hyperventilation, transient hypoxia, or lack of sufficient pre-oxygenation prior to RSI. Prospective multi-centre randomised trials are needed to avoid the inherent problems associated with the study designs.

▶ CLINICAL BOTTOM LINE

Prehospital endotracheal intubation is associated with increased mortality in patients with moderate to severe traumatic brain injury

Winchell RJ, Hoyt DB. Endotracheal intubation in the field improves survival in patients with severe head injury. *Archives of Surgery* 1997;**132**:592–597.
Sloane C, Vilke GM, Chan TC, *et al*. Rapid Sequence Intubation in the field versus hospital in trauma patients. *J Emerg Med* 2000:**19**(3):259–64.
Murray JA, Demetriades D, Berne TV, *et al*. Prehospital intubation in patients with severe head injury. *J Trauma Inj Infect Crit Care* 2000;**49**:1065–70.
Eckstein M, Chan L, Schneir A, *et al*. Effect of prehospital advanced life support on outcomes of major trauma patients. *J Trauma Inj Infect Crit Care* 2000;**48**:643–8.
Bochichhio GV, Ilahi O, Joshi M, *et al*. Endotracheal Intubation in the field does not improve outcome in trauma patients who present without an acutely lethal traumatic brain injury. *J Trauma Inj Infect Crit Care* 2003;**54**:307–311.
Davis DP, Hoyt DB, Ochs M, *et al*. The effect of paramedic rapid sequence intubation on outcome in patients with severe traumatic head injury. *J Traum, Inj Infect Crit Care* 2003;**54**:444–53.
Stockinger ZT, McSwain NE Jr. Prehospital Endotracheal intubation for trauma does not improve survival over bag-valve-mask ventilation. *J Trauma, Inj Infect Crit Care* 2004;**56**:531–6.
Wang HE, Peitzman AB, Cassidy LD, *et al*. Out-of-hospital Endotracheal Intubation and outcome after traumatic brain injury. *Ann Emerg Med* 2004;**44**:439–50.
Davis DP, Peay J, Sise MJ, *et al*. The impact of prehospital endotgracheal intubation on outcome in moderate to severe traumatic brain injury. *J Trauma Infect Crit Care* 2005;**58**:933–9.

Headache in paediatric head injury

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doi: 10.1136/emj.2005.031724

Abstract

A short cut review was carried out to establish whether headache was a significant indicator of the severity of head injury in children. 301 papers were found using the reported searches, of which 2 presented the best evidence to answer the clinical question. The author, date, and country of publication, patient group studied, study type, relevant outcomes, results, and study weaknesses of these best papers are tabulated. It is concluded that headache is not an independent risk factor for intracranial injury in children.

Clinical scenario

A 10 year old girl has presented on several occasions since a recent head injury with a persistent headache. Clinical examination has previously been documented as normal. You wonder how significant the headache is with respect to the initial head injury.

Three part question

In [a child with a head injury] does [the presence of headache] predict [intracranial injury]?

Search strategies

Medline 1966- Week 4 August 2005 [exp brain injuries/ or brain injur$.mp. or exp craniocerebral trauma/ or head injur$.mp.] AND [exp headache/ or headache.mp.] AND [BestBETs Paediatric filter] LIMIT to human AND English. Embase 1980–2005 week 37 [craniocerebral trauma.mp. OR exp Head Injury/ OR exp Brain injury/ OR brain injur$.mp] AND [exp headache/ OR headache.mp.] LIMIT to Human, English Language, Abstracts and (infant <to one year> or child <unspecified age> or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>) The Cochrane Library Issue 3 2005 Exp brain injuries [MeSH] OR exp craniocerebral trauma [MeSH] AND exp headache [MeSH] AND exp Child [MeSH]

Search outcome

Altogether 301 papers were found, of which one was a meta-analysis. One further paper postdated the meta-analysis. These two papers are shown in the table.

Comments

The consensus opinion is that the presence of headache does not correlate with the presence of or severity of intracranial injury in children. Several retrospective studies found high levels of association between extradural haemorrhage and initial presentation symptoms including headache. However, these were a highly selected group of patients and small numbers were involved.

▶ CLINICAL BOTTOM LINE

Headache does not appear to be an independent risk factor for intracranial injury in children.

Dunning J, Batchelor J, Stratford-Smith P, *et al*. A meta-analysis of variables that predict significant intracranial injury in minor head trauma. *Arch Dis Child* 2004;**89**:653–59.
Chan HC, Aasim WAW, Abdullah NM, *et al*. Characteristics and clinical predictors of minor head injury in children presenting to two Malaysian accident and emergency departments. *Singapore Med J* 2005;**46**:219–23.

