

## ACTH IS A RESCUE TREATMENT FOR INTRACTABLE TRIGEMINAL NEURALGIA

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### ABSTRACT

Trigeminal neuralgia (TN) is a common disease impairing quality of life. It's still difficult to control. The predicted site of pain ectopic impulses is local demyelination at root entry attributed to compression by an adjacent blood vessel. Brain cells are target and source of melanocortins. A number of studies validated the neuroprotective and Immunoregulation properties of neuronal melanocortin receptors. This study was attempting treatment of severe TN by ACTH. The study included 26 Trigeminal neuralgia patients meeting the diagnostic criteria of Headache Classification Committee of the International Headache Society in whom pain is not controlled by ordinary TN drugs. Their Numering Rating Scale (NRS-11) score were 7 or more. Each patient counted the number of pain attacks by a Finger-Held Digital counter for 1 day before receiving ACTH (Tetracosactide acetate Depot ampoule 1mg/ml) by a single intramuscular daily injection for 3 consecutive days. Patients were followed up at days 4<sup>th</sup>, 10<sup>th</sup> and 28<sup>th</sup> by counting the number of pain attacks and pain intensity by (NRS-11). For all patients There was a decline of 30 (45.9%), 39 (57.3%) and 46 (67.6%) of mean number of pain attacks /day (npa/d) at 4<sup>th</sup>, 10<sup>th</sup> and 28<sup>th</sup> days respectively. Furthermore number of patients have reduction of more than 50% of pretreatment npa/d were 10 (38.5%), 12 (46.2%) and 15 (57.7%) at 4<sup>th</sup>, 10<sup>th</sup> and 28<sup>th</sup> days consecutively. And 11 (42.3%), 13 (50%) and 14 (53.8%) patients had a drop of (NRS-11) score below 3 at days 4<sup>th</sup>, 10<sup>th</sup> and 28<sup>th</sup> after ACTH injections sequentially. ACTH injections significantly improve pain of severe Trigeminal neuralgia.

**Keywords:** ACTH, treatment, Trigeminal neuralgia.

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### INTRODUCTION

It's stated "Trigeminal Neuralgia is the worst pain in the world,"<sup>1</sup>. Trigeminal neuralgia (TN) was known since ancient times, it's mentioned by Ibn Sina (980–1073) as "pain in the bones of the face" and "spasmodic type laque" for describing "tic douloureux"<sup>2</sup>. TN is a common disease impairing quality of life. Its prevalence is 4 /100,000 in general population and commonly occur in people of age more than 50 years<sup>3</sup>. Although

various treatments were used to alleviate TN, still it's difficult to control. Microvascular decompressions will relief pain in most intractable type, however 27% of them have recurrence<sup>4</sup>. Still the pathophysiology of TN is unclear and almost no cause was detected<sup>5</sup>. Depending on clinical observations TN is commonly attributed to a vascular contact at the root entry zone<sup>6</sup>. Local pressure causes demyelination that leads to abnormal depolarization resulting in ectopic impulses<sup>7</sup>. Frequently, Local demyelination is found at the root entry site of TN<sup>8</sup> creating hyperexcitable neurons<sup>9</sup> which is the main expected site of ectopic pain impulses<sup>10</sup>. Supported by a large number of studies; melanocortin receptors have neuroprotection properties<sup>11</sup>, Immunoregulation<sup>12</sup> and control of inflammation<sup>13</sup>. Brain cells are target and source of melanocortins. Melanocortinergic terminals are found in various hypothalamic regions, spinal cord and dorsal root ganglion<sup>14</sup>. Some studies had verified the immunomodulation<sup>11</sup> and neuroprotective effect of melanocortin receptors directly on neuron<sup>15</sup> or indirectly by its influences on Glial cells<sup>16</sup>. As natural and synthetic melanocortins have neuroprotective action in many preclinical models of neural injury of vascular, inflammatory, and traumatic origin<sup>15</sup>. Furthermore; several investigators reported that melanocortins enhance regeneration of injured peripheral nerve<sup>18, 10</sup>. Adrenocorticotrophic hormone (ACTH) by unexplained mechanism is significantly effective in elimination of Infantile Spasm<sup>20</sup> by reducing neuronal excitability<sup>21</sup>. It's also formerly used in treatment of acute exacerbations of multiple sclerosis, owing to its anti-inflammatory properties<sup>22</sup>. In general TN is hyperexcitability of Trigeminal nerve as a consequence to inflammatory response. So we intend to explore whether melanocortins have efficacy in the management of TN where there is no response to current medical treatment.

