

LETTER TO THE EDITOR

THYROTROPIN-RELEASING HORMONE DECREASES PLASMA
BETA-ENDORPHIN LEVEL IN TRAUMATIC TETRAPLEGICS -
A POSSIBLE THERAPEUTIC AGENT

Sir,

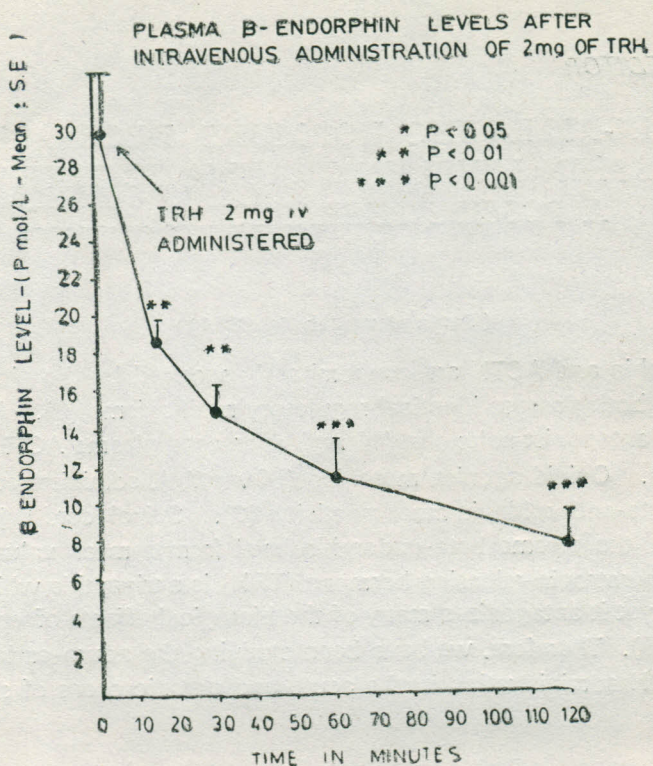
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Beta-endorphin and ACTH are concomitantly secreted by the pituitary in response to acute stress and both possess identical regulatory mechanisms (1). Intravenous administration of opioid antagonist naloxone (10 mg) decreased plasma ACTH levels in schizophrenic patients (2). Opioid agonist, morphine (50 mg/kg), administered intraperitoneally elevated plasma beta-endorphin immunoreactivity (3). Spinal cord injury is associated with an increase in the plasma beta-endorphin level from a mean value of 6 pgm/ml to 71 pgm/ml (4). Thyrotropin-releasing hormone (TRH) is a tripeptide which does not bind to opiate receptors yet it antagonizes many of the biological effects of endorphins without altering analgesia (5). Therefore, we have been studying the neuro-endocrinal and urological aspects of TRH administration in the acute and chronic cases of spinal cord injury (6,7,8,9).

Todate, eight traumatic tetraplegics have participated in this study during spinal shock phase. Five ml of blood was taken at 0900 hr in an ice-chilled tube containing 7.5 mg of EDTA for estimation of basal beta-endorphin level. Two mg of TRH was administered (iv) and blood samples were taken 15, 30, 60 and 120 min thereafter. Plasma beta-endorphin levels were determined with the RIA kit purchased from Immunonuclear Corporation, Stillwater, U.S.A. The minimal detectable amount of beta-endorphin was 3 pmol/l. Statistical significance was determined by paired student's t-test.

No adverse effect was observed to the administration of TRH. The basal beta-endorphin level was 29.53 ± 3.14 pmol/l and it decreased by 11.09 ± 2.32 pmol/l at 15 min. 14.8 ± 3.13 pmol/l at 30 min. 18.33 ± 2.76 pmol/l at 60 min and 21.83 ± 2.58 pmol/l at 120 min after TRH administration (Fig. 1).

The present study shows that TRH decreased plasma beta-endorphin levels following spinal cord injury in humans. TRH functionally antagonizes opiate-induced hypothermia, catalepsy and other behavioural effect (10). TRH, in a dose related way, improved arterial pressure, pulse pressure, heart rate and respiratory rate in experimental models of endotoxic and haemorrhagic shock (11). Survival was also significantly improved after TRH



injection (12). A comparison of TRH, naloxone and dexamethasone treatments in an experimental study where the spinal cord was traumatised at C-7, using the Allen method, revealed TRH-treated cats showed significantly better neurologic recovery than either naloxone- or dexamethasone-treated animals thus indicating that TRH treatment was most effective (13). TRH has already been approved for human use for other purposes, has a high therapeutic index and has been used with minimal side effects in doses upto 20 mg iv (14). In a preliminary study on nine traumatic tetraplegics and one traumatic paraplegic, one mg of TRH was administered (iv) as a bolus 12 hourly for 5 days, baseline neuro-urological assessment was made immediately after arrival to this hospital. Reassessment 4 weeks post-injury showed significant sensory recovery with early return of reflex bladder function (15). Further studies are warranted to correlate the decrease in plasma beta-endorphin levels observed after TRH administration with neuro-urologic recovery.

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