Ambulation in patients managed with intrathecal baclofen for MS-related spasticity

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Background

- Spasticity is a frequent (up to 84%) disabling symptom in patients with MS.
- Spasticity has been defined as, "disordered sensorimotor control resulting from an upper motor neuron lesion, presenting as intermittent or sustained involuntary activation of muscles" (1)
- Management is based around: physical strategies, oral treatments include: baclofen, tizanidine, gabapentin, benzodiazepines and dantrolene, focal treatment with Botulinum toxin and nerve blocks.
- Intrathecal baclofen (ITB) is an effective option in those resistant to above approaches.
- In people with MS it is usually recommended for those who are no longer ambulant.
- Prior case reports in mixed patient cohorts have reported preserved ambulation in people with Cerebral Palsy, spinal cord injuries and some people with MS

Aim

- To evaluate the effect of ITB on a small cohort of ambulatory patients with MS-related spasticity.

Methods

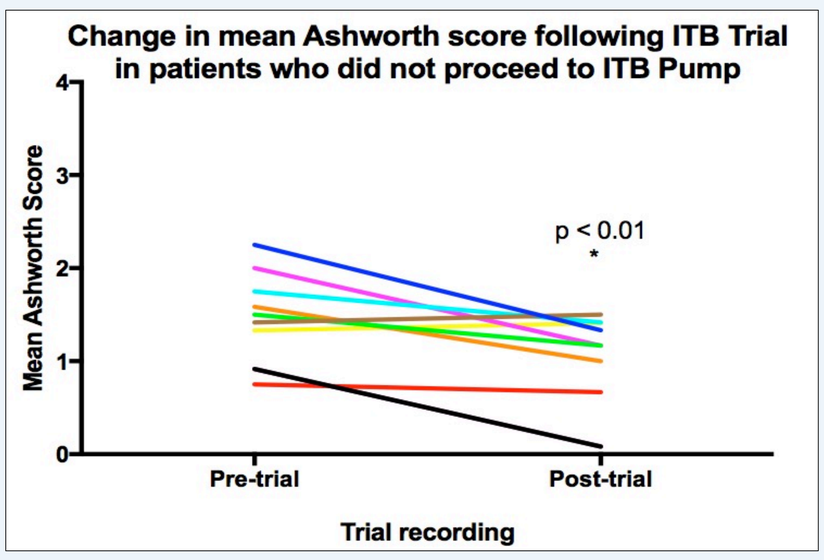
- A single centre observational cohort study was performed between 2009 - 2017.
- Ambulatory subjects with spasticity resistant to two or more standard agents including THC:CBD (Nabiximols - Sativex®) were offered ITB.
- Subjects were admitted for trial via lumbar puncture and effect assessed and subsequent.
- IT dose baclofen ranges from 25 – 75 mcg generally
- Data collected prospectively at baseline, at peak trial effect and longitudinally after trial and pump implant. Data: baseline demographics, EDSS, spasticity scores (Ashworth), spasm score (Penn), 10m timed walk seconds (10MTW), mobility aids, other spasticity treatment, ITB dose.