## MATERIAL AND METHODS

This study included 26 idiopathic TN patients meeting the diagnostic criteria of Headache Classification Committee of the International Headache Society<sup>23</sup> were received in the neurological outpatient clinic of Al-Diwaniyah teaching hospital. All participants had TN pain not responding to the ordinary TN medications for more than 10 days and score 7 and more according to (NRS-11)<sup>24</sup>. All of them were underwent a high resolution MRI scans T1 and T2 weighted images with contrast. Exclusion criteria include secondary TN, Diabetes mellitus, bronchial asthma, peptic ulcer, Cushing's syndrome, hypertension and patients already on steroids, febrile patient and presence of any source of infection. After consent taken from the patient, with continuation of current medications, each patient counting the number of pain attacks within 24 hours (npa/d) by a Finger-Held Digital Counter before receiving ACTH in form of Tetracosactide acetate Depot ampoule 1mg/ml by a single intramuscular daily injection for 3 successive days. After ACTH injections for each patient the npa/d and (NRS-11) pain score reevaluated at the 4<sup>th</sup>, 10<sup>th</sup> and 28<sup>th</sup> days. A reduction of more than 50% of initial npa/d and decline of (NRS-11) to score 3 and below was regarded significant improvement of pain intensity.

## RESULTS

Totally a 26 patients took part in the study, 16 (66.4%) were female and 8 (33.3%) were male. The patients mean age 64 years (range 49 -78 years) (Table 1).

Table 1: The characteristics of patients

Total patients	Female	Male
Number	16	8
100%	66.4%	33.3%
Age (mean)	63 year	67 year

The mean pan/d for all patients through first month after ACTH injections was 38, 29 and 22 at 4<sup>th</sup>, 10<sup>th</sup> and 28<sup>th</sup> days consecutively compared to 68 pretreatment (Table 2) (Fig. 1). The outcome was decline of mean pan/d 30 (45.9%), 39 (57.3%) and 46 (67.6%) at 4<sup>th</sup>, 10<sup>th</sup> and 28<sup>th</sup> days respectively (Table 2). Individually; the number of patients had significant decline of mean pan/d 10 (38.5%), 12 (46.2%) and 15 (57.7%) at 4<sup>th</sup>, 10<sup>th</sup> and 28<sup>th</sup> days respectively (Table 2) (Fig. 2). Moreover at 28<sup>th</sup> day 5 (19.2%) patients are free of pain (Table 2). Likewise 11 (42.3%), 13 (50%) and 14 (53.8%) patients had significant improvement in (NRS-11) score at days 4<sup>th</sup>, 10<sup>th</sup> and 28<sup>th</sup> after ACTH injections respectively (Table 2) (Fig 3). Consequently, the results shows linear improvement of both mean pan/d and (NRS-11) score (Fig 4).

Table 2: Results of pain score reevaluation

		Before	4 <sup>th</sup> day	10 <sup>th</sup> day	28 <sup>th</sup> day
mean pan/d	Number	68	38	29	22
	%	100%	55.9%	42.6%	32.4%
decline of mean pan/d	Number	68	30	39	46
	%	100%	45.9%	57.3%	67.6%
patients had decline of > 50% mean pan/d	Number	26	10	12	15
	%	100%	38.5%	46.2%	57.7%
patients are free of pain	Number	26	2	3	5
	%	100%	7.7%	11.5%	19.2%
(NRS-11) score < 3	Number	26	11	13	14
	%	100%	42.3%	50%	53.8%

