An analysis of symptoms and signs of adrenal insufficiency in children with CAH admitted to hospital in Australia

Georgina Chrisp[1], Ann Maguire[2], Maria Quartararo[1], Henrik Falhammar[3], Bruce King[4], Shihab Hameed[5], Craig Munns[6], David Torpy[7], & R. Louise Rushworth[1].

[1]School of Medicine Sydney, The University of Notre Dame Australia. [2]Endocrine and Diabetes, The Children's Hospital, Westmead. [3]Department of Endocrinology, Metabolism and Diabetes, Karolinska University Hospital; Department of Molecular Medicine and Surgery, Karolinska Institutet; Menzies School of Health Research and Royal Darwin Hospital.[4]The Department of Paediatric Diabetes and Endocrinology, John Hunter Children's Hospital, Newcastle; The School of Medicine and Public Health, University of Newcastle. [5]Endocrine Department, Sydney Children's Hospital, Randwick; School of Women's and Children's Health, University of NSW. [6]Endocrine and Diabetes, The Children's Hospital Westmead; Paediatrics and Child Health, Sydney Medical School, The University of Sydney. [7]Endocrine and Metabolic Unit, Royal Adelaide Hospital and The University of Adelaide.

Correspondence: georgina.chrisp1@my.nd.edu.au

Background

Congenital Adrenal Hyperplasia (CAH) is the most common cause of adrenal insufficiency in childhood and has an estimated incidence of 1/10,000 to 1/20,000 births (1). Adrenal crises (AC) are a life-threatening complication of CAH, occurring at an estimated frequency of 5-6/100 patient years (2,3). AC events are more common in younger patients (4) and can be fatal (5). Signs and symptoms of an AC include hypotension, reduced level of consciousness, abnormal electrolytes, vomiting and abdominal pain. AC prevention involves glucocorticoid (GC) stress dosing during times of physiological stress, administration of parenteral GC when oral doses cannot be taken or absorbed; and prompt attendance for medical treatment. Despite this, episodes of symptomatic AI/AC continue to occur.

Aim

The aim of the study was to determine the spectrum of symptoms and signs of AI in children with diagnosed CAH who attended hospital for an acute illness and to evaluate the use of stress dosing and parenteral hydrocortisone (HC) in these children.

Method

We audited the records of all patients with a diagnosis of CAH who attended a large paediatric hospital for treatment of an acute medical illness between 2000 and 2015. All patients were on GC replacement therapy. 156 admissions were considered eligible but 12 admissions were later excluded due to an unconfirmed CAH diagnosis. Chi squared tests were used to test differences in the distribution of categorical variables. Multivariable logistic regression models were used to identify predictors of hospital admission and the use of IV HC.

Results

There were 144 hospital attendances for children with CAH and 86 (59.7%) of these were in females. Children aged 1-4 years had the highest number of attendances (66 (45.8%)). An AC was diagnosed in 4 (2.8%); IV hydrocortisone was administered in 53 (36.8%); and 92 (63.9%) attendances resulted in a hospital admission. In 83 (57.6%) episodes of treatment there was a history of prodromal illness; 73 (50.7%) had vomited and 31 (21.5%) had diarrhoea. 79 (54.9%) children had been given GC stress doses; and 14 (9.7%) had been given IM HC. Three children were admitted to ICU, one child had an encephalopathy but no patients died.

Stress dosing varied by age group (p<0.001), being most common in children aged 1-4 years (48, 72.7%) (figure 1). More patients who had used stress doses (36, 46.8%) were given IV HC compared with those who had not taken stress doses (16 (24.6%)) (p<0.01) but a greater proportion of those who had not taken stress doses were admitted compared with those who had taken stress doses (73.8% cf 55.7%, p<0.05). Among those who had vomited, 55 patients (75.3%) were stress dosed compared with 18 (24.7%) who were not (p<0.001) (figure 2).

Logistic regression demonstrated that vomiting was the only factor that was significantly associated with the administration of IV HC, with an odds ratio of 7.4 (3.3,16.3). Parenteral administration of HC was a significant predictor of hospital admission with IV HC having an OR of 8.4 (3.2,22.0)) and IM HC having an OR of 6.2 (1.4,27.5). By comparison oral HC stress dosing was associated with a lower likelihood of admission (OR 0.2 (0.07,0.44)).

