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Anaesthetic Drugs and Defibrillation Threshold Testing

We read with interest the article entitled "Effect of Drugs on Defibrillation Capacity" by Dopp et al.[1] in issue 68 (5) of *Drugs*. Among all the effects of drugs described, we think that the influence of anaesthetic agents are of particular importance as defibrillation threshold (DFT) testing of implantable cardioverter-defibrillator (ICD) is always performed under anaesthesia or deep sedation. As the authors mentioned, the available data in this regard are limited and conflicting; however, there are a few animal studies testing the effects of anaesthetics on DFT in the literature worth mentioning. Although an ideal animal model has not been established, canine models may be more comparable with human cardiac electrophysiology.[2] Canine studies have shown that the DFT current and energy requirements are less under surgical level of pentobarbital anaesthesia than that required in the awake state.[3] In another canine study, DFT was increased with inhalational agents, whereas fentanyl analgesia reduced it.[4] Similarly, statistically significant reductions in energies required for 50% (E50) and 80% success in defibrillation were observed with fentanyl when compared with pentobarbital anaesthesia.[5] However, no significant difference in DFT was observed between pentobarbital, halothane and isoflurane anaesthesia in another canine experiment, although a significant difference in E50 was noticed when the methods used to defibrillate were taken into consideration.[6] Similar results were also observed by Jarvis and Lahtinen,[7] where only a single agent was used for both induction and maintenance of anaesthesia during DFT testing. In clinical settings, as in animal studies, results again remain unclear. In addition to the clinical studies described by the authors, significant decreases in DFT were observed in two patients who received ICD under isoflurane anaesthesia.[8] This is in contrast to another large clinical study where no significant difference in DFT was observed under general anaesthesia or conscious sedation.[9]

Although the data are ambiguous, the potential for anaesthetics to alter DFT suggests that the threshold values measured in the laboratory may not reflect the 'true DFT' when the patient is at home ('at home DFT') or during an arrhythmic event. Propofol, as a result of its excellent induction and emergence characteristics, has become one of the most commonly used anaesthetic agents for ICD implantation and DFT testing sessions. However, studies addressing the effects of propofol on DFT are very limited and data regarding the dose-related response of propofol on DFT are not available. This information is pivotal as extra doses of propofol are commonly administered without proper titration of the depth of anaesthesia during DFT testing sessions. Use of standardized anaesthetic depth assessment techniques, such as the Bispectral Index or Narcotrend Index, may be considered in these situations.[10] Similarly, the effects of polypharmacy as a result of the use of opioids and other adjuvant anaesthetic agents at the time of implantation when compared with the sole DFT testing sessions (without surgery) may also influence DFT values. Additionally, the influence of recreational drugs and/or alcohol can have an additive depressive effect on the myocardium under anaesthesia. Such patients may require larger doses of anaesthetic agents to achieve adequate anaesthetic depth, again confounding myocardial DFT measurements. Similarly, anti-arrhythmic medications, which potentially have varying effects on DFT, may also have interactions with anaesthetic agents, thus affecting DFT. For example, verapamil may increase DFT,[11] but its concurrent administration with midazolam may increase verapamil tissue concentrations,[12] which may possibly augment its effect on DFT.

Another interesting aspect of DFT testing is the measurement of upper limit of vulnerability (ULV). ULV is the strength at or above which ventricular fibrillation is not inducible when a stimulus is delivered during the vulnerable phase of the cardiac cycle. This measurement is often used as an alternative for DFT assessment without inducing ventricular fibrillation.[13] Although this method is widely

used, there are no published studies that have evaluated the effect of anaesthetic agents on ULV and its correlation with DFT under different depths of anaesthesia.

High DFT is a growing clinical problem with regard to ICD therapy. Several techniques, including surgical alterations (subcutaneous shocking coil implantations) and/or device modifications (changing to high energy ICDs) are performed in order to attain the adequate 'safety margin'. Given the conflicting evidence of effects of anaesthetics on DFT, it is imperative to recognise the true effect of anaesthetic agents on DFT and ULV. Hence, more data from well designed animal and/or clinical studies addressing this aspect of drug effect are of crucial importance in order to determine the 'true DFT', thus preventing unwanted procedures and assure patient safety.

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