recorded in diaries), sleep interference, SF-MPQ scores, PGIC, CGIC and quality of life (SF-36 QOL)	All CI 95% *Mean pain score There was a significant difference from gabapentin to placebo at the end point in decrease in pain score; -1.2 (-1.9 to -0.6), $p < 0.001$. Analysed per week this difference was significant from week 2 to week 8 ($p < 0.05$). *Mean sleep interference There was a significant decrease in sleep interference for gabapentin compared with placebo at the end point; -1.47 (-2.2 to -0.8), $p < 0.001$. *SF-MPQ For the total SF-MPQ scores there was a significant decrease for gabapentin compared with placebo; -5.9 (-8.8 to -3.1), $p < 0.001$. This was also noted for both the VAS; -16.9 (-25.3 to -8.4), $p < 0.001$ and the PPI scale; -0.6 (-0.9 to -0.3), $p < 0.001$. *PGIC and CGIC For both of these scales patients treated with gabapentin had significantly greater improvement in pain than patients randomised to placebo ($p = 0.001$)	Not stated

			were similar between groups.					<p>*SF-36 QOL There were significant increases (denotes improvement) in three areas of the SF-36 for gabapentin compared with placebo:</p> <ul style="list-style-type: none"> - bodily pain, 7.8 (1.8 to 13.8), p=0.01 - mental health, 5.4 (0.5 to 10.3), p=0.03 - vitality, 9.7 (3.9 to 15.5), p=0.001 <p>*Adverse events There was a significantly higher number of adverse events of dizziness (n=20 gabapentin, n=4 placebo, p<0.001) and somnolence (n=19 gabapentin, n=5 placebo, p=0.004) for those in the gabapentin group compared with placebo</p> <table border="0"> <tr> <td>*Discontinuation</td> <td>n</td> <td>(%)</td> </tr> <tr> <td>Gabapentin</td> <td>14</td> <td>16.7</td> </tr> <tr> <td>- adverse events</td> <td>7</td> <td>8.3</td> </tr> <tr> <td>Placebo</td> <td>16</td> <td>19.8</td> </tr> <tr> <td>- adverse events</td> <td>5</td> <td>6.2</td> </tr> </table>	*Discontinuation	n	(%)	Gabapentin	14	16.7	- adverse events	7	8.3	Placebo	16	19.8	- adverse events	5	6.2	
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F. J. GomezPerez, A. PerezMonteverde, O. Nascimento, P. Aschner, M. Tagle, K. Fichtner, P. Subbiah, E. M. Mustiya, and B. Parsons. Gabapentin for the treatment of painful diabetic neuropathy: Dosing to achieve optimal clinical	Open-label, multi centre 1+	N=339 (N=303 T2D) 33 Latin American centres	Inclusion criteria: Type 1 or 2 diabetes, experienced painful polyneuropathy for 1-5yrs, HbA1c ≤11%, pain intensity score of ≥40mm on the VAS of SF-MPQ Exclusion	N=170 Gabapentin, fixed-dose 300mgs TID	N=169 Gabapentin TID, titrating dose (900, 1200, 1800, 2400, 2700 and 3600 mg/day) up to the end of week 3, stable dose weeks 4-7 (Titrated to clinical effect ≥50%	8 week 1 week screening, 7-week treatment	Per cent reduction in final weekly mean pain score (11-point Likert scale), Responder rate, VAS of SF-MPQ, sleep interference, CGIC, PGIC, SF-36 QOL	The mean daily dose in the titration-to-clinical-effect group was 1,936mg/day * Mean pain score Gabapentin showed significantly greater reduction in final weekly mean pain scores when titrated to clinical effect compared with a fixed-dose of 900mg/day; 53.6% vs 43.3%, p=0.009. *Responder rate Responder rate (≥50% reduction in final weekly pain score from baseline) was significantly higher in the titration to clinical effect group compared with the fixed dose group (64.5% VS 47.5%, P=0.002)	Pfizer															