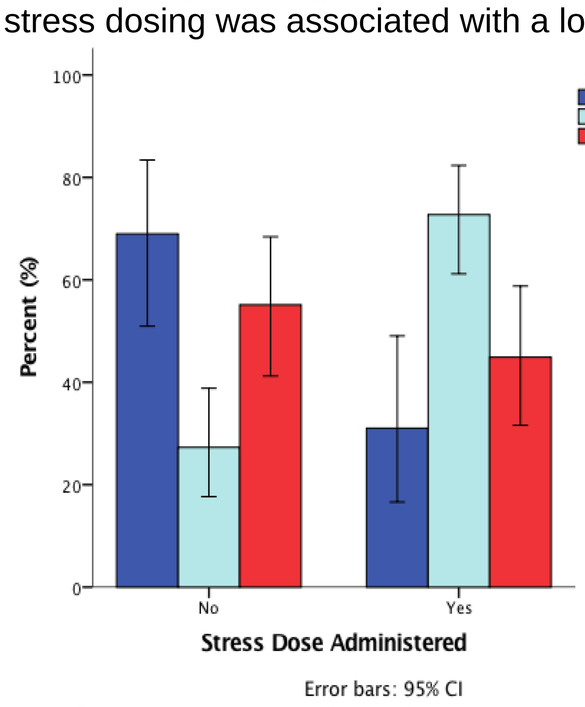

Figure 1: Stress dose by age group

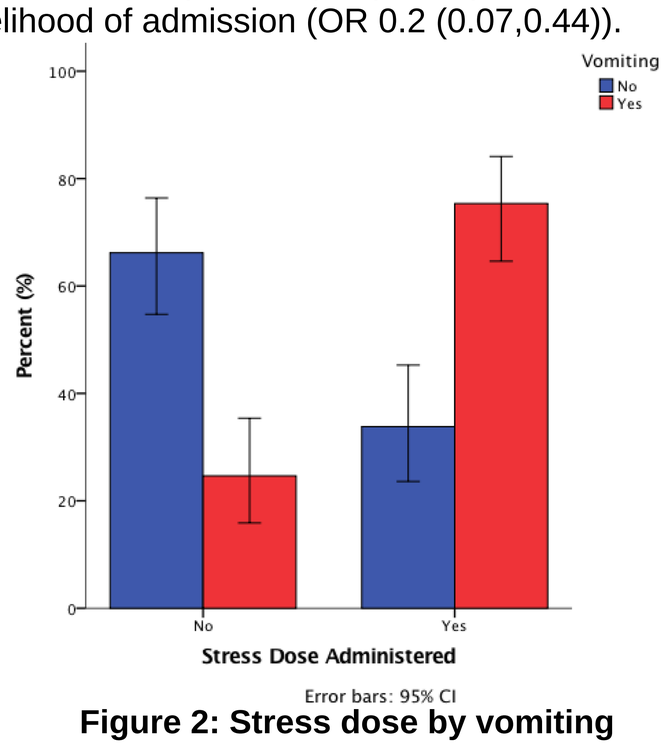

Figure 2: Stress dose by vomiting

Table 1:Demographic characteristics, frequencies of signs and symptoms of AI and treatments by admission status

Category	Outpatient (n=52) (n %)	Inpatient (n=92) (n %)
Age		
- <12 months (n=29)	11 (37.9)	18 (62.1)
- 1-4 years (n=66)	28 (42.4)	38 (57.6)
- 5+ years (n=49)	13 (26.5)	36 (73.5)
Males	22 (37.9)	36 (62.1)
Prodromal Illness	34 (41.0)	49 (59.0)
Vomiting	24 (32.9)	49 (67.1)
Diarrhoea	15 (48.4)	16 (51.6)
Fever	17 (32.1)	36 (67.9)
Infection	23 (41.1)	33 (58.9)
Stress Dose*	35 (44.3)	44 (55.7)
IM Injection	3 (21.4)	11 (78.6)
IV Hydrocortisone**	9 (17.0)	44 (83.0)
Seizure	1 (11.1)	8 (88.9)
Hyponatraemia (n=96)	4 (23.5)	13 (76.5)
Hyperkalaemia* (n=88)	0 (0.0)	7 (100.0)
Hypoglycaemia (n=76)	2 (22.2)	7 (77.8)
Hypotension/ Capillary Refill >3s	0 (0.0)	6 (100.0)
Lethargy	15 (34.1)	29 (65.9)
Reduced Consciousness	3 (16.7)	15 (83.3)
Diagnosed Adrenal Crisis	0 (0.0)	4 (100.0)

*p=<0.05
**p=<0.01

Conclusion

Admission to hospital with problems indicating acute AI is common in children with treated CAH but a diagnosis of an AC is rare in this group.

References

1. Speiser PW, Azziz R, Baskin LS, Ghizzoni L, Hensle TW, Merke DP, Meyer-Bahlburg HF, Miller WL, Montori VM, Oberfield SE, Ritzen M, White PC. Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2010;95(9):4133-60
2. Reisch N., Willige M., Kohn D., et al. Frequency and causes of adrenal crises over lifetime in patients with 21-hydroxylase deficiency. Eur J End. 2012;167(1):35–42.
3. Odenwald B, Nennstiel-Ratzel U, Dörr HG, Schmidt H, Wildner M, Bonfig W. Children with classic congenital adrenal hyperplasia experience salt loss and hypoglycemia: evaluation of adrenal crises during the first 6 years of life. Eur J Endocrinol. 2016;174(2):177-86.
4. Rushworth RL, Falhammar H, Munns CF, Maguire AM, Torpy DJ Hospital Admission Patterns in Children with CAH: Admission Rates and Adrenal Crises Decline with Age. Int J Endocrinol. 2016:5748264. doi: 10.1155/2016/5748264.
5. Swerdlow A. J., Higgins C. D., Brook C. G. D., et al. Mortality in patients with congenital adrenal hyperplasia: a cohort study. Journal of Pediatrics. 1998;133(4):516–520.

55ESPE 12--LBP
Late Breaking
Georgina Chrisp
DOI: 10.3252/pso.eu.55ESPE.2016
Poster presented at: ESPE 2016 PARIS
PosterSessionOnline.com