S-100b protein levels as a predictor for long-term disability after head injury

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doi: 10.1136/emj.2005.031732

Abstract

A short cut review was carried out to establish whether levels of S-100b were predictive of long-term disability after head injury. 200 papers were found using the reported searches, of

Table 2

Author, country, date	Patient group	Study type	Outcomes	Key results	Study weaknesses
Dunning J *et al*, 2004, UK	1136 children reported in 4 studies	Meta-analysis	Relative risk of intracranial haemorrhage in children with headache	1.02 (CI 0.62–1.69)	
Chan HC *et al*, 2005, Malaysia	265 children aged 2–18 years admitted to hospital with head injury	Prospective cohort	Odds ratio of intracranial injury	20.8 (CI 3.9–25.2)	Only children admitted to hospital

Table 3

Author, country, date	Patient group	Study type	Outcomes	Key results	Study weaknesses
Waterloo K *et al*, 2005, Norway	7 patients with high S-100b after mild head injury matched with 7 patients with no detectable S-100b	Case control study	Overall cognitive function	No difference	
			Reaction time	Increased in raised S-100b group	
			Attention	Reduced in raised S-100b group	
Rothoerl *et al*, 1998, Germany	30 patients with a severe head injury (GCS<=9) and 11 with minor head injury (GCS 13-15) admitted to a neurosurgical unit	Diagnostic Cohort study (4)	Glasgow Outcome Scale on discharge (Mean day 19 in severe group and mean day 1.3 in minor head injury group)	Patients with GOS 3-5 S-100 level mean 1.2mcg SD 1.8	Non-independent gold standard
	S-100 levels measured mean 2.5 hrs after injury		Detectable level of S-100 (>0.5mcg/l)	Patients with GOS 1-2 (unfavourable) S-100 level mean 4.9mcg/l SD 5.3 P=0.0025	Small, selected cohort of patients
				25 of 27 Elevated S-100 levels were found in the minor head injury group	
Raabe A *et al*, 1999, Germany	82 patients after severe head injury (GCS<=8)	Diagnostic cohort study (2b)	Glasgow outcome score at 6 months	For S-100 level of >2.5mcg/l, unfavourable outcome was predicted with	No confidence intervals presented
	s-100 taken at admission and every 24 hours		Unfavourable outcome defined as severe disability or vegetative state	Sensitivity 44%	Non-consecutive
				Specificity 97%	
Woertgen *et al*, 1999, Germany	44 patients after severe head injury (GCS score <=8)	Diagnostic cohort study (3b)	Glasgow outcome score calculated at mean 11 months after trauma (GOS 1-3 unfavourable)	For S-100 level of >2mcg/l, PCS symptoms predicted with	Tables 2, 3 and 4 are incorrect, with erratum printed in a later edition
	S-100 taken 1-6 hrs after injury			Sensitivity 95%	
				Specificity 70%	
Ingebrigtsen *et al*, 1999, Sweden	50 patients with minor head injury and LOC (GCS 13-15) referred to Neurosurgery dept after CT scan	Diagnostic Cohort study (3b)	Neuropsychological testing at 3 months (for attention, psychomotor speed, trail-making test, memory, digit span) In 36 patients	11/36 patients had S-100 >0.2mcg/l	Very small study with no sample size estimates
	S-100 taken hourly up to 12 hours		MRI and CT scan findings within 48hrs	There were non significant trends to reduced impairment in the S-100 negative group	Non consecutive
				4 of 5 patients with brain contusion had S-100 >0.4mcg/l Sensitivity 80% (p=0.035)	Only 36 of 50 patients followed up at 3 months
Ingebrigsten *et al* 2000 Scandinavia (3 centres Sweden, Denmark, Norway)	182 patients from 3 centres with GCS 13-15 and brief Loss of Consciousness.	Diagnostic Cohort Study (2b)	Rivermead postconcussion symptoms questionnaire score (RPQ)	Patients with a positive S-100 had mean RPQ 6.0 vs 4.0 in S-100 negative group p=0.07	No sensitivities or specificities given for prediction of long term disability
	S-100 taken on admission		Intracranial Pathology on CT scan at <24 hours	Detectable S-100 predicted intracranial pathology with: Sensitivity 90%, Specificity 65%	
Mussack T *et al*, 2000, Germany	80 patients presenting with a history of minor head trauma (GCS 13-15)	Diagnostic study (4)	S-100 in Minor Head Trauma pts	Patients discharged <=6hrs 0.29 +/- 0.11 ng/ml	No gold standard outcome measures
	Also 10pts with severe head injury (GCS<8) S-100 taken at 0h, 6h and 24hrs post admission		Patients with Severe head Injury GCS<8	Patients discharged >= 24hrs 0.70 +/- 0.19 ng/ml	Non consecutive
				Patients subsequently admitted to ICU 5.03 +/- 3.18 ng/ml	Results not clearly presented
	50 patients GCS 13-15 after normal CT scan			5.26 +/- 1.56ng/ml	Non significant findings between groups Low number of patients
Herrmann *et al*, 2001, Germany	69 patients admitted to a neurosurgical unit (mostly GCS >13) S-100 taken at 1, 2 and 3 days	Diagnostic study (3b)	Intracranial pathology on CT scan at 2 weeks and 6 months, or focal neurology	At 2 weeks, S-100 of >0.14mcg/l predicted positive outcome:	Inclusion criteria for patients unclear
				Sensitivity 69%	Only 29 patients followed up to 6 months
				Specificity 90%	
				At 6 month, S-100 of >0.14mcg/l predicted positive outcome: Sensitivity 65%	
				Specificity 89%	
Chatfield DA *et al*, 2002, UK	20 patients with severe head injury (GCS<=8) admitted to neurosurgical unit s-100 on admission	Diagnostic cohort study (4)	Glasgow outcome score at 6 months after trauma (GOS 1-3 unfavourable)	Patients with GOS 1-3 S-100 mean level 2.46 +/-0.32mcg/l	Data not clearly presented
				Patients with GOS 3-5 S-100 mean level 0.6 +/-0.1mcg P<0.05	Small study
					No cut off points or ROC curves calculated
Townend WJ *et al*, 2002, UK	148 adult head injury patients (GCS 4-15) in 4 hospitals. Most had a minor head injury S-100 levels taken within 6 hours of head injury	Diagnostic study (2b)	Extended Glasgow outcome score at 1 month	S-100>0.32mcg/l predicted severe disability (15 patients with GOSE<5):	Wide confidence intervals
				Sensitivity 93% (63%-100%)	Non consecutive
				Specificity 72% (54%- 79%)	Wide definition of head injury (including no LOC)
				NPV 99% (93%-100%)	80% follow up rate
Spinella *et al*, 2003, USA	27 children (<18yrs) with traumatic brain injury	Diagnostic cohort study (3b)	Pediatric Cerebral performance category score (PCPC) assessed at discharge and 6 months	For s-100 level of >2.0mcg/l, unfavourable outcome was predicted with	Very small study
	S-100 taken within 12 hours			Sensitivity 86%	Confidence intervals not given
				Specificity 95%	Non consecutive
Savola O & Hillbom M, 2003, Finland	172 consecutive patients with mild head injury (GCS 13-15)	Diagnostic cohort study (2b)	Post concussional symptoms defined by Rivermead Post-Concussion Symptoms Questionnaire at 2–6 weeks	For s-100 level of >0.50mcg/l, PCS symptoms predicted with	No confidence intervals or sample size calculations
				Sensitivity 27%	
				Specificity 93%	

