EDITORIAL VIEW

Malignant hyperthermia, dantrolene and apathy

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ABSTRACT

Malignant hyperthermia is a genetically transmitted hypermetabolic syndrome, and thus will always continue to surface and test the wits of the anesthesiologists. This editorial compliments two case reports published in this issue, as well as a brief story on the related topic in the journal's permanent chapter 'My Most Unforgettable Experience'©. The high rate of mortality due to non-availability of dantrolene, and thus the need to chalk out a well-linked system to make dantrolene available even in the farthest corner of the country, with the help of army aviation, when the need arises, is emphasized.

Key words: Malignant hyperthermia; Hypermetabolism; Dantrolene; Mortality; Morbidity

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Malignant hyperthermia (MH) is a well-known clinical syndrome of hypermetabolism of the skeletal muscles of the human body. It is also well-known for its associated morbidity and mortality, which is a result of excessive catabolism in the muscles leading to increased carbon dioxide production, combined metabolic and respiratory acidosis, high oxygen consumption in the body, activation of the sympathetic nervous system, heat production, and electrolyte disturbances involving hyperkalemia. Disseminated intravascular coagulation (DIC), and multiple organ dysfunction and failure are the endpoints.[1] The syndrome is not alien to the practicing anesthesiologists, and most of us might have one or more encounters with it during our clinical careers.

Not long before, it was a common belief that MH is not a disease of the subcontinent. The natives were thought to be somehow resistant to this disease syndrome. Perhaps it was a result of lack of adequate communication system and failure to report by the specialists in the peripheral parts of the countries. It was not before year 2000, when J Punj et al[2] reported a case report of MH in The Internet Journal of Pharmacology, quoting, "...it is reasonable to suppose that in a busy, tertiary care hospital in which about 15 –20,000 anaesthetics are conducted annually, one would expect to come across 1-2 cases annually, at the very least. Classic malignant hyperpyrexia, typically heralded by hyperthermia, tachypnoea, tachycardia and muscle rigidity along with rhabdomyolysis and myoglobinuria, has surprisingly never been reported from the Indian sub-continent, neither as published case reports or as presentations in clinical meetings or conferences. We, therefore, feel it necessary to report the first case of malignant hyperthermia, from the subcontinent of India...".

In this issue of the journal a case report[3] is being published, which is very similar to the above quoted case report by J Punj et al[2]. Although the onset and the initial clinic-pathological features were similar, including the fact that dantrolene – the drug of choice, was not available so not used in both cases, the outcome was different. Another case report in this issue of this journal[4] has reported a different scenario. A two years old girl underwent cleft surgery, was recovering in the recovery, when she developed hyperpyrexia. In this case the patient was lucky as the cleft team from UK had had dantrolene available with them. They used it and the life of the girl was saved. After these two cases were posted on social media, e.g. facebook and 'Anaesthetist Support Group' on whatsapp, news from all over poured in; the centers which had dantrolene available with them reported higher rates of survival, but the mortality was much higher at centers where dantrolene was not available. In fact, during the course of events of the management of the patient cited by Jadoon H et al, a country wide search was made on telephone from all the major medical institutions of Pakistan, and sadly none of them had had dantrolene available.[3] Both of these incidences generated a stir in the anesthesia circles, and the author was specially invited to highlight the topic in the 36th Conference of PSA Karachi. It was here that Prof. Akhtar Wahid, a renowned

anesthesiologist, disclosed that he once indented the full dose of the drug for Liaquat National Hospital Karachi, but after two years the drug was expired and was never replaced with fresh stock afterwards. The talk generated a lengthy discussion in the forum and various proposals were discussed.

The cost of the drug and the shelf life are definitely an issue. Average shelf life of dantrolene vials id two years. Dentrium™ (dantrolene sodium) comes as 20 mg per vial, and 12 vials would be required in an adult paient for the first dose. An additional 24 vials would be required in the same patient subsequently. One vial costs $65, hence total 36 vials would cost $65 x 36 = $2340 = Rs. 2,35,000. Ryanodex is the latest development of dantrolene, which is more concentrated and has less problems of drug solving in water for injection. It was developed by Eagle Pharmaceuticals in 2015, and is available as 5 ml vials of 50 mg/ml. One vial of this drug is equivalent to 12 vials of the older formulation (Dentrium™). Three vials of it required for a single patient cost $2300 x 3 = $ 6900 = Rs. 6,95,000. Punj J et al stated in their case report that, "...it is reasonable to suppose that in a busy, tertiary care hospital in which about 15 –20,000 anaesthetics are conducted annually, one would expect to come across 1-2 cases annually, at the very least...".[2] We can easily conclude that at least one full dose must be available in at least one major hospital in all metropolitan cities. Suppose no MH case happens in that city; it will be a wastage of $2340 = Rs. 2,35,000. But it will be a life insurance for the entire population of that city for two years.

The availability of dantrolene in a particular hospital, and the contact numbers of the responsible person in the lending hospital, must be known to all practicing anesthesiologists in the city as well as the surrounding towns. A network can be woven around army corps headquarters in the country, in which the drug is stored in the nearest military hospital, and army aviation helicopters are utilized to deliver or drop the drug in the peripheral hospitals. Please note that only six or seven main cities in Pakistan will have to be supplied with dantrolene to cover the whole of the country at the expense of 2,35,000 x 6 = Rs. 1,410,000 for two years.

Dantrolene has been shown to reduce MH related mortality from 70-80% to 5%. In the North American MH Directory 291 MH episodes were recorded and there were 8 cardiac arrests and 4 deaths between 1987 and 2006, and the median age of patients experiencing cardiac arrest or death was 20 years in the USA, and 1 or 2 deaths are reported to the MH hotline each year.[5] In UK 0-2 reported deaths per year is the estimated mortality due to MH. The health reporting systems and statistical data facilities in our countries are virtually non-existent as compared to USA or UK. And in the wake of non-availability of dantrolene, its any one's guess about the death toll in our country due to this syndrome. We need to act and prevent one of the most dreadful deaths due to anesthesia related cuses.

Let us see if wisdom prevails or apathy proves itself once again to be the ruling principle of this nation.

Conflict of interest: Nil

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