<p>response. <i>British Journal of Diabetes & Vascular Disease</i> 4 (3):173-178, 2004.</p>			<p>criteria: Pain due to other causes, other neurological conditions, other serious diseases, prohibited medications.</p> <p>Groups were well matched, though the titration to clinical effect group had a longer mean duration of diabetes (12.9yrs) than the fixed dose group (10.7yrs).</p>		<p>reduction in pain)</p>		<p>*SF-MPQ VAS This score showed a significant decrease in favour of the titration to clinical effect group compared with fixed dose ($p < 0.001$)</p> <p>*Sleep interference There was a significantly greater reduction in final weekly mean sleep interference score for the titration to clinical effect group compared with fixed dose (57% vs 37.2%, $p = 0.013$)</p> <p>*CGIC There was a significant improvement in CGIC for the titration to clinical effect group compared with the fixed dose group ($p = 0.02$)</p> <p>*PGIC There was no significant difference between the two groups in improvements in PGIC</p> <p>*SF-36 QOL There was no significant difference between the two groups in SF-36 QOL domains</p> <p>*Adverse events The most common adverse events in the titration to clinical effect group and fixed dose groups were somnolence (20.1% vs 15.3%) and dizziness (16.6% vs 13.5%)</p> <table border="0" data-bbox="1529 1157 2033 1324"> <tr> <td>*Discontinuation</td> <td>n</td> <td>(%)</td> </tr> <tr> <td>Total</td> <td>16</td> <td>4.8</td> </tr> <tr> <td>Fixed dose</td> <td></td> <td></td> </tr> <tr> <td>- adverse events</td> <td>9</td> <td>5.3</td> </tr> <tr> <td>Titration doses</td> <td></td> <td></td> </tr> <tr> <td>- adverse events</td> <td>7</td> <td>4.1</td> </tr> </table>	*Discontinuation	n	(%)	Total	16	4.8	Fixed dose			- adverse events	9	5.3	Titration doses			- adverse events	7	4.1	
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<p>C. M. Morello, S. G. Leckband, C. P. Stoner, D. F. Moorhouse, and G. A. Sahagian. Randomized double-blind study comparing the efficacy of gabapentin with amitriptyline on diabetic peripheral neuropathy pain. <i>Arch Intern Med</i> 159 (16):1931-1937, 1999.</p>	<p>RCT, double blinded, crossover, single centre 1+</p>	<p>N=25 (N=22 T2D), USA</p>	<p>Inclusion criteria: >18yrs, stable glycaemic control defined as HbA1c between 4.3% and 7.9% within 3 mths, chronic daily pain >3mths consistent with diabetic neuropathic pain Exclusion criteria: non-neuropathic pain, severe depression, other serious conditions Patient characteristics given for all participants not per group.</p>	<p>N=12 Gabapentin, titrated for 2 days and dosage adjusted based on clinical response and adverse events. Doses for gabapentin were; 65% 1800mg/day, 26% 1200 mg/day and 9% 900 mg/day.</p>	<p>N=13 Amitriptyline, titrated for 2 days and dosage adjusted based on clinical response and adverse events. Doses for amitriptyline were: 54% 75 mg/day, 29% 50 mg/day and 17% 25 mg/day</p>	<p>15 weeks 2 week wash out of any medications being used to treat neuropathic pain, 6 week treatment periods with 1 week washout, followed by 6 week crossover</p>	<p>Pain Scale Rating System, Global Rating Scale</p>	<p>* Pain intensity score There were significant reductions in the end of treatment pain scores for both gabapentin (p<0.001) and amitriptyline (p<0.001). However, there was no statistically significant difference in pain scores between gabapentin and amitriptyline at the end of treatment. * Global pain score There was no statistical difference in pain relief between the groups. * Adverse events With the exception of weight gain with amitriptyline (p<0.03) there was no significant difference in occurrence of adverse events between the drugs. Adverse effects included sedation, dry mouth, dizziness, postural hypotension, weight gain, ataxia and lethargy. *Discontinuation 19 (76%) participants completed 6 weeks of treatment with both study arms, 2 (one from each group) crossed over early due to adverse events and completed the study</p>	<p>Not stated</p>
