Glucocorticosteroids for Refractory Migraine in the ED

Specific Care Question:

In the pediatric patient diagnosed with a refractory migraine, is glucocorticosteriods an effective treatment for the prevention of migraine relapse (return to ED or provider for relapse of the same migraine within 24-72 hours)?

Question Originator:

Migraine Therapy in the ED CPG Team

Plain Language Summary from The Office of Evidence Based Practice:

Based on very low quality evidence, the Migraine in the ED CPG Team makes a conditional recommendation against the use of glucocorticosteriods for either the treatment of acute migraine headache, or the prevention of migraine relapse. Huang et al. (2013) conducted a sound systematic review with meta-analysis on eight RCTs that evaluated this question (See Table 1). For the outcome prevention of relapse of migraine headache, treatment with dexamethasone had the absolute effect of preventing relapse in 11 of 100 subjects (range 5-15 fewer). It did not have a significant treatment effect on the outcome total headache resolution (4 more subjects of 100 subjects had total headache resolution after being treated with dexamethasone, but the range is form 2 fewer to 12 more total headache resolutions per 100 subjects) The only adverse event that was significantly different between treatment groups was dizziness. It occurred more frequently in the group treated with dexamethasone. Dexamethasone had the absolute effect of causing dizziness in 3 of 100 subjects (range 0-12 more). Although the results of the meta-analysis are promising, the characteristics of patients who would benefit from glucocorticosteriods are not clear. Long-term effects of chronic glucocorticosteriods use were not evaluated, nor were the appropriate doses of glucocorticosteriods determined.

The evidence is graded as very low quality evidence due to different doses of dexamethasone (inconsistency) all of the studies were performed in adults (indirectness), and finally in the combined studies there are small number of events, (imprecision). The results of a case series reported by (Legault, Eisman, and Shevell (2011) did not find a difference in "bounce" backs in children treated with steroids, versus those who were not. Larger, prospective studies are needed to clarify the migraine recurrence and treatments that are efficacious to prevent migraine headache and recurrence.

Literature read and analyzed by:

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Search Strategy and Results:

No.	**Query**	**Results**
#18	#7 AND [embase]/lim NOT [medline]/lim AND 'antihistaminic agent'/de	**2**

15

#17
#7 AND [embase]/lim NOT [medline]/lim AND 'steroid'/de

966

#16
#7 AND [embase]/lim NOT [medline]/lim

7

#15
#7 AND ('drug therapy':lnk OR 'prevention':lnk OR 'therapy':lnk) AND 'triptan derivative'/de AND [embase]/lim NOT [medline]/lim

12

#14
#7 AND ('drug therapy':lnk OR 'prevention':lnk OR 'therapy':lnk) AND 'valproic acid'/de AND [embase]/lim NOT [medline]/lim

72

#13
#7 AND ('drug therapy':lnk OR 'prevention':lnk OR 'therapy':lnk) AND 'valproic acid'/de

37

#12
#7 AND ('drug therapy':lnk OR 'prevention':lnk OR 'therapy':lnk) AND 'triptan derivative'/de

23

#11
#7 AND ('controlled study'/de OR 'major clinical study'/de) AND ('drug therapy':lnk OR 'prevention':lnk OR 'therapy':lnk) AND 'triptan derivative'/de

Studies included in this review:
Huang et al., 2013
Legault et al., 2011

Excluded Studies and Reason for Exclusion:

Study	Reason for exclusion
Singh, Alter, & Zaia, 2008	Huang MA includes more recent studies
Soleimanpour et al., 2012	Does not answer the question

Method Used for Appraisal and Synthesis:
The Cochrane Collaborative computer program, Review Manager (RevMan 5.3.5) (Higgins & Green, 2011), was used to recreate the meta-analysis reported in Huang 2013. GradePro was used to assess the methodological quality of the meta-analysis.

Updated March 7 2016

Tables:

Table 1. GRADE Summary of Huang, 2013

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirect-ness**	**Imprecision**	**Other considerations**	**Glucocorticosteroids**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Migraine recurrence (follow-up 24-72 hours)												
8	randomized trials	serious	no serious inconsistency	serious[1]	serious	none	128/469 (27.3%)	166/436 (38.1%)	OR 0.6 (0.45 to 0.79)	111 fewer per 1000 (from 54 fewer to 164 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
Adverse events- Dizziness (follow-up 24-48 hours)												
4	randomized trials	no serious risk of bias	serious[2]	serious[1]	serious[3]	none	15/246 (6.1%)	4/226 (1.8%)	OR 0.35 (0.12 to 0.96)	11 fewer per 1000 (from 1 fewer to 16 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
Totally resolved migraine headache (follow-up median 48-72 hours)												
6	randomized trials	no serious	serious[2]	serious[1]	serious	none	160/368 (43.5%)	131/340 (38.5%)	OR 0.82 (0.6 to 1.12)	46 fewer per 1000 (from 112	⨁◯◯◯ VERY LOW	CRITICAL

		risk of bias								fewer to 27 more)		

[1] Although heterogeneity was assessed at 0%, there were different doses of dexamethasone (10, 15, and 24 milligrams); route for the medication varied among studies (IV, IM, or oral) and two of the eight studies described the "standard" therapy while six did not.

