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CORRESPONDENCE

Perioperative gabapentin and delirium following total knee arthroplasty: a *post-hoc* analysis of a double-blind randomized placebo-controlled trial

Krupa Dighe, MD · Hance Clarke, MD, PhD · Colin J. McCartney, MD · Camilla L. Wong, MD

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To the Editor,

Delirium is characterized by a new onset of fluctuating attention and confusion and is often linked to various triggering factors. Developing delirium is associated with an increased risk of post-discharge mortality, functional decline, longer hospitalization, hospital-acquired complications, persistent cognitive deficits, increased costs, and long-term institutionalization.[1]

Postoperative delirium is associated with pain severity as well as the effects of opioids on the central nervous system. Although gabapentin has opioid-sparing effects and reduces postoperative pain,[2] it is uncertain whether its opioid-sparing properties and reduction in pain scores translate into less postoperative delirium.

We report an analysis of a double-blinded randomized placebo-controlled trial that was designed primarily to compare gabapentin with placebo with respect to postoperative pain and in-hospital rehabilitation after total knee arthroplasty (TKA).[3] This report addresses the *post-hoc* analysis of postoperative delirium in the two groups.

A separate Sunnybrook Health Sciences Centre Research Ethics Board approval was obtained for this *post-hoc* analysis. Details on enrolment criteria, participant recruitment, and study duration are in the primary publication.[3] A computerized list of random numbers was generated for block randomization, treatment allocation was concealed, and gabapentin and placebo medications were identical and identically packaged. Physicians, nurses, patients, and data abstractors were blinded to treatment allocation. The sample size was based on the estimate for the primary outcome of the original trial.

Gabapentin 600 mg or placebo was administered two hours before surgery along with celecoxib 400 mg. Patients received femoral and sciatic nerve blocks along with spinal anesthesia. Postoperatively, patients received placebo or gabapentin 200 mg *tid* for four days, as per randomization. All patients received celecoxib 200 mg every 12 hr for 72 hr and morphine intravenous patient-controlled analgesia for 24 hr. OxyContin 5 mg q8hr was started the morning after surgery.

Incident postoperative delirium was identified via a validated medical chart abstraction tool.[4] The first episode of delirium was included for each given patient. Duration of delirium was also identified by the validated medical chart abstraction tool or by discharge date, whichever occurred first. Potential risk factors for delirium were abstracted (cognitive impairment, APACHE II score, visual impairment, and preoperative dehydration). A subset of 27 records was abstracted independently by a second investigator for inter-rater reliability of incidents of delirium.

K. Dighe, MD
Mackenzie Health, Richmond Hill, ON, Canada

H. Clarke, MD, PhD
Sunnybrook Health Sciences Centre, Toronto General Hospital, University of Toronto, Toronto, ON, Canada

C. J. McCartney, MD
Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada

C. L. Wong, MD
Li Ka Shing Knowledge Institute of St. Michael's Hospital, Toronto, ON, Canada

C. L. Wong, MD (✉)
St. Michael's Hospital, University of Toronto, Toronto, ON, Canada
e-mail: camilla.wong@utoronto.ca

Table Baseline characteristics of patients and outcomes

	Placebo $n = 78$	Gabapentin $n = 83$
Demographics		
Age in yr, mean (SD)	62.9 (7.2)	62.5 (6.5)
Female, *n* (%)	37 (47%)	44 (53%)
History of falls, *n* (%)	2 (3%)	3 (4%)
Previous stroke, *n* (%)	2 (3%)	3 (4%)
Risk factors for delirium on admission		
Cognitive impairment, *n* (%)	1 (1%)	2 (2%)
Vision impairment, *n* (%)	1 (1%)	0 (0%)
APACHE II > 16, *n* (%)	0 (0%)	0 (0%)
Dehydration (BUN:Cr ≥ 0.1), *n* (%)	19 (24%)	19 (23%)
Hospitalization-related factors		
Intensive care unit, *n* (%)	0 (0%)	1 (1%)
Postoperative hemoglobin, mean (SD)	105.3 (13.2)	105.1 (2.7)
Length of stay (days), mean (SD)	5.90 (1.54)	5.80 (1.15)
Death, *n* (%)	0 (0%)	0 (0%)
Clinical outcomes		
Incident delirium, *n* (%)	7 (9%)	10 (12%)

BUN:Cr = blood urea nitrogen to serum creatinine ratio

One hundred seventy-nine patients were randomized (84 to placebo and 95 to gabapentin). In this intention-to-treat analysis, complete data were available for 78 and 83 participants in the placebo and gabapentin groups, respectively. Inter-rater reliability for delirium assessments was good ($\kappa = 0.80$). The characteristics of the two groups were comparable (Table).

Delirium occurred in 17 (10.6%) of all participants. There was no difference in the incidence of postoperative delirium between the placebo and gabapentin groups (7/78 = 9% of participants *vs* 10/83 = 12% of participants, respectively; $P = 0.53$). The absolute risk reduction of delirium in the gabapentin compared with the placebo group was −3.1% (95% confidence interval −12.5 to 6.4). The maximum duration of delirium in both groups was one day.

Our study did not find a difference between gabapentin and placebo regarding the incidence or duration of postoperative delirium among elective TKA patients. This result contrasts with the results of another study of perioperative gabapentin among spinal surgery patients where there was less delirium in patients receiving perioperative gabapentin.[5] Limitations of this *post-hoc* analysis include a small sample size. This study had very few patients at higher risk for delirium and may limit generalizability to the frail orthopedic population. Lastly, the use of the validated chart abstraction tool for delirium is limited by the accuracy of the tool itself.[4] Larger studies in higher risk patients are needed to clarify the role of this multimodal medication in postoperative delirium.

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Competing interests None declared.

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