<p>D. A. Simpson. Gabapentin and venlafaxine for the treatment of painful diabetic neuropathy. <i>Journal of Clinical</i></p>	<p>RCT, double-blind * Reporting</p>	<p>N=60 (N=49 T2D)</p>	<p>Inclusion criteria: pain attributed to diabetic neuropathy for 3mths-1.5yrs,</p>	<p>N=30 gabapentin 4 week titration period up to 3600mg/day,</p>	<p>N=30 placebo</p>	<p>9 weeks 1 week screening, 8 weeks treatment</p>	<p>Mean pain scores (11-point Likert scale) Sleep</p>	<p>*Mean pain score There was a significant decrease in mean pain score for gabapentin compared with placebo, -2 vs -0.5, p<0.01. *SF-MPQ, sleep interference and SF-36</p>	<p>Not stated</p>

<p><i>Neuromuscular Disease 3 (2):53-62, 2001.</i></p>	<p>only on part 1 of the study – gabapentin vs placebo.</p> <p>1+</p>		<p>type 1 or 2 diabetes from 6mths-17yrs, pain score of ≥ 40mm on the VAS of SF-MPQ, av score of 4 on an 11-point Likert scale over one week.</p> <p>Exclusion criteria: other severe pain, renal failure, prohibited medications.</p> <p>Groups were similar for demographics.</p>	<p>1200mg TID as tolerated¹, followed by 4 week fixed dose</p>			<p>interference, PGIC, CGIC, SF-36 QOL</p>	<p>QOL Changes in mean sleep interference scores, the SF-36 QOL and SF-MPQ total pain scores also revealed significant improvement in the gabapentin-treated group</p> <p>*PGIC and CGIC There were 55.5% (n=15) in the much/moderately improved category in the gabapentin treated group compared with 25.9%(n=7) in the placebo group; 41% (n=11) compared with 59.3% (n=16) in the minimally improved/no change group and 3.5% (n=1) compared with 14.8% (n=4) who considered they were worse.</p> <table border="0"> <tr> <td>*Discontinuation</td> <td>n</td> <td>(%)</td> </tr> <tr> <td>Gabapentin</td> <td>3</td> <td>10</td> </tr> <tr> <td>- due to adverse events</td> <td>2</td> <td>6.6</td> </tr> <tr> <td>Placebo</td> <td>3</td> <td>10</td> </tr> <tr> <td>- due to adverse events</td> <td>2</td> <td>6.6</td> </tr> </table>	*Discontinuation	n	(%)	Gabapentin	3	10	- due to adverse events	2	6.6	Placebo	3	10	- due to adverse events	2	6.6	
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<p>K. C. Gorson, C. Schott, R. Herman, A. H. Ropper, and W. M. Rand. Gabapentin in the treatment of painful diabetic neuropathy: a placebo controlled, double blind, crossover trial. <i>J Neurol.Neurosurg.Psychiatry</i> 66 (2):251-252, 1999.</p>	<p>RCT, double-blind, crossover</p> <p>1-</p>	<p>N=40 (number T2D not specified)</p>	<p>Inclusion criteria: diabetes for >6 mths on a stable dosage of insulin or oral hypoglycaemic agent, daily neuropathic pain for >3 mths</p> <p>Exclusion criteria: renal insufficiency, other painful</p>	<p>N=19 gabapentin increased up to 900mg/day maintenance dose first phase, 3 week wash out and crossover</p>	<p>N=21 placebo first phase, 3 week wash out, followed by crossover</p>	<p>15 weeks</p> <p>6 weeks dosed, 3 weeks wash out, crossover and 6 weeks dosed</p>	<p>MPQ, global assessment of pain relief</p>	<p>*MPQ and global assessment of pain The mean decrease in the MPQ score was 8.9 with gabapentin compared with 2.2 for placebo (p=0.03). There were no differences in the VAS and PPI scores.</p> <p>The global assessment of pain relief showed no significant differences between gabapentin and placebo.</p> <p>*Adverse events Adverse events were significantly more common with gabapentin compared with placebo (p<0.001), commonest with the gabapentin were drowsiness (n=6), fatigue (n=4) and imbalance (n=3).</p>	<p>Warner Lambert (Parke-Davis Pharmaceuticals)</p>															

			conditions, other causes of neuropathy					*Discontinuation Not reported	
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¹ Titration incremented in 300mg increases over 4 weeks