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Understanding and Treating Emergence Delirium

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Abstract

This paper examines our current understanding of the phenomena of emergence delirium, which can occur following general anesthesia. Much research has been conducted to elucidate the causative factors of this condition, with findings ranging from anxiety to volatile agents and the neurodevelopment of the brain (Aono, Ueda, & Mamiya, 1997; Kain et al., 2004; McLott, Jurecic, Hemphill, & Dunn, 2013). While much of our understanding of emergence delirium has come from studying children, who are more prone to this condition, we can attempt to learn even more by examining the increased incidence of emergence delirium that occurs in those with post-traumatic stress disorder or PTSD (Lovestrand, Phipps, & Lovestrand, 2013). Not only has our understanding of brain structure and function increased in recent years, but our improved ability to target specific receptors with pharmacological agents has also enabled us to discover ways to lessen the incidence of this upsetting and potentially dangerous response to general anesthesia (Dahmani et al., 2010). Current treatments that target GABA, opioid and alpha-2 receptors appear to demonstrate the greatest effect, however, there is wide variability within these receptor classes and various side effects that must also be considered. Individual genetic variations in receptor subtypes only complicates the picture, and may be the focus of future research as our understanding of and attention to the human genome increases.

Understanding and Treating Emergence Delirium

Emergence delirium, also referred to as emergence agitation and emergence excitement, is a condition that can occur following the administration of general anesthesia. This condition was first described by Dr. Eckenhoff in the 1960s, who referred to it as post anesthetic excitement and considered it a dissociated state of consciousness (Mohkamkar et al., 2014). Emergence delirium can be defined as a state of mental confusion, agitation and disinhibition marked by hyperexcitability, crying, restlessness and hallucinations during emergence from general anesthesia (Stamper, Hawks, Taicher, Bonta, & Brandon, 2014). During this period, attempts to reorient the patient through verbal and other means are ineffective. Although emergence delirium is most likely to occur during the first 30 minutes following anesthesia and tends to last for between 15 and 30 minutes, it has been reported to occur as long as 45 minutes following emergence and to last for upwards of two days in the most extreme cases (Dahmani, Delivet, & Hilly, 2004; Munk, Anderson, & Gogenur, 2013). Emergence delirium appears to affect children more often than adults, with studies showing that it occurs at rates of three to eight times greater in children (Stamper et al., 2014).

Literature Review

Emergence delirium causes a great deal of stress for anesthesia and nursing personnel, as well as for the patient and the patient's family. Not only is there increased psychological stress as a result of the patient's condition; the agitation, flailing arms, and inability to reason with and control the patient places them at great risk for injury (Lepouse, Lautner, Liu, Gomis, & Leon, 2006; Sikich & Lerman, 2004). During this

period there is increased risk of physical harm from pulling out IV lines and drains, as well as the risk of self-extubation and other bodily injury (Wofford & Vacciano, 2011). In addition, the demands placed upon staff are greatly increased, as nearly 50% of those who develop emergence delirium require extra PACU personnel to take care of them (Hudek, 2009).

When emergence delirium was first recognized in the 1960s, it was thought to be due primarily to the effects of postoperative pain and the resulting discomfort and agitation that ensued. During this time period the primary anesthetic agents being used were ether and cyclopropane, which were both felt to contribute strongly to emergence excitement (Eckenhoff, Kneale, & Dripps, 1961). Although no specific studies comparing the incidence of emergence delirium from one anesthetic agent to another were conducted during this time, it does not appear that anesthesiologists felt there was a greater propensity for delirium or agitation with any specific agent over another. In subsequent decades, when halothane was the primary anesthetic agent in use, discussion of emergence delirium went by the wayside; this was presumably due to a decreased incidence of such effects with the use of halothane. It was not until the advent of more volatile modern agents such as sevoflurane and desflurane that discussion of emergence delirium once again made its way back into the literature.

Despite more than four decades of exploration on emergence delirium in the literature, researchers still do not have a full grasp of the exact cause of this condition. Although various factors appear to place an individual at greater risk for developing this condition, no single factor has emerged as the primary cause. One of the reasons it has been so difficult to determine the exact causative factors of emergence delirium is that

there has not been a consistent grading scale for the verification of emergence delirium in postoperative patients (Munk, Andersen, & Gogenur, 2013). In fact, more than fifteen measurement tools have been used over the years to define and grade emergence delirium, and few of these tools have been able to effectively differentiate between pain and agitation or delirium, as they present with many similar characteristics (Nasr & Hannallah, 2011).

