

Glucocorticoid and Mineralocorticoid Insufficiency on Treatment with Tramadol

Mansoor Shaikh¹, Catrin Searell² & Anthony Wilton¹

¹Department of Endocrinology, Ysbyty Gwynedd, Bangor, United Kingdom

²Department of Blood Sciences, Ysbyty Gwynedd, Bangor, United Kingdom



GIG
CYMRU
NHS
WALES

Bwrdd Iechyd Prifysgol
Betsi Cadwaladr
University Health Board

Opioids are known to suppress the hypothalamo-pituitary-adrenal axis. The fourfold increase in the number of opioid prescriptions in the last 20 years has resulted in patients with this side effect and its consequences presenting to specialties other than Endocrinology.

Case History

A 32 year old female presented to the emergency medicine department with recurrent episodes of collapse with hypotension. She had variously taken tramadol 100 mg qds, morphine sulphate 10-20 mg od and codeine phosphate 60 mg qds for pain due to endometriosis. A random cortisol of 110 nmol/L led to endocrine referral and opiate-induced hypoadrenalism was considered and investigated.

Investigations

Results of basal pituitary tests at 09:00h were as follows:

Cortisol	109 nmol/L	(185-624)
ACTH	3.2 ng/L	(7-63)
FT4	12.3 pmol/L	(7.0-17.0)
FT3	3.7 pmol/L	(3.5-6.5)
TSH	1.18 mU/L	(0.35-5.50)
FSH	6.8 IU/L	
LH	12.1 IU/L	
Prolactin	438 mU/L	(71-556)
IGF-1	14.0 nmol/L	(10.0-39.0)

Short synacthen test: (commenced 09:00h, on tramadol 100 mg qds)

Time (min)	Cortisol (nmol/L)	ACTH (ng/L)
0	182	6.0
30	397	-

Urea & electrolytes and pituitary MRI were normal.

The following investigations were conducted after withdrawal of opiates:

Cortisol & ACTH day profile with morphine challenge:

Morphine sulphate 5 mg given 09:00h (morphine half life 1.5-4.5h)

Time	Cortisol (nmol/L)	ACTH (ng/L)
09:00	542	43.5
10:00	405	10.4
11:00	246	4.3
12:00	154	3.0
13:00	467	13.1
14:00	298	5.9
15:00	486	11.8

Cortisol & ACTH day profile with tramadol challenge:

Tramadol 100 mg given 09:00h (tramadol half life 6-7h)

Time	Cortisol (nmol/L)	ACTH (ng/L)
09:00	175	6.1
10:00	140	4.7
11:00	91	2.4
12:00	64	2.0
13:00	66	3.9
14:00	85	6.8
15:00	57	3.0
16:00	42	2.4

Glucagon test: (commenced at 08:30h) off tramadol for 3 weeks

Time (min)	Glucose (mmol/L)	Cortisol (nmol/L)	GH (µg/L)
-30	4.6	425	3.13
0	4.4	344	6.98
90	3.8	186	0.44
120	6.6	140	1.63
150	4.3	156	14.50
180	3.6	304	25.30
210	3.5	279	13.30
240	3.9	227	5.38

Aldosterone <100 pmol/L Renin 0.6 nmol/L/h (supine)
Aldosterone <100 pmol/L Renin 1.4 nmol/L/h (ambulant)

Discussion

The results demonstrate hypothalamo-pituitary-adrenal axis suppression with tramadol and morphine, both of which are Mu opiate receptor agonists. The hypo-reninaemic hypoaldosteronism whilst taking tramadol is a novel finding with its relevance to the presentation being unclear (there is evidence that naloxone increases secretion of renin at rest and during exercise). The patient was advised of the need for hydrocortisone if treated with opiates and did so during a recent labour/delivery during which she received morphine analgesia with no untoward effects.