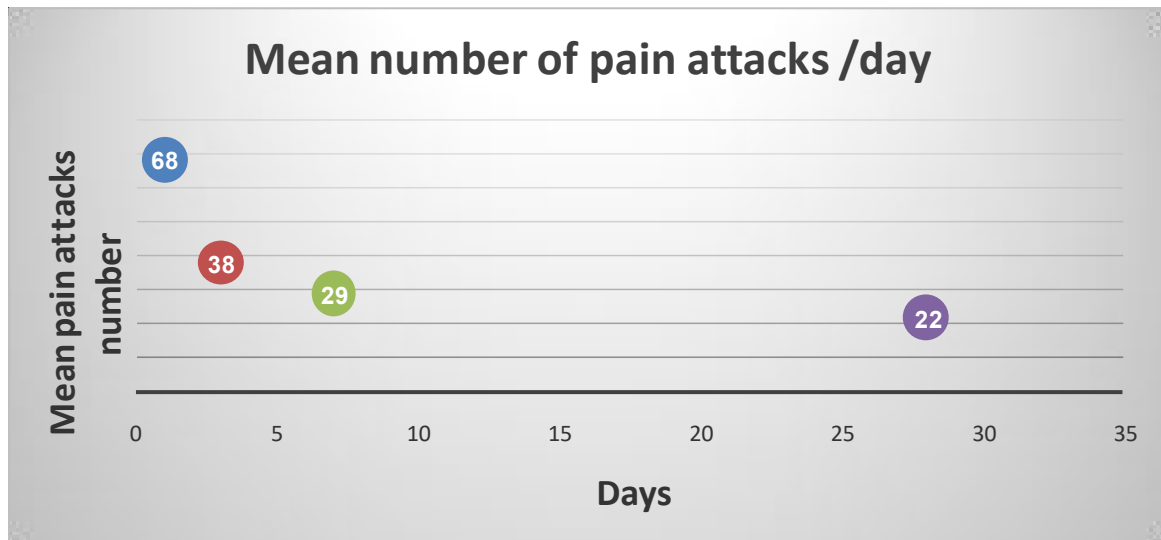


Figure 1: The mean npa/d after ACTH injections

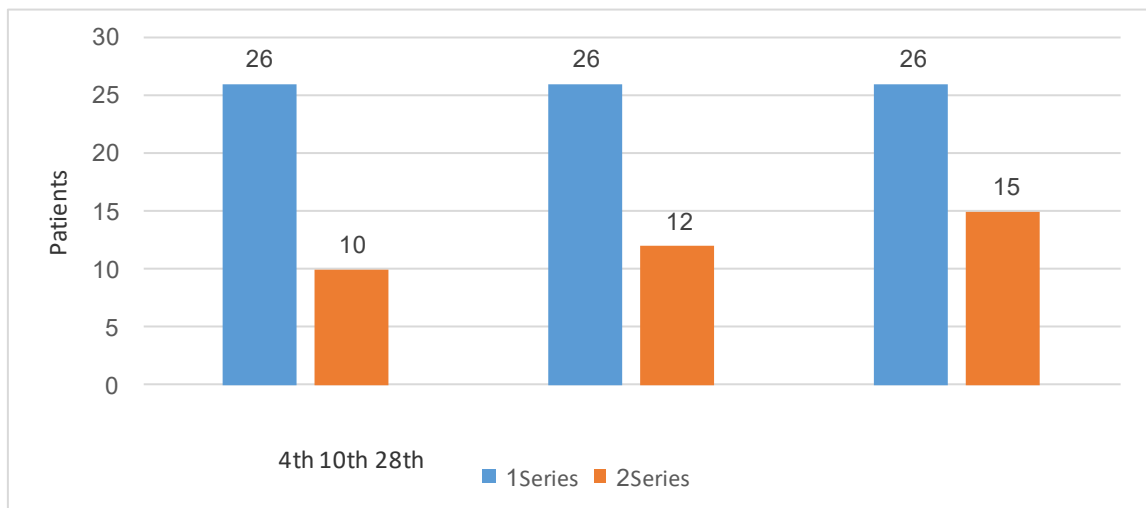


Figure 2: The number of patients had reduction of more than 50% of npa/d

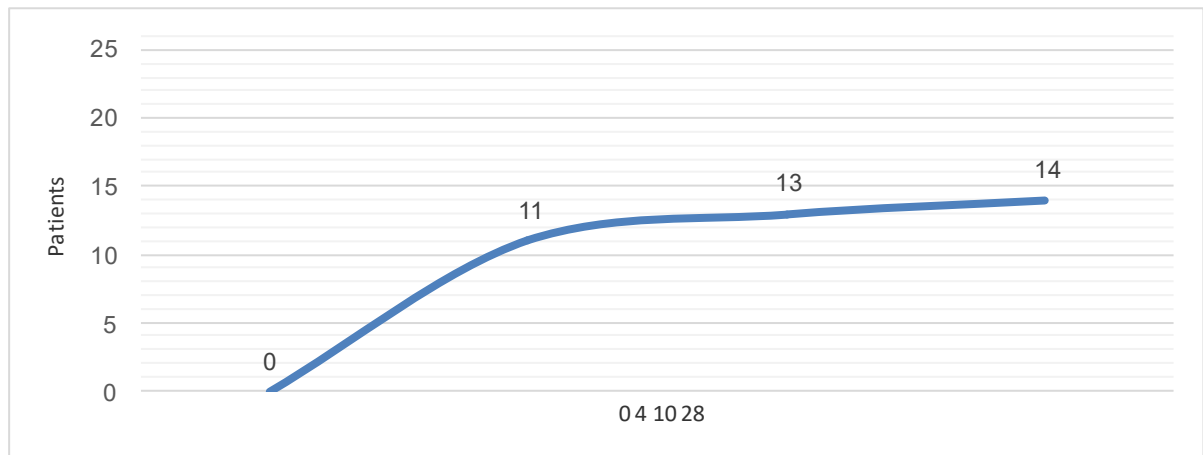


Figure 3: The number of patients had significant improvement in (NRS-11) score after ACTH injection.

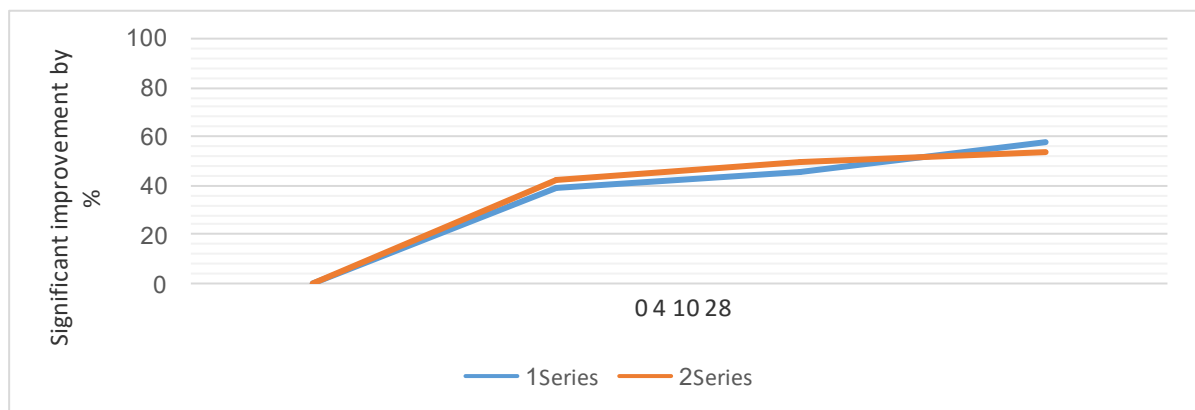


Figure 4: The improvement of both mean npa/d and (NRS-11) score by percentile, Series 1: mean npa/d, Series 2: (NRS-11) score.

## DISCUSSION

ACTH was significantly eliminated 45.9% of mean npa/d at 4<sup>th</sup> day increased to 67.6% at 28<sup>th</sup> day certifying its short onset and long duration of effectiveness. In addition it reduced more than 50% of initial mpan/d in 57.7% of patients at 28<sup>th</sup> day and about 1/3 of them (5/15) were free of pain. A possible explanation is the early local effect of ACTH on trigeminal neuronal excitability and later allowing myelination due to its anti-inflammatory properties.

Furthermore ACTH significantly improved pain severity since 42.3% of patients had an early decline in pain score from sever to mild at 4th day. The effect extended to 28<sup>th</sup> day to include 53.8% of patients. Probably this attributed to direct anti-inflammatory effect on trigeminal nerve permitting its regeneration or modulating central sensory pathways by melanocortin receptors.

## CONCLUSION

ACTH significantly improved pain of severe TN. An option of ACTH may be considered in any case of severe TN.

## RECOMMENDATIONS

In our study ACTH significantly improved TN, studying the ACTH attempt initially for TN is a substantial choice, it could affect later outcome and prognosis.

## ETHICAL CLEARANCE

The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

## CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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