Pituitary dysfunction following traumatic brain injury

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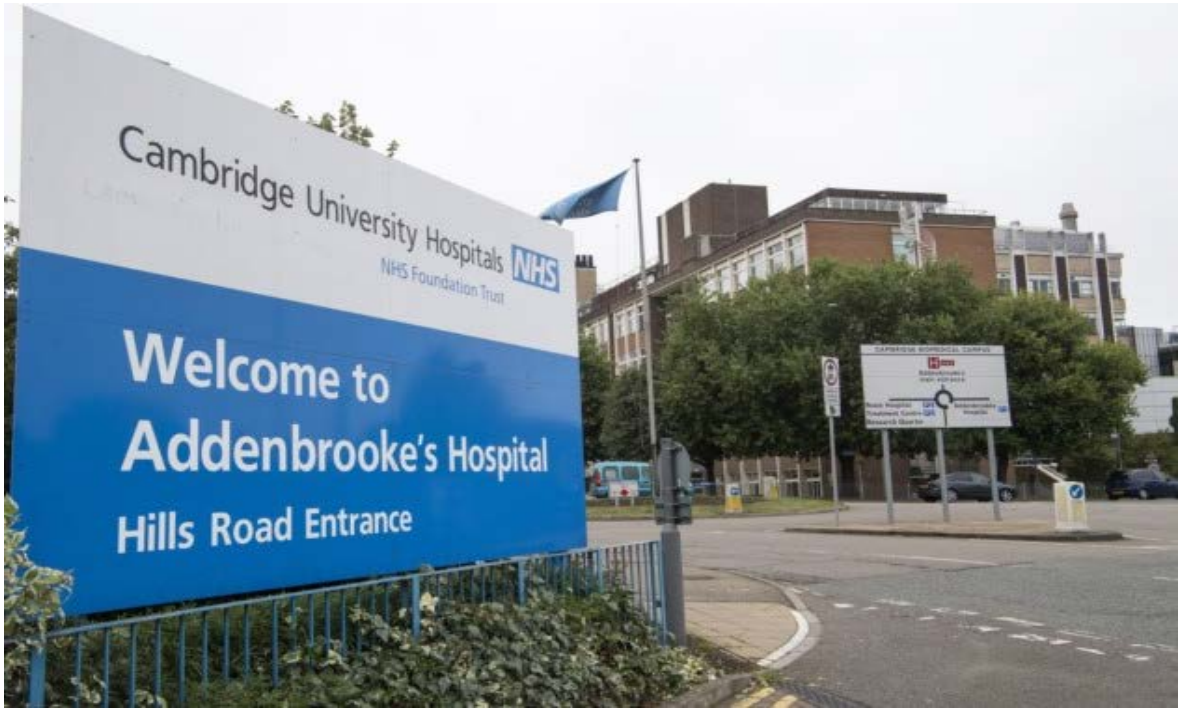
Cambridge study ,S.A. Alavi et al, British journal of neurosurgery, volume 30, 2016.

- Incidence of pituitary dysfunction following traumatic brain injury: A prospective study from a regional neurosurgical centre.2009-2012

- SA ALAVI
- Chinlik Tan
- DK Menon
- H L Simpson
- PJ Hutchinson



Cambridge study ,S.A. Alavi et al.

- TBI patients were studied in 2 cohorts
- Serial cohort: 58 patients.
- Cross sectional late cohort: 47 patients.

Methods

- Subjects for this study were TBI patients admitted to the neurosurgical unit or reviewed in the neurotrauma clinic at Addenbrooke's Hospital, Cambridge, UK; recruited and followed-up between August 2009 and January 2012. Subjects were aged 16–65, and all had abnormal CT head findings.

- Assessments of the pituitary function were performed in the total of 105 patients recruited in two cohorts:

  (i) Serial cohort

  (ii) Cross-sectional late cohort

Serial cohort

• 58 consecutive patients (41 male, 17 female) who were admitted to the neuro critical care unit with TBI.

•Serum cortisol level was performed within 7 days of their admission (acute phase). Patients with low cortisol level were further assessed with short synacthen test during their hospital admission.