Of the measurement tools used, the most frequently chosen are the Watcha scale, the Cravero scale and the more recently created Pediatric Anesthesia Emergence Delirium (PAED) scale. Each of these scales has been designed primarily to examine emergence delirium in the pediatric population. Both the Watcha and Cravero scales are similar and relatively easy to use as they rank order a child's behavior from asleep or obtunded to wild and thrashing (Reduque & Verghese, 2013). The concern with these two scales is that they both involve the rating of behaviors that are not necessarily specific to emergence delirium, but could simply be a reflection of untreated pain (Sikich & Lerman, 2004). The PAED scale was developed in an attempt to address this and examines disturbances in consciousness, such as reduced awareness of the environment and an inability to focus or shift attention, rather than simply a child's degree of physical restlessness (Sikich & Lerman, 2004). In order to rate these more subtle disturbances, the PAED scale requires the practitioner to evaluate eye contact and whether the child makes purposeful movements. The degree to which each behavior is demonstrated is further rank-ordered, making the PAED scale a much more time consuming and cumbersome measurement tool than the others, and limiting its utility in clinical assessment. Another issue further hampering the routine use of the PAED scale is that the developers of this

scale never defined the numeric value for which a diagnosis of emergence delirium would be attributable. Consequently, various studies have been conducted to compare the results of the most frequently used scales to the more recently created PAED scale, and a consensus has begun to develop that defines emergence delirium as being consistent with a PAED scale rating of greater than 10 to 12 (Bajwa, Costi, & Cyna, 2010; Nasr & Hannallah, 2011).

Over the years the study of emergence delirium has been primarily focused on pediatric anesthesia as it has been observed to be a condition more common to this population. Consequently, there has been a paucity of studies examining this phenomenon as it occurs in the overall surgical population (Wilson, 2014). Due to the wide range in scoring criteria used over the years the incidence of emergence delirium in the pediatric population has been considered to be as low as 20% by some reckonings and as high as 80% according to others (Rahimzadeh, Faiz, Alebouyeh Dasian, & Sayarifard, 2014), although most studies put the figure at closer to the 20% mark (Bong & Ng, 2009). More recently, emergence delirium has gained additional attention outside the realm of pediatric anesthesia as there has been increased attention placed upon posttraumatic stress disorder (PTSD) in the adult population. The primary cause of this increased attention has come from the rise in the incidence of PTSD in the military population, as a result of the prolonged conflicts in Afghanistan and Iraq. It is quite possible that the renewed attention placed upon this phenomenon will help us not only better understand and treat this condition, but more importantly, prevent its occurrence in the first place.

There are a number of factors that appear to bear a strong correlation with the development of emergence delirium. These precipitating factors include age (younger patients between the ages of 2 and 6, as well as those over 65), increased levels of preoperative anxiety, postoperative pain, short surgical duration, use of sevoflurane, surgery involving the head and neck, and rapid emergence from anesthesia (Aono, Ueda, & Mamiya, 1997; Kain et al., 2004; Lepouse et al., 2006; Nasr & Hannallah, 2011; Radtke et al, 2010; Stamper et al., 2014; Yu, Chai, Sun, & Yao, 2010). Although emergence delirium is possible following total intravenous anesthesia, it has been found to be nearly four times more common when inhalation anesthetics are used (Yu et al., 2010). In addition, the common perception that individuals who experience a rough induction of anesthesia often experience a rough emergence may not simply be an anecdotal finding, as Mohkamkar et al. (2014) discovered when they found that individuals who were agitated during induction of anesthesia had a higher risk of developing emergence agitation.

A number of explanations have been put forward in an attempt to explain why these various factors appear to be connected with an increased incidence of emergence delirium. Eckenoff, Kneale and Dripps (1961) speculated that a sense of suffocation upon emergence from anesthesia was responsible for the frequent agitation seen following surgery on the neck and throat. The increased incidence of emergence delirium following surgical procedures of short duration has been proposed to be due to a rapid washout of inhalation anesthetic agent before analgesic medication has had a chance to reach its peak effect (Mohkamkar et al., 2014). The newer, more rapid acting volatile agents such as sevoflurane and desflurane have been speculated to cause emergence

delirium due to the fact that they result in a rapid emergence. This last theory, however, was disproved by Vlajkovic and Sindjelic (2007), who found that even a step-wise decrease in sevoflurane - made in such a way as to slow emergence - did not appear to change the frequency of emergence delirium. The fact that the rapid emergence from propofol anesthesia is not associated with emergence delirium further debunks this theory (Cohen, Finkel, & Hannallah, 2002).

