Supplementary Online Content

Chang AK, Bijur PE, Esses D, Barnaby DP, Baer J. Effect of a single dose of oral opioid and nonopioid analgesics on acute extremity pain in the emergency department: a randomized clinical trial. *JAMA*. doi:10.1001/jama.2017.16190

Imputation process

eTable 1. Numerical Rating Scale (NRS) Pain Scores and Decline in Pain Score by Treatment Groups with Imputation of NRS scores for Patients Who Received Rescue Analgesia

eTable 2. Between-Group Difference in Mean Change in Numerical Rating Scale (NRS) Pain Scores with Imputation of NRS scores for Patients Who Received Rescue Analgesia

eTable 3. Post hoc Analysis of Subset of Patients with Severe Pain (NRS = 10 or Documented Fracture)

This supplementary material has been provided by the authors to give readers additional information about their work.

Imputation process

Missing data for the NRS pain score at arrival, 1 hour, and 2 hour was imputed using the chained equations approach which is based on conditional density of a variable given other variables. In this method the imputed values are generated from a series of univariate models, in which a single variable is imputed based on a group of variables. Statistical software STATA's user-written program *ice* (Imputation by Chained Equations) was used. The ice imputations do not require multivariate joint distribution assumption and imputes missing values in by using switching regression, an iterative multivariable regression technique. This method estimates a series of univariate models and can accommodate larger imputation models than the multivariate normal approach and may even have lower sample size requirements that the multivariate normal approach. Imputed data for 2-hour pain score was bound within the interval of 0 and 10 and imputation model for interval data included NRS pains scores at other time points, drug group, emergency department procedure, interventions, age and gender. Five imputations were done and the imputed data sets were analyzed using STATA's *mi estimate* command that adjusts coefficients and standard errors for the variability between imputations according to the combination rules by Rubin (1987). The change in pain score at 2 hours from baseline was then compared for the four drug groups using pairwise comparisons and the respective Bonferroni corrected 95% confidence intervals (or 99.2% CI).

eTable 1. Numerical Rating Scale (NRS) Pain Scores and Decline in Pain Score by Treatment Groups with Imputation of NRS scores for Patients Who Received Rescue Analgesia

	NRS Pain Score, Mean (95% CI)[a]				
	Ibuprofen and Acetaminophen[b]	Oxycodone and Acetaminophen[c]	Hydrocodone and Acetaminophen[d]	Codeine and Acetaminophen[e]	*P* Value[f]
No. of subjects	101[g]	104[h]	103[i]	103[j]	
Primary end point: decline in score to 2 h	4.2 (3.7, 4.7)	4.3 (3.8, 4.7)	3.6 (3.0, 4.1)	3.6 (3.0, 4.1)	0.07
Baseline score	8.9 (8.6 ,9.1)	8.7 (8.4, 8.9)	8.6 (8.4, 8.9)	8.6 (8.3, 8.8)	0.47
Score at 1 h	5.9 (5.5, 6.4)	5.5 (5.1, 6.0)	6.2 (5.8, 6.7)	5.8 (5.4, 6.3)	0.25
Score at 2 h	4.6 (4.1, 5.1)	4.4 (3.9, 4.9)	5.1 (4.6, 5.6)	5.0 (4.4, 5.5)	0.22
Decline in score to 1 h	2.9 (2.5, 3.4)	3.1 (2.7, 3.6)	2.4 (2.0, 2.9)	2.7 (2.3, 3.2)	0.13

[a] Pain intensity was assessed using an 11-point NRS in which a score of 0 indicates no pain and a score of 10 indicates the worst possible pain
[b] Patients received 400 mg ibuprofen and 1000 mg of acetaminophen
[c] Patients received 5 mg of oxycodone and 325 mg of acetaminophen
[d] Patients received 5 mg of hydrocodone and 300 mg of acetaminophen
[e] Patients received 30 mg of codeine and 300 mg of acetaminophen
[f] Calculated using analysis of variance
[g] Includes 19 patients with imputed NRS values
[h] Includes 15 patients with imputed NRS values
[i] Includes 19 patients with imputed NRS values
[j] Includes 24 patients with imputed NRS values

eTable 2. Between-Group Difference in Mean Change in Numerical Rating Scale (NRS) Pain Scores with Imputation of NRS scores for Patients Who Received Rescue Analgesia

Comparison	Between-Group Difference in Mean Change in NRS Pain Score (99.2% CI)[a]	
	From Baseline to 1 h	From Baseline to 2 h
Ibuprofen and acetaminophen vs oxycodone and acetaminophen	-0.2 (-1.0, 0.6)	-0.0 (-1.0, 1.0)
Ibuprofen and acetaminophen vs hydrocodone and acetaminophen	0.5 (-0.3, 1.3)	0.7 (-0.3, 1.6)
Ibuprofen and acetaminophen vs codeine and acetaminophen	0.2 (-0.6, 1.0)	0.7 (-0.4, 1.7)
Oxycodone and acetaminophen vs. hydrocodone and acetaminophen	0.7 (-0.1, 1.5)	0.7 (-0.3, 1.7)
Oxycodone and acetaminophen vs. codeine and acetaminophen	0.4 (-0.4, 1.2)	0.7 (-0.3, 1.6)
Hydrocodone and acetaminophen vs. codeine and acetaminophen	-0.3 (-1.1, 0.5)	-0.0 (-1.0, 1.0)

[a] Indicates mean change in pain of first analgesic minus mean change in pain from second analgesic. Pain intensity was assessed using an 11-point NRS in which a score of 0 indicates no pain and a score of 10 indicates the worst possible pain.

eTable 3. Post hoc Analysis of Subset of Patients with Severe Pain (NRS[a] = 10 or Documented Fracture)

	NRS Pain Score, Mean (95% CI)[a]				
	Ibuprofen and Acetaminophen[b]	Oxycodone and Acetaminophen[c]	Hydrocodone and Acetaminophen[d]	Codeine and Acetaminophen[e]	*P* Value[f]
No. of subjects	52	48	50	49	
Primary end point: decline in score to 2 h	4.4 (3.6, 5.1)	4.5 (3.7, 5.3)	3.9 (3.1, 4.6)	4.1 (3.3, 4.9)	0.69
Baseline score	9.6 (92,9.9)	9.2 (8.9, 9.5)	9.6 (9.3 9.9)	9.2 (8.9, 9.6)	0.24
Score at 1 h	6.6 (5.9, 7.2)	6.0 (5.3, 6.7)	7.0 (6.3, 7.7)	6.2 (5.5, 6.9)	0.20
Score at 2 h	5.2 (4.5, 6.0)	4.7 (3.9, 5.5)	5.7 (4.9, 6.5)	5.1 (4.4, 5.9)	0.38
Decline in score to 1 h	3.0 (2.4, 3.6)	3.3 (2.6, 3.9)	2.6 (2.0, 3.3)	3.1 (2.4, 3.7)	0.59

[a] Pain intensity was assessed using an 11-point NRS in which a score of 0 indicates no pain and a score of 10 indicates the worst possible pain
[b] Patients received 400 mg ibuprofen and 1000 mg of acetaminophen
[c] Patients received 5 mg of oxycodone and 325 mg of acetaminophen
[d] Patients received 5 mg of hydrocodone and 300 mg of acetaminophen
[e] Patients received 30 mg of codeine and 300 mg of acetaminophen
[f] Calculated using analysis of variance