which 12 presented the best evidence to answer the clinical question. The author, date, and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of these best papers are tabulated. It is concluded that a raised level of S-100b is a marker of poorer long-term outcome after both major and minor head injury.

Clinical Scenario

A 17 year old male presents to the Emergency Department after a road traffic accident. His GCS was 8 on arrival but an immediate CT scan showed no focal abnormality. His GCS returned to 14 after 4 hours. You are talking to his mother who is reassured that he does not need urgent neurosurgery, but she asks whether he will suffer any long term consequences from this injury. You tell her that it is difficult to predict. You have recently heard that S-100 protein measurement is available in your hospital for research purposes. You wonder whether S-100 could help predict his long term prognosis.

Three part question

In [patients with a head injury] do [levels of S-100B protein] predict [long-term disability]?

Search strategy

Medline 1966-Week 4 August 2005 using the OVID interface [(exp S100 Proteins/ OR s100.mp OR s-100.mp) AND (exp Brain Injuries/ OR brain injury.mp OR exp Craniocerebral trauma/ OR head inj$.mp)] Embase 1980-2005 week 37 [exp Protein S 100/ OR s100.mp OR s-100.mp] AND [exp Brain Injury/ OR brain injury.mp. OR craniocerebral trauma.mp. or exp Head Injury/] LIMIT to Human and English Language The Cochrane Library Issue 3 2005 Exp Brain injuries [MeSH] OR exp Craniocerebral trauma [MeSH] AND exp S100 proteins [MeSH]

Search outcome

200 papers were found of which 13 were found to be relevant. Two relevant papers described the same patient population. The remaining 12 papers are shown in the table.