Serial cohort

- Thirty-eight of the patients who underwent assessment in the acute phase had their pituitary function re-assessed subsequently at 6 months post-TBI using fT4, TSH, 9am cortisol, LH/FSH and testosterone/oestradiaol E2 levels.

Cross-sectional late cohort

•A convenience sample of 47 post-TBI patients (37 male, 10 female), assessed ≥6 months post-injury in the neurotrauma clinic and judged to be symptomatic constituted this cohort and had the following investigations:

serum urea and electrolytes (U&Es), free T4 (fT4), TSH, 9am serum cortisol, LH/FSH, testosterone and/or oestradiol (E2) levels.

•This group of patients did not have cortisol level checked during their acute phase as either their head injury were occurred before starting our study or they had been managed by other hospitals in our region during their acute phase and later referred to our neuro-trauma clinic for follow-up.

Symptoms

- Poor rehabilitation
- Fatigue
- Low tolerance for stress
- Muscle weakness
- Sensitivity to cold or difficulty staying warm
- Loss of under arm and pubic hair

Men :

- Loss of interest in sexual activity
- Erectile dysfunction
- Decrease in facial or body hair

Women:

- Irregular or no menstrual periods
- Infertility
- Inability to produce milk for breast-feeding

Result: Serial cohort

- We found that pituitary function as observed in the acute phase did not necessarily predict its longer-term status.
- Ten patients with normal cortisol production in the acute phase were found to have developed some form of hypopituitarism after 6 months.
- In addition, out of six patients with low cortisol level in the acute phase, only one patient showed persistent abnormality in cortisol production and two patients recovered their adrenal function, but developed abnormalities in other pituitary axes, with one having low LH and testosterone levels while the other having low TSH and fT4 levels.

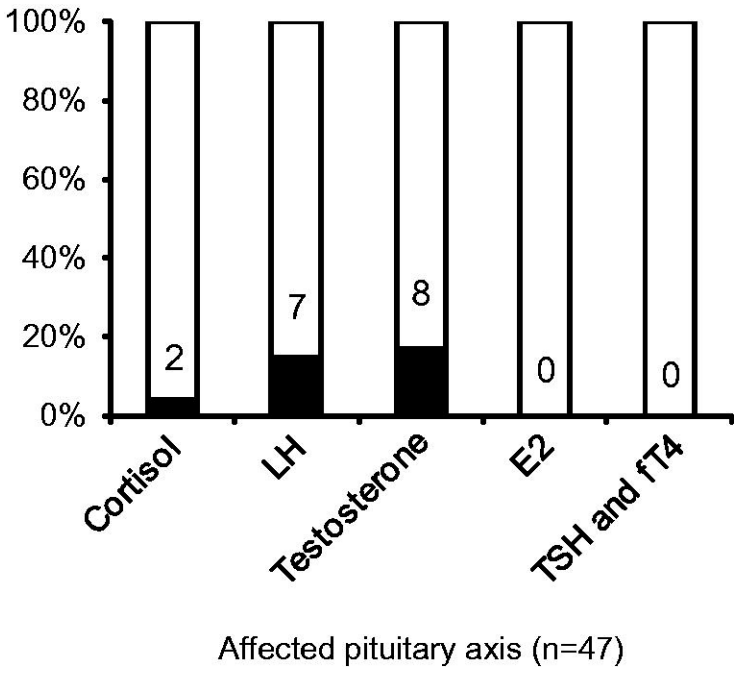
Result: cross-sectional late cohort

- Ten of them (21.3%) had an abnormal result in at least one of the pituitary axes, i.e:

- Four had low LH (<1.5 IU/L) and testosterone (<8 nmol/L) levels, two had low testosterone, two had low LH, one had low cortisol (<200 nmol/L), LH and testosterone levels, one had low cortisol and testosterone levels.

