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Melatonin - marvel in the making?

Ever since Aaron Bunsen Lerner isolated melatonin (N-acetyl-5-methoxytryptamine) from pineal glands of cattle in 1958, the hormone has been found to have several uses in humans. Endogenous melatonin is well recognised for its role in regulation of the circadian rhythm.^[1] Exogenous melatonin has been studied for various indications in anaesthesia such as hypnosis, anxiolysis, sedation and analgesia. It has also been used effectively for the prevention of emergence agitation and delirium in postoperative as well as intensive care unit patients. Melatonin's antioxidative, immunomodulatory and cardioprotective properties have found utility in a variety of surgical procedures such as organ transplantation, liver resection and cardiovascular surgery.^[2-5]

Systematic reviews and meta-analyses have shown that oral melatonin (0.05–0.2 mg/kg or 3–15 mg bolus) decreases the preoperative anxiety in adults scheduled for a wide range of surgeries. It is also devoid of amnesic effects unlike benzodiazepines. Conflicting evidence exists in literature regarding melatonin's ability to provide postoperative anxiolysis, pain intensity reduction and probable opioid sparing effects.^[6,7] Limited evidence suggests that melatonin may reduce the induction dose requirements of intravenous induction agents^[8,9] but not of sevoflurane.^[10] Melatonin is a poor facilitator of paediatric steal induction compared to clonidine.^[11] Melatonin administration improves the baroreflex response and decreases the sympathetic output without affecting cardiac contractility.^[12] A study in this issue of Indian Journal of Anaesthesia (IJA) explores the possibility of melatonin for suppressing pressor response to direct laryngoscopy and intubation.^[13]

Children form a special group where preoperative anxiety can be very severe and can have serious

sequelae. Their anxiety can be due to fear of the unknown, parental separation, hospital atmosphere, past experience of needles, bitter medications, etc. Several studies show the beneficial effects of oral melatonin in alleviating preoperative anxiety in children. Although conflicting evidence exists regarding melatonin's superiority over oral midazolam in this regard, melatonin may be favoured over midazolam as it has least hangover effects and other adverse effects attributable to midazolam.^[14-18] In a study of 100 children aged 5–15 years posted for elective surgery, published in this issue of IJA, oral melatonin 0.75 mg/kg provided better preoperative anxiolysis without affecting cognitive or psychomotor behaviour.^[19]

Exogenously administered melatonin has very few side effects with virtually no serious or life-threatening complications attributable even at a dose of 1 g/day or 50 mg/kg administered as a bolus.^[20,21] Although benzodiazepines are commonly used for sedation and anxiolysis in anaesthesia and intensive care, melatonin appears to have a distinct edge due to its ability to provide the same without any hangover or other side effects associated with benzodiazepines. Blood melatonin levels are known to be subnormal in a large variety of disease conditions.^[4] All these factors along with its ease of availability (classified as a dietary supplement) are encouraging clinicians to delve into further depths of related research. However, one should note that the long-term consequences of high-dose melatonin are yet to be ascertained – it has been shown to contribute to altered sperm motility in healthy men and its use as a contraceptive has been contemplated.^[22-24]

The high therapeutic index of melatonin, lack of life-threatening adverse effects, ease of access coupled

with its beneficial effects on various organ systems and in a variety of pathological conditions hint at a marvel in the making. The evidence is convincing regarding its anxiolytic and sedative properties, but robust evidence is lacking in other areas. Future studies regarding appropriate dose and timing of administration of melatonin for other indications might unravel the true potential of melatonin.

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