The beta-2-agonist terbutaline for the treatment of painful polyneuropathy. A randomized, active- and placebo-controlled trial.

Summary data.

Study design

Randomised, double-blind, and active- and placebo-controlled trial with 3 treatment periods of 5 weeks duration, each preceded by 1 week for baseline observations, and with 1 week for washout between the baseline-treatment sections.

Outcomes

Primary: Weekly median of average daily pain rated with 0-10 points numeric rating scales (NRS).

Secondary: Patient global impression of change (PGIC), weekly median of average daily rating of specific pain symptoms with 0-10 NRS, numbers needed to treat (NNT) to obtain more than 50% pain relief.

Patients

Demographics and baseline characteristics

	mITT	PP
Patients, n	47	32
Age, median (range), y	59 (20-76)	62 (20-74)
Sex (female/male), n	22/25	16/16
Etiology of polyneuropathy, n (%)		
Idiopathic	16 (34.0)	12 (37.5)
Diabetes	10 (21.3)	4 (12.5)
Alcohol	5 (10.6)	3 (9.4)
Drug-induced	4 (8.5)	3 (9.3)
Other*	12 (25.5)	10 (31.3)
Pain		
Pain duration, months, median (range)	40 (10-156)	44 (10-156)
Total pain baseline 1, NRS, median (range)	6 (4-10)	6 (4-10)
Spontaneous pain symptoms, n (%)		
Deep aching	29 (61.7)	16 (50.0)
Pressing	16 (34.0)	9 (28.1)
Burning	32 (68.1)	21 (65.6)
Stabbing pain	35 (74.5)	23 (71.9)
Evoked pain symptoms, n (%)		
Touch-evoked	21 (44.7)	13 (40.6)
Pressure-evoked	19 (40.4)	10 (31.3)
Cold-evoked	12 (25.5)	8 (25.0)
Previous neuropathic pain treatment, n (effect)		
TCA	25 (12)	17 (7)
SNRI	3 (1)	1 (0)
Gabapentin, pregabalin	23 (7)	14 (5)
Opioid, incl. tramadol	11 (4)	6 (3)

***Other: Mb. Sjøgren, MGUS-associated, Guillain Barré sequelae, Mb. Crohn, Mb. Waldenstrøm**
mITT: modified intention to treat population
PP: per protocol population
Spontaneous and evoked pain: possible to choose none, one or several symptoms
TCA: tricyclic antidepressant
SNRI: serotonin and norepinephrine reuptake inhibitors
Effect: patients own experience

Results

Effect of terbutaline and imipramine as compared to placebo for pain symptoms, sleep disturbance and use of escape medication in the total population