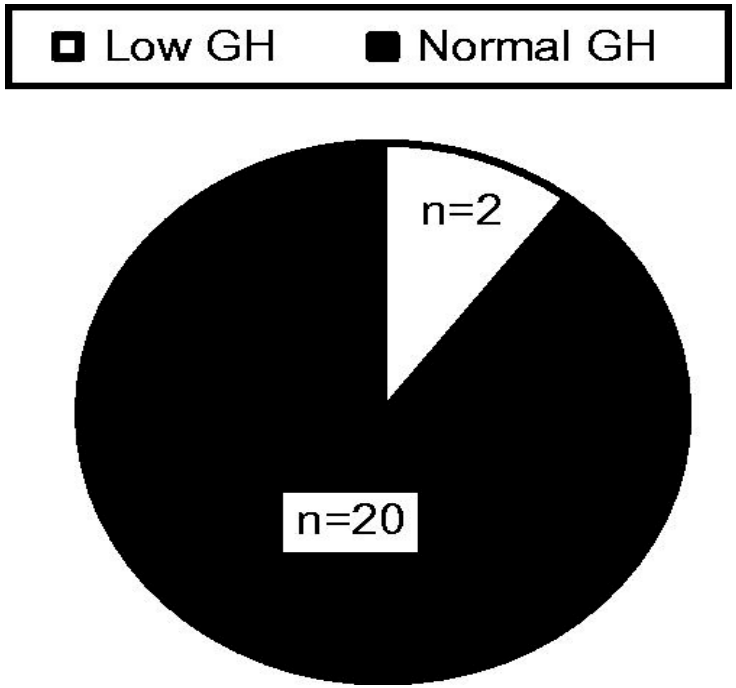
Result: cross-sectional late cohort

- Fig. 1. Hypopituitarism in the cross-sectional late cohort at ≥6 months post-TBI (some patients were deficient in more than one hormone).



