EDITORIAL

Evaluating The Efficacy of Phototherapy Devices

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The field of newborn phototherapy (PT) has clearly arrived at a strategic period of transition from the use of traditional light sources, such as fluorescent, halogen and halogen/fiberoptic, towards the use of presently fast developing, versatile solid state light emitting diode (LED) technology. The time also appears to be ripe for the replacement of ineffective, defective, and worn-out devices that deliver inadequate therapy, as has been demonstrated through recent surveys in India, Nigeria, and Brazil [1-3]. Because of a rapidly expanding global market for PT devices, the medical device industry, particularly in India, appears to be actively engaged in the production of newer and, undoubtedly, more effective and affordable LED-based devices.

In order to assist physicians, hospitals, and clinic administrators with the selection of the most appropriate device for their clinical needs, it is important that uniform and comprehensive device characterizations and criteria be established and made available. Thus, it is becoming increasingly important that devices be evaluated for their physical and spectrophotometric characteristics as well as their clinical efficacy to affect the photochemical alteration of bilirubin (BR) in the newborn skin and circulation. The study reported by Subramanian, *et al*. [4] in this issue of *Indian Pediatrics* significantly adds to the efforts that have already been made towards this goal [5-7], while it also demonstrates the diversity of traditional and new technologies.

The primary parameters that determine the efficacy of a PT device are: the spectral quality of the light (optimal within the blue to green range of 400-520 nm) that is delivered, the irradiance (light intensity), and the treatable body surface area (BSA) of a patient (the light foot print). In addition to these device characteristics, patient and caregiver-related parameters also contribute significantly to the efficacy of treatment. These include, the initial plasma BR level and BR production rate of an infant and treatment initiation, duration of PT, and irradiance level chosen by the caregiver. Basic physical and spectrophotometric data are usually provided by device manufacturers. Frequently, some time after devices have been made commercially available, clinical studies may be performed by clinical researchers with a variety of more or less appropriate methods and measurement techniques that make meaningful comparisons difficult. For instance, measurements of irradiance using an inappropriate light meter can be a serious source of error [8].

Obviously, the most appropriate evaluation of device efficacy is through measurements of the decline of plasma BR levels or PT duration through clinical studies with jaundiced newborns under carefully defined conditions. However, besides the fact that it is morally indefensible to treat newborns with potentially inferior devices, when proven devices are available, it is also a strategic and practical problem to evaluate a new device or series of devices, on a sufficient number of jaundiced newborns over a reasonable time period to achieve statistical significance.

Thus, efforts are being made to comprehensively evaluate PT devices in the laboratory as a surrogate for *in vivo* clinical studies. Besides measuring the (spectro-) physical characteristics of devices, typical

methods include estimations of BR photodegradation through use of various concentrations of BR with or without human serum albumin in varying solvent systems, which are exposed to PT light with a carefully selected level of irradiance. The %BR remaining is then determined using various methods, ranging from direct spectrophotometry, diazo method, to HPLC with spectrophotometric or mass spectrometry detection.

Specifically, Subramanian, *et al*. exposed very low concentrations (1 ug/mL or 0.1 mg/dL) of BR, dissolved in methanol to the maximum (rather than the mean) irradiance of PT devices and measured the %BR left through measurements of lumirubin, a reaction product which represents one of the three recognized BR photoalteration mechanisms. The use of the latter strategy or endpoint may explain the observed leveling off for the observed %BR degraded. The authors also raised an interesting and important testing topic, stating that the devices were tested with "regulated" power. Obviously, it is appropriate to test devices with regulated voltage. However, it may also be valuable to test devices under conditions of voltage fluctuations and outages, which often occur under actual field and hospital conditions, especially in India and elsewhere. Information about electrical ruggedness could be of critical importance in the selection of the appropriate device for a particular clinical setting.

However, it needs to be kept in mind that the validity and value of bench-testing towards estimating *in vivo* device efficacy has its limitations, because it employs static (test tube) methodology to model the efficacy of a complex dynamic system. Furthermore, the method also ignores the aforementioned effects that patient and caregiver parameters contribute towards PT efficacy. Obviously, more effort needs to be made to refine the methodology used to date, particularly those aspects that relate to determining the relative BR photodegradation rate as a functional efficacy estimate. Interestingly, after half a century of PT research, many aspects, such as the optimum PT wavelength (range), the minimal effective, optimum, and maximum safe irradiance levels for both term and preterm infants are still being debated. Clearly these issues are very relevant to the design of safe and effective PT devices.

Hopefully, further research in this interesting field of endeavor will be carried out with the assistance and leadership of a new generation of young and enlightened researchers.

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