	TERBUTALINE		IMIPRAMINE		PLACEBO		TERBUTALINE	IMIPRAMINE
	Baseline NRS (SD)	**Week 5 NRS (SD)**	**Baseline NRS (SD)**	**Week 5 NRS (SD)**	**Baseline NRS (SD)**	**Week 5 NRS (SD)**	**Treatment effect as compared to placebo NRS, (CI), p-value**	
Total pain								
mITT	6,44 (1,83)	6,13 (2,34)	6,58 (1,91)	4,77 (2,43)	6,27 (1,74)	5,66 (1,91)	0,13 (-0,123;0,379), 0,316	-1,17 (-1,418; -0,921), <0,001
PP	6,50 (1,67)	6,03 (2,40)	6,39 (1,79)	4,47 (2,20)	6,27 (1,66)	5,69 (1,94)	0,23 (-0,047;0,514), 0,103	-1,17 (-1,459; -0,889), <0,001
Spontaneous pain								
Burning								
mITT	5,03 (2,59)	5,05 (2,97)	5,25 (2,97)	4,07 (3,02)	4,82 (2,69)	4,16 (2,57)	0,17 (-0,094;0,440), 0,204	-0,92 (-1,190; -0,658), <0,001
PP	5,06 (2,64)	5,00 (3,01)	5,00 (2,55)	3,59 (2,63)	4,91 (2,83)	4,25 (2,65)	0,29 (-0,001;0,586), 0,051	-0,93 (-1,234; -0,633), <0,001
Deep aching								
mITT	5,46 (2,64)	5,29 (2,86)	5,49 (2,60)	4,16 (2,87)	5,10 (2,23)	4,71 (2,40)	0,16 (-0,103;0,422), 0,233	-1,00 (-1,252; -0,739), <0,001
PP	5,50 (2,49)	5,08 (2,87)	4,98 (2,57)	3,69 (2,61)	4,98 (2,34)	4,75 (2,51)	0,25 (-0,041;0,548), 0,092	-1,05 (-1,345; -0,754), <0,001
Stabbing								
mITT	4,99 (2,77)	4,76 (3,08)	4,78 (2,84)	3,59 (2,82)	4,50 (2,78)	3,91 (2,69)	0,17 (-0,135;0,348), 0,386	-0,80 (-1,032; -0,567), <0,001
PP	5,09 (2,58)	4,53 (3,12)	4,27 (2,70)	3,13 (2,50)	4,36 (2,86)	3,86 (2,87)	0,20 (-0,069;0,472), 0,144	-0,81 (-1,074; -0,549), <0,001
Evoked pain								
Touch-evoked								
mITT	3,30 (2,19)	3,31 (3,01)	3,61 (2,98)	2,74 (2,91)	3,21 (2,92)	2,45 (2,65)	0,32 (0,120;0,511), 0,002	-0,36 (-0,549; -0,164), <0,001
PP	3,25 (3,04)	3,09 (3,16)	3,19 (2,89)	2,31 (2,75)	3,09 (3,05)	2,28 (2,71)	0,41 (0,195;0,628), <0,001	-0,21 (-0,427;0,008), 0,059
Pressure-evoked								
mITT	3,81 (3,12)	3,96 (3,07)	4,00 (3,10)	3,01 (2,84)	3,96 (2,97)	3,03 (2,74)	0,33 (0,111;0,550), 0,003	-0,44 (-0,659; -0,226), <0,001
PP	3,91 (3,11)	3,81 (3,14)	3,72 (3,00)	2,63 (2,60)	3,89 (2,98)	2,97 (2,78)	0,34 (0,091;0,589), 0,008	-0,41 (-0,661; -0,156), 0,002
Sleep disturbance								
mITT	4,99 (3,20)	4,97 (3,27)	5,42 (3,04)	4,09 (3,02)	4,92 (2,92)	4,84 (2,86)	-0,23 (-0,474;0,005), 0,055	-0,89 (-1,123; -0,652), <0,001
PP	5,05 (3,28)	4,74 (3,43)	4,84 (3,13)	3,56 (2,86)	4,84 (3,05)	4,87 (3,09)	-0,22 (-0,483;0,037), 0,092	-0,87 (-1,135; -0,611), <0,001
Paracetamol								
mITT	17,3 (16,6)	19,7 (17,4)	19,2 (20,0)	14,7 (16,7)	14,9 (17,9)	13,7 (14,5)	2,1 (0,658;3,450), 0,004	-2,0 (-3,341; -0,606), 0,005
PP	15,4 (15,4)	17,8 (17,5)	16,9 (20,3)	11,4 (16,6)	13,3 (18,0)	13,1 (14,9)	1,7 (0,159;3,312), 0,031	-2,3 (-3,858; -0,670), 0,005

mITT: modified intention to treat population
PP: per protocol population
***p-value: general liniear model for repeated measurements with baseline pain as co-variable**

PGIC

PGIC mITT	**PLACEBO**	**TERBUTALINE**	**IMIPRAMINE**
much improved	2 (5,6%)	1 (2,6%)	5 (12,2%)
moderately improved	4 (11,1%)	3 (7,7%)	11 (26,8%)
slightly improved	7 (19,4%)	5 (12,8%)	12 (29,3%)
unchanged	14 (38,9%)	14 (35,9%)	9 (22%)
slightly worse	2 (5,6%)	6 (15,4%)	1 (2,4%)
moderately worse	5 (13,9%)	8 (20,5%)	3 (7,3%)
much worse	2 (5,6%)	2 (5,1%)	2 (4,9%)
Total	36	39	41
p		0.56	0.056

PGIC PP	**PLACEBO**	**TERBUTALINE**	**IMIPRAMINE**
much improved	2 (6,7%)	1 (3,2%)	5 (16,7%)
moderately improved	3 (10%)	3 (9,7%)	7 (23,3%)
slightly improved	7 (23,3%)	5 (16,1%)	8 (26,7%)
unchanged	11 (36,7%)	10 (32,3%)	7 (23,3%)
slightly worse	1 (3,3%)	5 (16,1%)	0 (0%)
moderately worse	5 (16,7%)	6 (19,4%)	2 (6,7%)
much worse	1 (3,3%)	1 (3,2%)	1 (3,3%)
Total	30	31	30
p		0.543	0.111

NNT

	50% pain relief	NNT (95% CI)
Terbutaline	2/39	∞
Imipramine	12/44	5.16 (2.85-21.23)