[2] All studies were done in adults

[3] Small sample sizes with small number of events

Table 2. Risk of Adverse Events when treating with dexamethasone that did not reach significance

Adverse events that were not different	Number of reporting studies	Risk ratio, fixed effects [95% Confidence Interval]
Restlessness	2	1.46 [0.74, 2.90]
Drowsiness	3	0.75 [0.46, 1.23]
Nausea or vomiting	5	0.76 [0.46, 1.48]
Tingling, numbness, or swelling	5	1.56 [0.57, 4.26]
Mood change	2	0.80 [1.18, 3.52]
Other adverse events	6	0.71 [0.41, 1.21]

Note: Table is from Huang et al. (2013)

Characteristics of included studies (from Huang 2013):

Figures:

Study or Subgroup	Glucocorticosteroids Events	Total	Placebo Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Innes 1999	9	49	22	49	14.5%	0.28 [0.11, 0.69]	1999
Jones 2003	4	34	7	36	4.9%	0.55 [0.15, 2.09]	2003
Fiesseler 2006	19	44	20	41	9.5%	0.80 [0.34, 1.88]	2006
Friedman 2007	35	106	44	99	24.7%	0.62 [0.35, 1.09]	2007
Donaldson 2008	17	57	19	42	12.4%	0.51 [0.22, 1.18]	2008
Kelly 2008	10	31	8	32	4.3%	1.43 [0.48, 4.29]	2008
Rowe 2008	14	57	20	55	12.4%	0.57 [0.25, 1.29]	2008
Fiesseler 2011	20	91	26	82	17.3%	0.61 [0.31, 1.20]	2011
Total (95% CI)		**469**		**436**	**100.0%**	**0.60 [0.45, 0.79]**	
Total events	128		166				

Heterogeneity: Chi² = 5.75, df = 7 (P = 0.57); I² = 0%

Test for overall effect: Z = 3.57 (P = 0.0004)

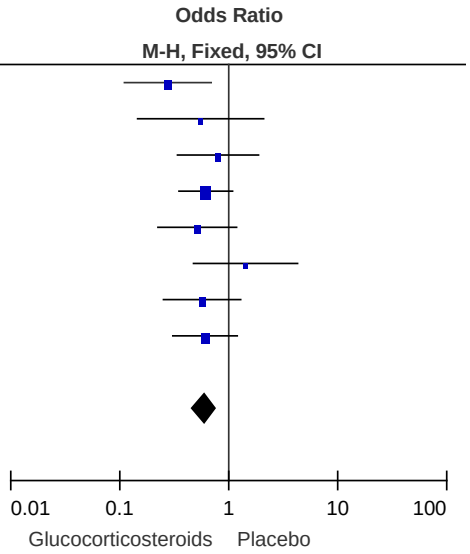

Figure 1. Comparison: Glucocorticosteroids versus. Placebo, Outcome: Migraine recurrence