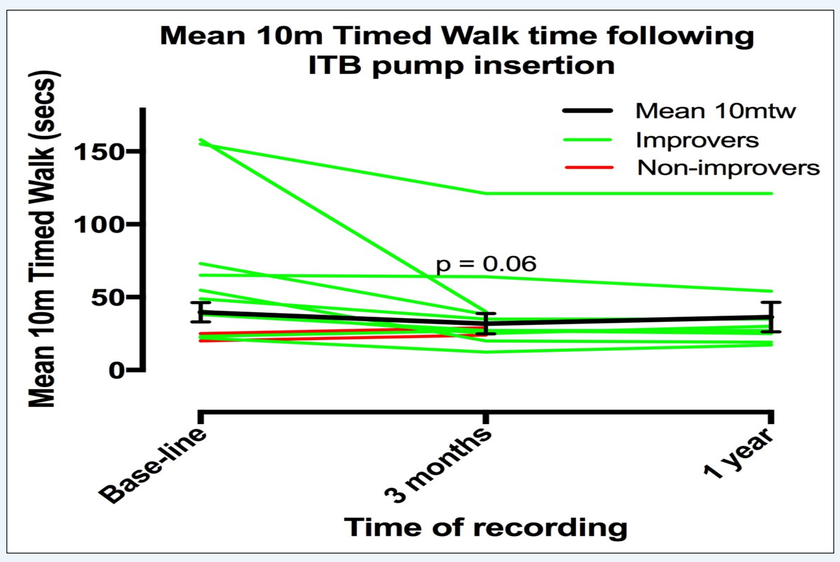
	Proceeded to pump	Did not proceed to pump
	n=	n=
Total patients:	21	10
Female	15	5
Male	6	5
Type of MS:		
Primary Progressive	4	0
Relapsing Remitting	4	0
Secondary Progressive	12	9
Mean EDSS	6.5	6.5
Age at ITB trial (years)	46.43	51.30
Time from diagnosis to ITB trial (years)	9.21	16.7
Time with ITB (years)	2.9 (1-9)	-
Anti-spasticity drugs		
1 agent	0	5
2 agents	13	1
3 or more agents	2	1

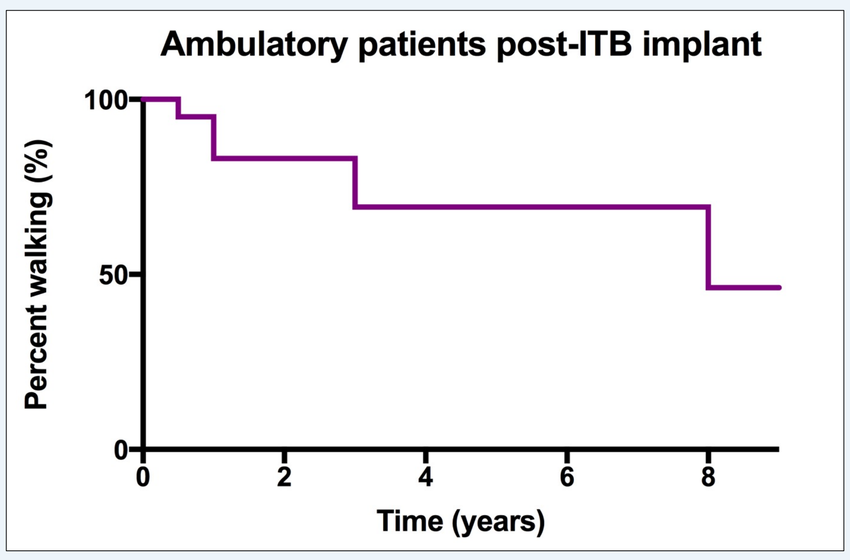
Results

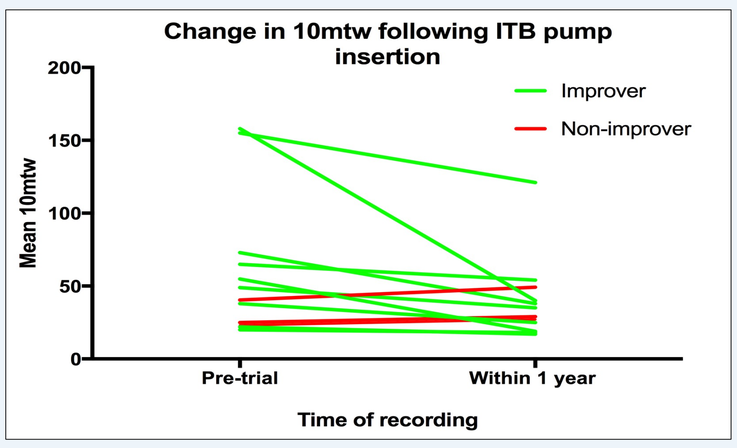
- 31 people were ambulatory at ITB trial.
- Females to males 20:11
- 29 were taking oral anti-spasticity treatment and 9 people on disease modifying drugs.
- 30 people responded to ITB trial with significant reduction in Ashworth (pre 1.34; post 0.72, $p<0.01$) and Penn (pre 3.14; post 1.08; $p<0.01$).
- Mean 10MTW pre-trial was 69.9s [20-186] and post-trial 67.3s [24-211] ($p=0.8$).
- 21 people (68%) proceeded with pump implantation and ten (32%) did not.
- Mean lower limb MRC power grade pre-trial was 3.16 (1.7-5.0) in those who proceeded to pump and 2.54 (1.4-3.7) in those who did not ($p = 0.017$).
- There was no statistically significant difference in 10mTW in those who proceeded up to 1 year as determined by one-way ANOVA ($F(3,24) = 1.7$, $p = 0.19$).
- 16 people (76%) discontinued other spasticity treatments post-pump.
- At review, 17 patients (80%) were ambulatory (mean follow up 3.4 years, range 1-9).
- 3 people (14%) lost their mobility at 1 year.
- Mean time to inability to walk was 2.1 years (0.5-4).
- Two people have remained ambulatory with bilateral aid for 8 and 9 years (EDSS pre pump 6.5 and 7).
- Further longitudinal monitoring is ongoing.
- Subjects reported other benefits including reduced fatigue and improved concentration.

