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Neuromodulators Are Effective for Treatment of Spastic Chest Pain After Heller Myotomy for Achalasia

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TO THE EDITOR: Chest pain (CP) affects 50-70% patients with achalasia and is often refractory to treatment.[1] Previous studies have reported persistent and even worsening of CP in patients undergoing Heller myotomy (HM) and up to one-third of patients with CP after HM have CP.[2] Neuromodulators such as tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) have previously been demonstrated to treat noncardiac CP and esophageal hypersensitivity in subjects without achalasia.[3] We hypothesized treatment with neuromodulators to be effective in treating CP in patients with achalasia after HM. After institutional review board approval, patients with achalasia who were prescribed neuromodulators (TCAs/SSRIs) for CP after HM were included retrospectively from 2016-2021. All patients had esophageal manometry following HM that demonstrated absent contractility. Five patients underwent pre-treatment timed barium esophagogram that did not reveal obstruction. Pain was assessed per Eckardt score ranging from 0-3 where 0 = no pain, 1 = occasional pain, 2 = daily pain, and 3 = pain with each meal.[4] Response to treatment at first follow up after starting neuromodulator was recorded using numeric modified Likert scale (symptom relief score [SRS]) from 1 to 5, where 1 = much worse, 2 = slightly worse, 3 = no change, 4 = slightly better, and 5 = much better.

Six patients (4 females) with a median age of 20.5 (range 16-47) years at time of HM were included (Table). CP was reported at a median time interval of 10.5 months (range 1-41) after HM. SSRIs and TCAs were started in 2 (33.3%) and 4 patients (66.7%), respectively. All 6 patients (100.0%) reported improvement in CP with a median SRS of 5 (much better) with 3 patients (50.0%) having complete resolution after a median follow-up of 282 (range 103-428) days. All included patients opted to continue treatment with neuromodulators and were doing

well at the last follow up. Patient No. 2 (47-year-old female) reported dry mouth with amitriptyline and was switched to escitalopram with maintained response.

CP occurring after HM is a poorly understood phenomenon for which no standardized treatment exists currently. In this retrospective study, neuromodulators were found to be a safe and effective for treatment of CP persisting after HM in patients with achalasia. Complete resolution of pain was seen in 50.0% of patients. Our results suggest modulation of pain sensitivity can be a safe and effective option for treatment of CP after HM.

The pathophysiology of CP after HM remains unknown with recent studies showing no relationship between age and occurrence of CP in achalasia patients. De-novo occurring CP is observed in 8.3% patients undergoing HM.[2] No manometric parameters have been reported to correlate with CP in achalasia arguing against a "mechanical" pathophysiology.[5] All of the patients in our study had an "aperistaltic" esophagus effectively ruling out esophageal spasms as a cause of CP. We postulated the origin of CP to be related to altered pain perception and esophageal hypersensitivity similar to functional CP.[6] Esophageal tissue injury from repetitive ongoing insult in achalasia patients may have led to peripheral and/or central sensitization leading to CP. Similar mechanisms have been reported in functional CP where the hypersensitivity may persist event after removal of the inciting stimulus is removed.[6] Neuromodulators including TCAs and SSRIs are first-line treatment for functional CP by modulating hypersensitivity.[7] This prompted us to treat our achalasia patients with CP after HM. Potential other causes of CP, including acid reflux and CP as a result of myotomy itself, should be considered before initiating treatment with neuromodulators. Future research evaluating neuromodulators in prospective trials coupled with testing for esophageal hypersensitivity are needed to better manage this perplexing condition.

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Table. Characteristics of Patients Receiving Neuromodulator After Heller Myotomy for Achalasia

Serial No.	Type of surgery	Age at surgery (yr)	Gender	Time interval from surgery to onset of chest pain (mo)	Initial pain score (out of 3)	TBE prior to starting medication	Medication started	Dosage (mg)	Time interval between starting medication and first follow-up (day)	Pain score at first follow-up (out of 3)	Likert score	Continuing neuromodulator
1	Heller myotomy with Dor fundoplication	18	F	41	2	1 min: 3.0 x 4.0 cm 5 min: 4.0 x 3.5 cm	Escitalopram	20	428	1	4	Yes
2	Heller myotomy with Dor fundoplication	47	F	60	2	1 min: 11.7 x 1.5 cm 5 min: 0.0 cm	Amitriptyline	20	355	1	4	Switched to Escitalopram due to dry mouth
3	Heller myotomy with Dor fundoplication	16	M	96	3	1 min: 2.9 x 2.7 cm 5 min: 2.9 x 2.5 cm	Nortriptyline	10	107	0	5[a]	Yes
4	Heller myotomy with Dor fundoplication	22	F	43	2	1 min: 7.4 x 1.2 cm 5 min: 0.0 cm.	Fluoxetine	20	181	0	5[a]	Yes
5	Heller myotomy with Dor fundoplication	33	F	1	2	NA	Amitriptyline	20	103	0	5[a]	Yes
6	Heller myotomy with Dor fundoplication	19	M	4	2	1 min: 8.0 x 2.5 cm. 5 min: 5.0 x 2.5 cm	Amitriptyline	20	305	0	5	Yes

[a]Patient 3, 4, and 5 had complete resolution of chest pain.

TBE, timed barium esophagogram; F, female; M, male; NA, not applicable.