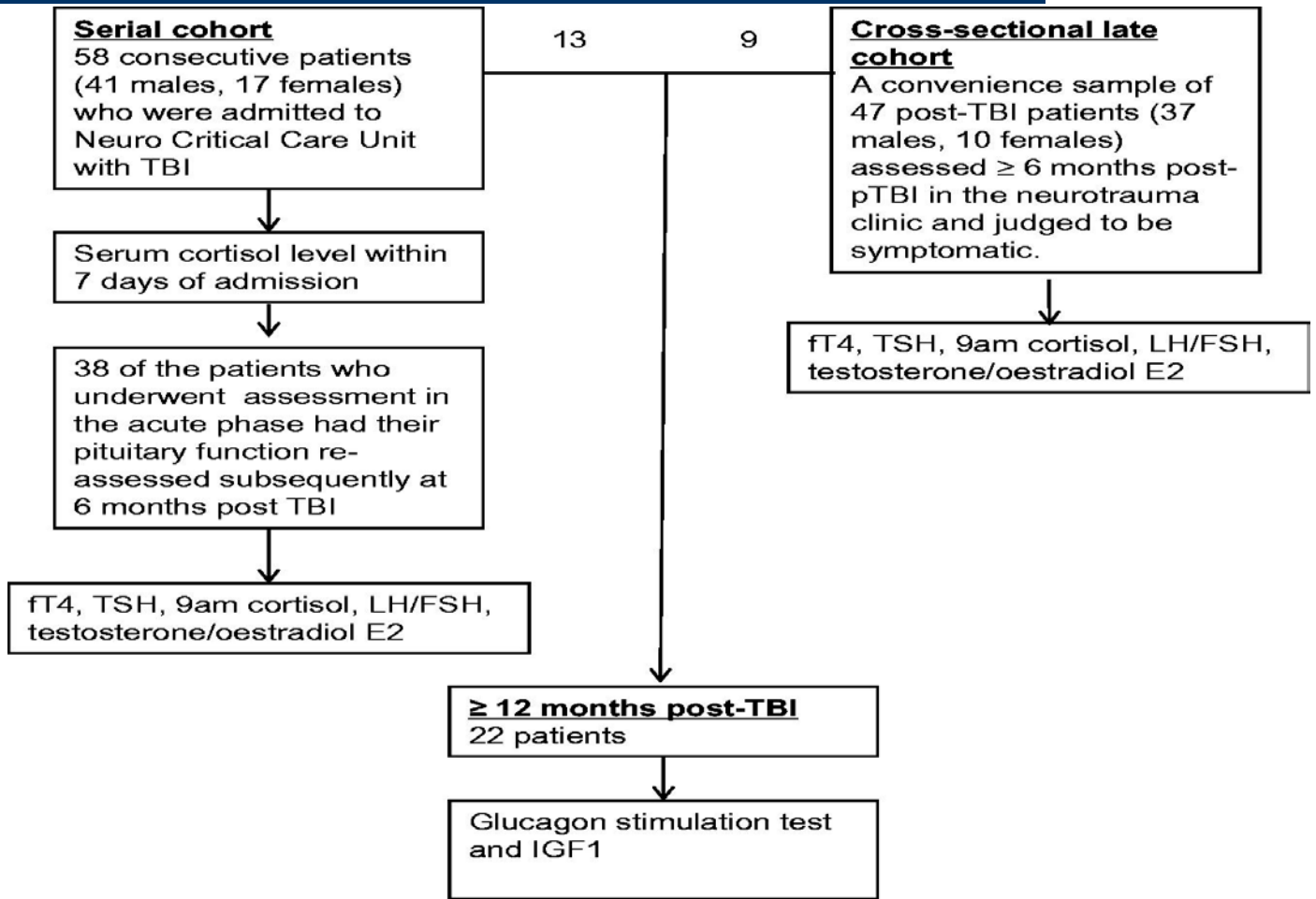
Result: GH assessment

- Fig. 2. Growth hormone (GH) deficiency at ≥12 months post-TBI.



Summary

Chart1. Demonstrating the number of patients recruited in each cohort and their subsequent follow-up.



Conclusion

- This study provides us with evidence that PTHP is a common condition in the Neuro Critical Care Unit (NCCU) and may be a significant cause of morbidity in TBI patients at follow-up.

- This along with data from previous studies suggests that PTHP is an important health issue, and efforts should be taken to ensure timely detection and appropriate treatment of the condition.

- Currently, there appears to be a lack of formal guidance on the investigation or screening for pituitary dysfunction after TBI, as well as for the management of PTHP.

Birmingham study, S.A. Alavi, E.Toman et al, 2013-2015

- SA ALAVI
- E Toman
- A Mason
- R. Mitchell
- A Toogood
- A Belli

Birmingham study, S.A. Alavi, E.Toman et al, 2013-2015

Pituitary dysfunction following traumatic brain injury:

- Incidence,
- Risk factors,
- Quality of life in a prospective study.

Birmingham study, S.A. Alavi, E.Toman et al, 2013-2015

Objectives:

Report the incidence, risk factors and outcome of post-traumatic hypopituitarism (PTHP), a recognised complication of traumatic brain injury (TBI).

Design:

Prospective observational study of TBI patients referred to a dedicated PTHP screening clinic.

Subjects:

163 TBI patients were identified over 2 years between the period from July 2013 to July 2015.

Birmingham study, S.A. Alavi,E.Toman et al, 2013-2015

Methods:

- TSH,fT4,
- IGF-1,
- Prolactin
- Testosterone / Oestrogen
- FSH,LH
- Short Synacthen Test,
- GH

**assessed 4-6 months and at 12 months after injury*

Outcome measures:

- Quality of Life after Brain Injury (QOLIBRI)
- Quality of Life Assessments of GH Deficiency in Adults (QoL-AGHDA)

Birmingham study, S.A. Alavi, E.Toman et al, 2013-2015

Multivariate analysis:

- predictors:
  - GCS
  - Age
  - Gender
  - Extra-cranial trauma
  - Hypotension
  - Hypoxaemia
  - Past medical history
  - Pre-hospital rapid sequence intubation
  - Frontal contusions / Marshall score
  - Vault or skull base fracture
  - Injury severity score (ISS)
  - New injury severity score (NISS)
  - Any neurosurgical procedures

Birmingham study, S.A. Alavi, E Toman et al, 2013-2015

Results:

- The incidence of PTHP was 21.5% (n=35) at first screening.
- The most common abnormalities were raised prolactin (n=8) and GH deficiency (n=7).
- Further changes in pituitary function were seen at 12 months.
- No strong predictors of PTHP were identified.
- Quality of life is significantly worse for patients with post-TBI pituitary dysfunction when using the QoL-AGHDA questionnaire (p-value:0.05) but not the QOLIBRI (p-value:0.49).