Pre-implant 10m timed walk in seconds (steps)	Trial Mobility (including 10mtw)	Post-implant 10m timed walk in seconds (steps)	1 year 10mtw	Latest 10m timed walk at time of review in seconds (steps)
54.8 (48)	43.8 (34)	20 (22)	19 (21)	39 (28)
Not recorded	107 (62)	72	Not measured	101 (52)
Not recorded (mobilises up to 15m)	Not measured	281 (66)	NA	-
158 (48)	70 (36)	40 (30)	Not measured	-
40.4 (26)	73 (35)	25 (25)	49.15 (30)	31 secs (25ft walk)
Able to take 4 effortful steps (EDSS 7)	Not measured ('less effortful walking')	N/A	NA	-
Effortful walking limited to 8m	Can walk 20m (compared to 8m pre-trial	159	Can only walk 5m	few steps with ++ support - walking worsening over previous few months
73 (88)	78 (55)	**38(32)**	Lost to follow up	Lost to follow up
49 (53)	47 (47)	35 (40)	35 (40)	Not measured - walking 10-20 with frame
65 (41)	84 (42)	64 (30)	54 (34)	54 (34)
22 (13)	23 (13)	12.2 (16)	17.2 (22)	17.2 (22)
38 (36)	109 (49) + 40 (38)	27 (40)	25 (30)	25 (30)
23 (28)	30 (28)	27 (25)	27 (25)	Can only mobilise 2m
Few steps	Difficult walking	Few steps	Not measured	10.84 (20)
Unable to stand due to spasms	Effortful standing	40 (70)	Not measured	0.41ft/sec
Standing - unable to take steps	Easier to stand	129	43.5 (30)	43.5 (30)
Unable to complete 10m. High falls risk	172 (56)	46 (32)	Lost mobility	Lost mobility
155	211	121	121	121
186 (72)	123 (73)	Not measured	Latest data 3mo	NA
25 (27)	29 (30)	29 (30)	Latest data 3mo	29 (30)
20 (24)	24 (29)	18 (24)	Latest data 3mo	18 (24)









Conclusions

- Intrathecal baclofen may increase/unmask lower limb weakness in people with MS.
- The dose of IT baclofen at trial was lower in ambulatory subjects in order to avoid this. The mean dose was 25 mcg (bolus), 50 mcg being a standard trial dose in non-ambulatory subjects.
- Some subjects required a second trial to aid decision making.
- 10 subjects did not proceed with IT pump due to weakness and others proceeded.
- In a small cohort mobility improved after proceeding with ITB and several subjects have had prolonged benefits with preserved mobility despite EDSS 6 / 6.5 at time of implant.
- Longer term follow up is required.
- People with relatively preserved lower limb power and better walking ability at baselines are most likely to benefit on measures of ambulation.
- Those with precarious transfers and ambulation need to be cautioned that ITB may not improve function

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Disclosures

Y Sammaraiee M Yardley, L Keenan, K Buchanan, V Stevenson have nothing to disclose.
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