Controversies in Malignant Hyperthermia

The current issue resolves one controversy concerning management of patients susceptible to malignant hyperthermia (MH) and raises another relating to diagnosis of susceptibility. The first concerns the use of preanesthetic dantrolene. Flewelling et al. demonstrate that intravenous dantrolene in volunteers results in predictable blood levels and avoids the pitfalls of oral doses—variable time to peak blood level (range 1–12 h), lower blood levels than expected, and necessity for large doses (400 mg/day) to achieve protective blood levels. These pitfalls may account in part for Fitzgibbons’ case, in which MH occurred despite the use of oral dantrolene. Most physicians pretreat susceptible patients with dantrolene: toxicity is minimal if used for less than 3 weeks, and it protects against unexpected triggering factors. Flewelling et al. have confirmed Dolan’s suggestion that the intravenous route is preferred. However, their half-life of 10–12 h is twice that observed in other human studies (including intravenous)* and therefore needs confirmation.

The second controversy concerns the interpretation of positive muscle biopsy contracture responses in patients with no personal or family history of MH, alluded to by Rosenberg. Experts generally agree that some disorders have an inconstant association with MH, wherein susceptibility sometimes may be involved, but not always. These include muscular dystrophy, central core disease, crib deaths (sudden infant death syndrome), and heat stroke. However, several laboratories have identified patients with various specific and nonspecific myopathies who coincidentally have positive contracture responses. No data directly relate these disorders to MH susceptibility, nor do we know whether positive contracture responses always signify it. This topic was debated fiercely by Hyam Isaacs (a muscle physiologist from Johannesburg) and other participants at the Fifth International Congress on Neuromuscular Diseases in Marseilles, France, September, 1982. It is Isaacs’ contention that such susceptibility is highly unlikely. There is at present no easy answer to this controversy.

Despite these concerns, the contracture response of a muscle biopsy remains the only confirmed diagnostic test (other than an unequivocal clinical episode). Two other tests have been proposed enthusiastically—platelet ATP depletion and calcium uptake of muscle. These tests constitute “shortcuts,” in that the specimen can be mailed. But there are problems: 1) verification of these techniques is incomplete, e.g., as correspondence or abstract; and 2) definitive studies directly contradict their findings. The burden of proof is on those proposing these tests to publish in a peer-reviewed journal a paired study comparing their results with those of contracture responses; otherwise the results of such testing remain uninterpretable.

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References