Comments

All studies were under 200 patients in size and most were under 100 patients. The studies find sensitivities from 27%–95% and specificities from 70% to 97%. The reasons for this great variation in findings may in large part be due to the small sample sizes. The specificities seem to perform better than the sensitivities and thus the finding of a high S-100 may indicate that your patient is at high risk of long term disability. The cut-points for a significant S-100 level differ between studies also and are generally much higher when applied to patients after a severe head injury. Most studies agree that S-100 levels must be taken within 6 hours of head injury.

► CLINICAL BOTTOM LINE

A high S-100 level is a marker of poorer long term outcome following minor and major head injury.

Waterloo K, Ingebrigtsen T, Romner B, *et al*. Neuropsychological function in patients with increased serum levels of protein S-100 after minor head injury. *Acta Neurochirug* 1997;**139**:26–32.
Rothoerl RD, Woertgen C, Holzschuh M, *et al*. S-100 serum levels after minor and major head injury. *Journal of Trauma-Injury Infection & Critical Care* 1998;**45**:765–7.
Raabe A, Grolms C, Seifert V. Serum markers of brain damage and outcome prediction in patients after severe head injury. *British Journal of Neurosurgery* 1999;**13**:56–9.
Woertgen C, Rothoerl RD, Metz C, *et al*. Comparison of clinical, radiologic, and serum marker as prognostic factors after severe head injury. *Journal of Trauma-Injury Infection & Critical Care* 1999;**47**:1126–30.
Ingebrigtsen T, Waterloo K, Jacobsen EA, *et al*. Traumatic brain damage in minor head injury: relation of serum S-100 protein measurements to magnetic resonance imaging and neurobehavioral outcome. *Neurosurgery* 1999;**45**:468–75.
Ingebrigtsen T, Romner B, Marup-Jensen S, *et al*. The clinical value of serum S-100 protein measurements in minor head injury: a Scandinavian multicentre study. *Brain Injury* 2000;**14**:1047–55.
Mussack T, Biberthaler P, Wiedemann E, *et al*. S-100b as a screening marker of the severity of minor head trauma (MHT)—a pilot study. *Acta Neurochirurgica—Supplement* 2000;**76**:393–6.
Herrmann M, Curio N, Jost S, *et al*. Release of biochemical markers of damage to neuronal and glial brain tissue is associated with short and long term neuropsychological outcome after traumatic brain injury. *Journal of Neurology, Neurosurgery & Psychiatry* 2001;**70**:95–100.
Chatfield DA, Zemlan FP, Day DJ, *et al*. Discordant temporal patterns of S100beta and cleaved tau protein elevation after head injury: a pilot study. *British Journal of Neurosurgery* 2002;**16**:471–6.
Townend WJ, Guy MJ, Pani MA, *et al*. Head injury outcome prediction in the emergency department: a role for protein S-100B? *Journal of Neurology, Neurosurgery & Psychiatry* 2002;**73**:542–6.
Spinella PC, Dominguez T, Drott HR, *et al*. S-100beta protein-serum levels in healthy children and its association with outcome in pediatric traumatic brain injury. *Critical Care Medicine* 2003;**31**:939–45.
Savola O, Hillbom M. Early predictors of post-concussion symptoms in patients with mild head injury. *European Journal of Neurology* 2003;**10**:175–81.

Aspirin and the risk of intracranial complications following head injury

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doi: 10.1136/emj.2005.031740

Abstract

A short cut review was carried out to establish whether pre-injury aspirin increases the risk of intracranial complications following head injury. 124 papers were found using the reported searches, of which three presented the best evidence to answer the clinical question. The author, date, and country of publication, patient group studied, study type, relevant outcomes, results, and study weaknesses of these best papers are tabulated. It is concluded that aspirin may increase the risk of developing intracranial complications. More research is needed.

Clinical scenario

A 65 year old man on aspirin presents to the Emergency Department having fallen sustaining a minor head injury. You wonder whether he is at higher risk of intracranial bleeding due to aspirin.

Three part question

In [adults with head injury] does [pre-injury aspirin] adversely [affect clinical outcome]?

Search strategies

Medline using the OVID interface 1966- August Week 4 2005 [exp brain injuries/ OR brain injur$.mp. OR exp craniocerebral trauma/ OR head injur$.mp.] AND [exp aspirin/ OR aspirin.mp. OR exp acetylsalicylic acid/ OR antithromb$.mp.] Limit to humans and English Embase 1980–2005 week 37 [craniocerebral trauma.mp. OR exp Head Injury/ OR exp Brain Injury/ OR brain injur$.mp] AND [aspirin.mp. or exp Acetylsalicylic Acid/ OR antithrom$.mp] LIMIT to Human, English Language and (adult <18 to 64 years> or aged <65+ years>) The Cochrane Library Issue 3 2005 Exp Aspirin [MeSH] AND exp brain injuries [MeSH] OR exp craniocerebral trauma [MeSH]