N₂O anesthesia may exacerbate hyperhomocysteinemia and endothelial dysfunction in patients with renal impairment

To the Editor: Patients with renal impairment have elevated homocysteine levels and are at high risk of cardiovascular complications [1]. Herein, we caution against the use of nitrous oxide (N₂O) anesthesia for these patients.

Under most conditions, N₂O appears to be inert, but prolonged exposure to the gas leads to significant increases in plasma homocysteine levels in patients presenting for elective craniotomy [2]. N₂O directly inhibits methionine synthase, which contains cobalamin as a prothetic group and catalyzes a folate-dependent conversion of homocysteine to methionine. Recently, Selzer et al [3] have described the neurologic deterioration and death of a child anesthetized twice with N₂O before the diagnosis of 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency was established. The N₂O-induced defect of methionine synthase superimposed on an inherited defect of MTHFR caused the death of the reported patient. The adverse effects of N₂O were reported in two other children with severe dietary cobalamin deficiency. One developed acute neurologic deficit six days after N₂O anesthesia, and the other showed hypotonia, dehydration, and acidosis three weeks after N₂O anesthesia.

Acute rise in plasma homocysteine level causes substantial impairment of endothelial function in healthy volunteers [4]. It is likely that when such endothelial dysfunction occurs in patients with renal impairment, it exacerbates the vascular dysfunction. The above-mentioned catastrophic events may provide us a cautionary message; plasma homocysteine and methionine levels should be closely monitored in patients with renal impairment undergoing N₂O anesthesia. Pretreatment with vitamins (folic acid, vitamin B₆, and B₁₂) may block the N₂O-induced increase in homocysteine level in at-risk individuals.

Failure to follow K/DOQI guidelines decreases effectiveness of access flow surveillance

To the Editor: The major drawback of the recent study on graft surveillance [1] is its failure to use major Kidney Disease Outcome Quality Initiative (K/DOQI) guidelines.

The K/DOQI ΔQa guideline (25% flow drop over 4 months, or a drop >20% within 1 month in the 1999 version) was not applied. Flow trends are considered to be more predictive of thrombosis than a single flow measurement (Qa). The authors argue that the application of the ΔQa criterion would not have altered the study outcome based on their previous study [2]. First, their previous study did not use interventions. Second, the results of that study have been disputed because of an incorrect statistic approach and multiple errors in calculations [3, 4]. Furthermore, when this study was analyzed by others [3, 4], it was shown to actually support the K/DOQI guidelines. Failure to apply both K/DOQI thresholds resulted in decreased preemptive percutaneous transluminal angioplasty (PTA) rate to 0.34/patient-years versus 0.54/patient-years in a study in which both flow thresholds were used [5], suggesting the patient’s undertreatment.

Qa should be measured during the first 1½ hour of hemodialysis (K/DOQI). The hemodynamic uncertainties related to patient status late in the treatment (15 minutes before the end, according to the authors’ protocol) could impact flow results significantly. This brings into question all access flow data.

The authors’ noncompliance with the K/DOQI guidelines decreased the quality of their clinical outcomes. Their article sends a misleading message to the hemodialysis community about the effectiveness of flow surveillance.

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Study is valid and helps define proper role of surveillance

Our publication is the first randomized controlled trial that has studied the influence of flow (Qa) surveillance on graft survival [1]. We share the disappointment of the nephrology community that surveillance did not prolong graft life.

Dr. Levine questions the validity of our study because we did not apply decrease in Qa (ΔQa), and did not restrict Qa measurements to early in dialysis. Our observation that ΔQa does not improve prediction of thrombosis [2] was confirmed by a second study that was reviewed by two statisticians [3]. In addition, we have shown that hemodynamic variation is so great that there is no value in limiting measurements too early in dialysis [1]. Moreover, risk of thrombosis increases with ultrafiltration volume [3]. This indicates that hemodynamic state at the end of dialysis influences thrombosis, suggesting that it may be better to measure Qa late rather than early in dialysis.

Dr. Levine has restated criticisms made by Krivitski and Gantela [4, 5] concerning our study that evaluated accuracy of Qa in predicting thrombosis [2].

(1) They claimed our calculations had multiple errors because a figure and a table did not have equal numbers of false positives [4]. This difference was expected because these two analyses did not include the same number of grafts [2]. The only error was in calculating predictive accuracy of Qa and ΔQa with the data in Table 1. Correction yielded a lower predictive accuracy [6].

(2) They claimed that reanalysis of our data shows Qa accurately predicts thrombosis [4]. Their analysis is not valid because they only considered ΔQa; they excluded grafts that thrombosed before ΔQa could be measured. Inclusion of all grafts yields a poor predictive accuracy (Table 1).

(3) They criticized our suggested guideline for adequate predictive accuracy [5]. Actual predictive accuracy was so poor that this criticism is irrelevant.

(4) They claimed we “have no basis for making any conclusions” without doing a harm-benefit analysis [5]. They have not applied this criticism to studies that favor Qa surveillance, and the information required to do such an analysis is not available [6].

In conclusion, our surveillance study [1] was properly designed, and our studies convincingly show that Qa is an inaccurate predictor of thrombosis [2, 3, 6]. Only by considering the results of such ongoing research can we hope to define the proper role of surveillance.

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References


Markers of oxidative stress in uremia

To the Editor: In their recent paper, Witko-Sarsat et al [1] hypothesized that advanced oxidation protein products (AOPP) behave as mediators of inflammation. A