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Morphine and Memantine Treatment of Long-Standing Complex Regional Pain Syndrome

Dear Editor:

Long-standing complex regional pain syndrome (CRPS) is difficult to treat and an effective oral regimen would be welcome. A recent randomized controlled trial in long-standing upper limb CRPS reported by Gustin et al. demonstrated significant pain relief, with minimal side effects in 10 patients, with an oral combination treatment of morphine and memantine [1]. Pain at rest/on movement was reduced by half or greater in 60%/70% of patients. Fifty percent of participants were male, and 60% had CRPS II. These characteristics are not typical for patients seen at our center. I therefore wished to confirm whether the described treatment would benefit my patients; I conducted a prospective registered audit.[1] Ten consecutive patients with long-standing CRPS diagnosed according to Budapest criteria [2] were treated, who attended over a period of 4 weeks in October/November 2010 and who had not responded to other medical treatments. The patients completed a Brief Pain Inventory [3] both before and 6 weeks into the audit. Variations between this audit and the published (intervention arm) data related to the patients' sex (10% vs 50% male), mean age (40 vs 51 years), the audit patients' higher disease duration (32 vs 15.6 months), CRPS type (type II in 10%/60%), the affected limb (upper in 20%/100%), the higher baseline pain (8.1–24 hours average pain numerical rating scale taken before the first treatment day—vs 67—visual analog scale average of rest and movement pain over 5 days before treatment), the endpoint (6/8 weeks after morphine

Table 1 Demographics, disease characteristics, and treatment outcome in 10 patients with CRPS treated over 6 weeks with 10 mg Morphine TDS and 20 mg BD Memantine using a recently published uptitration protocol [1]

Patient Audit No.	M/F	Age (Years)	Duration (Months)	U/L	CRPS I/II	Pain Pre	Pain Post	BPI Pre	BPI Post	Side Effects/Comments
#1	F	46	25	L	I	9	6	10	10	Good tolerance
#2	F	43	30	L	I	8	6	10	9	Spaced out, tired, dizzy, lethargic*
#3	F	29	30	U	I	8	7	8	7	Good tolerance
#4	F	45	36	U	I	10	9	9	8	Good tolerance
#5	F	51	34	L	I	9	9	8	9.5	Drunk, sick, not with it†
#6	F	27	11	L	II	8	8	9	8.5	Good tolerance Some benefit from morphine
#7	F	35	126	L	I	9	9	9.5	9.5	Good tolerance
#8	F	52	9	L	I	7	7	8.5	10	Very depressed, mind messed up, not able to get words out, can't drive
#9	F	31	182	L	I	6	5	5	5	Not in own body‡
#10	M	42	60	L	I§	7	7	8.5	4.5	Good tolerance
Average	NA	40	32 (Med)	NA	NA	8.1	7.3	8.6	8.1	NA

* This patient reduced her dose to 10 mg BD from end of week 2.
† This patient reduced her dose to 15 mg BD from end of week 2.
‡ This patient dropped her dose to 5 mg BD after 3 days on full dose.
§ CRPS NOS: This patient had several specialist-documented limb signs in the past, but did only have one sign on examination.
M = male/F = female; U/l = upper/lower limb; Pain pre/post = 24 h average pain intensity before/6 weeks into treatment; Med = median; NA = not applicable.
BPI = Brief Pain Inventory interference subscale (the ability to walk was not calculated in patients with upper limb CRPS) [3].
One patient (#10) felt that the BPI pain value did not reflect his dramatic improvement. He subsequently wrote two letters indicating that he obtained excellent and meaningful, ongoing pain relief. Three patients (#1, #3, #10) decided to continue their treatment after the audit had ended.

start—in the study the results of the 6 and 8 weeks were congruent), and participant adherence (33% vs 0% were unable to continue on full dose). At 6 weeks, none of my patients had experienced pain reduction by half or more, and some recorded bothersome side effects (Table 1).

Patient characteristics and/or selection criteria may be responsible for the dramatic differences in efficacy observed between the two studies, but larger trials are required to investigate predictive factors for a beneficial response. These data suggest that patients considered for this treatment should be told that the probability for success is currently uncertain, and that severe cognitive adverse reactions may occur not infrequently.

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Note

1. In the UK, clinical audit is a quality improvement process that seeks to enhance patient care and outcomes through systematic review of care against explicit criteria, and consequent implementation of change. Ethical approval was not sought following advice from local Research Managers and in accordance with NHS National Research Ethics Service guidance (http://www.nres.npsa.nhs.uk/applications/apply/is-your-project-research).

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References

1 Gustin SM, Schwarz A, Birbaumer N, et al. NMDA-receptor antagonist and morphine decrease CRPS-pain and cerebral pain representation. Pain 2010;151: 69–76.

2 Harden RN, Bruehl S, Stanton-Hicks M, Wilson PR. Proposed new diagnostic criteria for complex regional pain syndrome. Pain Med 2007;8:326–31.

3 Tan G, Jensen MP, Thornby JI, Shanti BF. Validation of the Brief Pain Inventory for chronic nonmalignant pain. J Pain 2004;5:133–7.