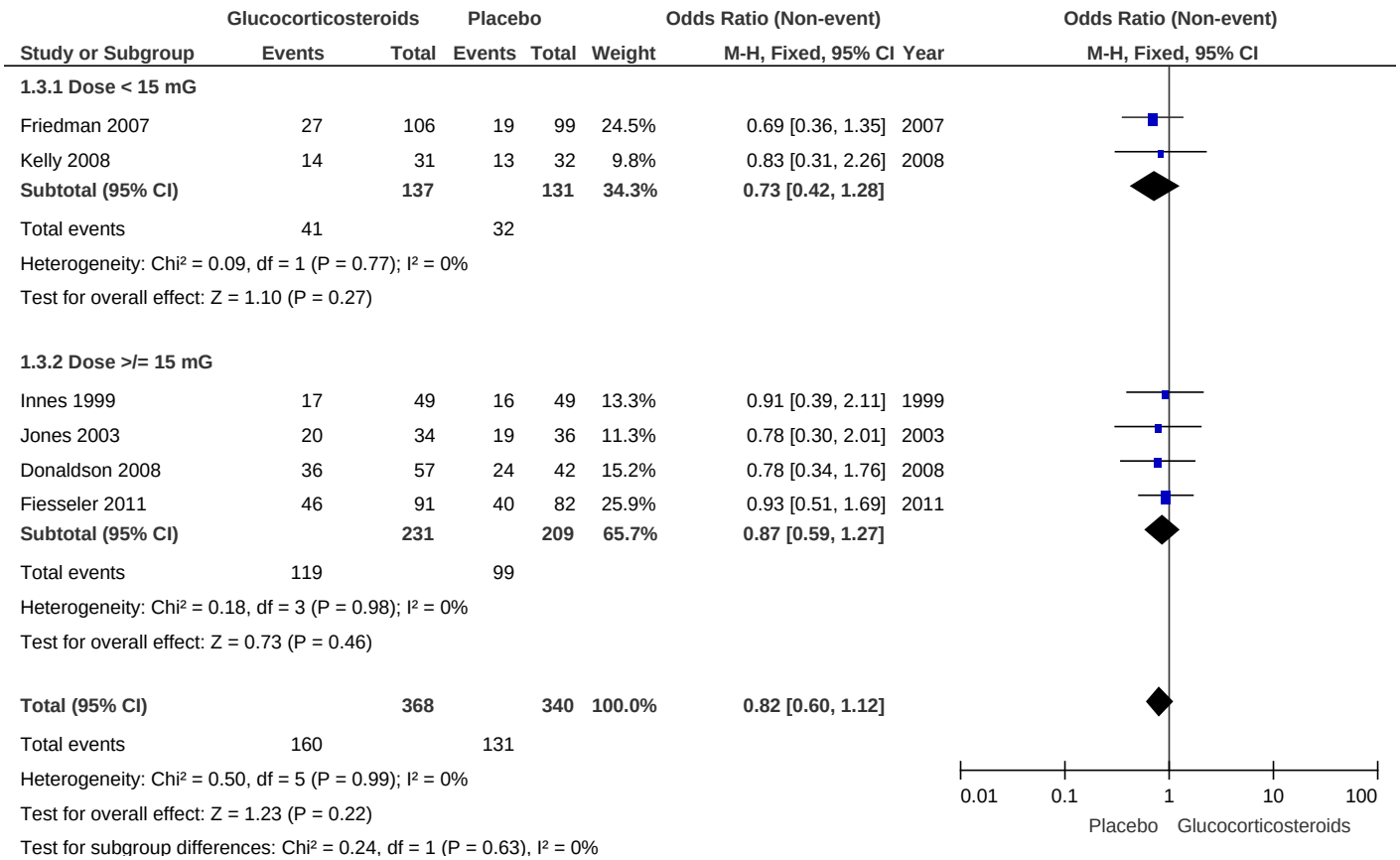

Figure 2. Comparison: Glucocorticosteroids versus Placebo, Outcome: Totally resolved migraine

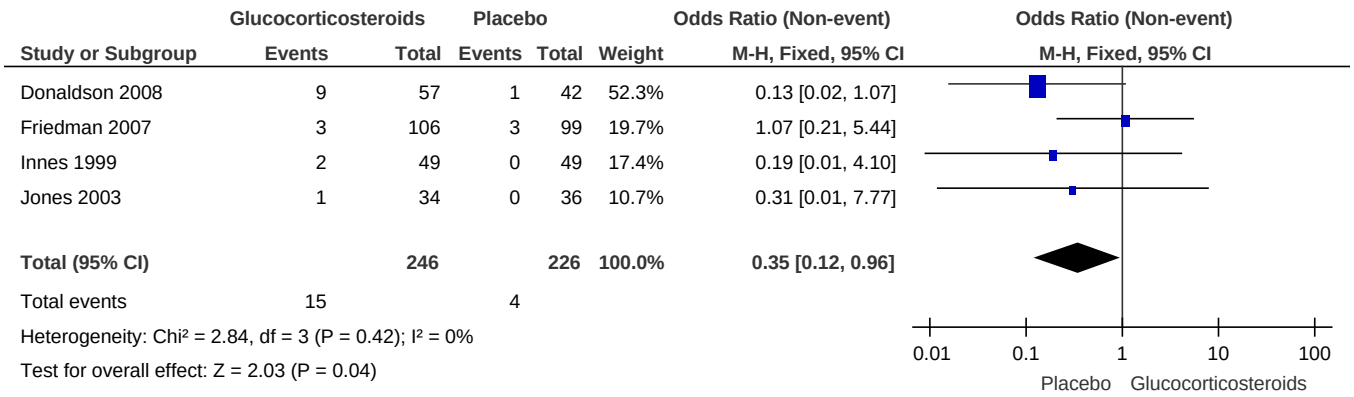

Figure 3. Comparison: Glucocorticosteroids versus placebo, Outcome: Adverse event (dizziness)