Hormone deficiencies

Hormone	Number of abnormal results in the cohort
T4 and TSH	2 (1.2 %)
IGF-1	7 (4.2%)
Prolactin	8 (4.9 %)
Testosterone	4 (2.4%)
FSH	4 (2.4%)
LH	0
Estradiol (E2)	4 (2.4%)
GH	7 (4.2%)
Short Synacthen Test	3 failed (1.8%)

Normal value

TSH	0.3-4.5 mIU/L	
T4	10.0-22.0 pmol/L	
IGF-1	Age in years 16-20 21-30 31-45 >45	nmol/L 25-64 14-48 13-37 8.0-32
Prolactin	♀ non-pregnant ♂ adult	100-500 mIU/L 85-325 mIU/L
Testosterone	Adult ♀ Adult ♂	<1.9 nmol/L 7.0-27.0 nmol/L
Oestrogen	At any stage of menstrual cycle	>50 IU/L
FSH	At any stage of menstrual cycle	1.5-12.4 IU/L
	Adult ♂	> 1.5 IU/L
LH	At any stage of menstrual cycle	1.7-8.6 IU/L
	Adult ♂	> 1.5 IU/L
Short Synacthen test	30 minute cortisol >550	
Growth hormone	Peak growth hormone level more than 3 ug/litre following glucagon stimulation test.	

Summary Information by Outcome Group

Variable	Abnormal (n=35)	Not Abnormal (n=128)	Diff [95% CI]	p-value
Age				
Mean (SD)	38.9 (16.6)	43.0 (19.0)	-4.07 [-10.6, 2.49]	0.22
Gender				
Male (%)	28 (80%)	102 (80%)		1.00
Female (%)	7 (20%)	26 (20%)		
ISS				
Mean (SD)	24.6 (8.14)	23.2 (9.5)	1.39 [-5.07, 7.85]	0.6
NISS				
Mean (SD)	40.1 (10.03)	41.0 (17.3)	-0.85 [-9.18, -7.49]	0.8
Hypoxemia				
Yes (%)	4 (20%)	16 (21%)		1.0
No (%)	16 (80%)	59 (79%)		
Missing	15	53		
Hypotension				
Yes (%)	2 (10%)	6 (8%)		1.0
No (%)	18 (90%)	69 (92%)		
Missing	15	53		
GCS on Scene	(n=29)	(n=101)		
Median (IQR)	13 (3, 15)	13 (6, 15)	0	0.65
GCS on Discharge	(n=34)	(n=122)		
Median (IQR)	15 (15, 15)	15 (15, 15)	0	0.63
RSI				
Yes (%)	12 (39%)	33 (29%)		0.41
No (%)	19 (61%)	81 (71%)		
Missing	4	14		

Variable	Abnormal (n=35)	Not Abnormal (n=128)	Diff [95% CI]	p-value
Marshall Grade				
1 (%)	5 (15%)	14 (12%)		0.15
2 (%)	15 (45%)	62 (51%)		
3 (%)	3 (9%)	5 (4%)		
4 (%)	4 (12%)	4 (3%)		
6 (%)	6 (18%)	36 (30%)		
Missing	2	7		
Frontal Contusion				
Yes (%)	12 (35%)	49 (40%)		0.73
No (%)	22 (65%)	72 (60%)		
Missing	1	7		
Skull Base				
Yes (%)	5 (15%)	33 (27%)		0.20
No (%)	29 (85%)	88 (73%)		
Missing	1	7		
Skull Vault				
Yes (%)	14 (40%)	38 (31%)		0.46
No (%)	21 (60%)	83 (69%)		
Missing	0	7		
Surgery				
Yes (%)	13 (37%)	41 (32%)		0.71
No (%)	22 (63%)	87 (68%)		
Missing	0	0		
AGHDA	(n=29)	(n=113)		
Median (IQR)	17 (9, 23)	15 (6, 19)	2	0.05
QOLIBRI	(n=21)	(n=78)		
Mean (SD)	61.2 (16.9)	64.1 (15.0)	-2.83 (-11.11, 5.46)	0.49

Birmingham study, S.A. Alavi,E.Toman et al, 2013-2015

Conclusion:

- This represents one of the largest studies of PTHP.
- The incidence of this complication was high.
- Poor quality of life associated with pituitary dysfunction.
- Routine post-acute neuroendocrine screening is worthwhile for all TBI patients admitted to neurosurgery (there is no clear way to select patients for screening).

Questions?

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