Although most studies seem to relate emergence delirium to sevoflurane anesthesia, studies of desflurane - and to a lesser extent isoflurane - have also consistently demonstrated a link to increased rates of emergence delirium (Vlajkovic & Sindjelic, 2007). Additionally, inadequate pain control is a rather hazardous predictive measure as well, due to the fact that so many of the criteria used to define emergence delirium, such as physical agitation, can also be caused by pain. To further support the notion that pain is too simple a criterion upon which to base emergence delirium, is the fact that even painless procedures such as MRI have been found to result in emergence delirium (Bonhomme et al., 2012). It appears that there is something in the nature of volatile agents that is responsible for the development of emergence delirium. The fact that it occurs more often in children between the ages of 2 and 6, likely has to do with the underlying nature of neurodevelopment in children. That increased levels of preoperative anxiety correlate strongly with the development of emergence delirium also suggests that there is a psychological component at work as well; perhaps it is some combination of these two factors that is ultimately responsible.

A lot of research has been conducted examining the connection between preoperative anxiety and emergence delirium. A study by Kain et al. (2004) found that

children with preoperative anxiety had a 12.5% increase in maladaptive behavioral changes following surgery, and that every ten point increase in a child's anxiety score correlated with an approximately 10% increase in the rate of emergence delirium. Not only do more anxious children tend to develop emergence delirium at nearly six times the frequency of less anxious children, but studies also indicate that more anxious children also report more pain during their hospital stay, as well as during their first three days at home (Kain et al., 2006). Kain et al. (2004) also found that in addition to child-related factors influencing the rate of emergence delirium, the parents of anxious children are significantly more anxious in the holding area and upon separation from their child en route to the OR. All of these findings underscore the importance of parental and child education within the perioperative setting to lessen procedural-related anxiety and thus emergence delirium. To further support the case for effective preoperative preparation, it has been found that previous history of illness decreases the risk of emergence delirium in the adult population. This is speculated to be due to the fact that these patients are more accustomed to the hospital environment and are therefore less anxious (Lepouse et al., 2006).

When looking into emergence delirium and anesthesia in general, it does not take long before an examination of the mechanism of action of anesthetic agents and their effect on the central nervous system becomes a primary focus. Interestingly, in the more than one hundred years that we have been using pharmacological agents to induce a state of anesthesia, we still cannot say with certainty just how these agents work upon the body to produce their desired effect. While it was initially postulated that the effects of anesthetic agents were due to their lipid solubility and impact on the lipid bilayer of

neuronal membranes, it has since been proven that this basic explanation is not only too simplistic, but also incorrect (Bonhomme, Boveroux, Brichant, Laureys, & Boly, 2012). More modern hypotheses of the pharmacodynamics of volatile agents vacillate between the creation of a global inhibitory state and a more targeted, specific inhibition of various brain regions.

The primary receptor responsible for inhibitory neurological impulses is the GABA receptor. It is upon this receptor that agents such as benzodiazepines, alcohol and propofol have their effect; volatile agents are also believed to have some effect upon these receptors. The chronic stress of PTSD has been found to result in neural remodeling of GABA receptors, with a consequent decrease in binding sites, which causes benzodiazepines to be less effective in reducing hyperarousal (Geuze, van Berckel, & Lammertsma, 2008). Researchers speculate that the same reduction in benzodiazepine binding sites may occur with respect to the binding sites for volatile anesthetics, and that this may play a role in the increased agitation that can occur following general anesthesia with these agents. They further speculate that the effect of chronic stress from PTSD on GABA receptors may be somehow similar to the stress of general anxiety, which may be the reason for the increases in emergence agitation exhibited by more anxious individuals.

Several studies have demonstrated that the amygdala is an important area for the inhibitory effects of anesthetic agents. In a review of relevant literature by McLott, Jurecic, Hemphill, and Dunn (2013), the authors showed that GABA receptors exist in large quantities within the amygdalocentric neurocircuitry, that area of the brain comprising the amygdala and its connections to the medial prefrontal cortex and the

hippocampus. It is these areas of the brain that are responsible for the amnestic effects of general anesthetics (Alkire & Nathan, 2005). Interestingly, the stress response has been intricately linked to the amygdala as well, as it is this area of the brain that is associated with the transmission of fear and excitation to the hypothalamus (McLott, Jurecic, Hemphill, & Dunn, 2013).

Further underscoring the link between emergence delirium and activity within the amygdala, studies have shown that auditory stimulation activates that part of the amygdala responsible for fear conditioning. Researchers have also found that chronic stress causes a down-regulation of Ca⁺-activated potassium channels, which results in increased activity within the amygdala in response to auditory stimuli (Guo et al., 2012). As hearing is the first sense to return during emergence from general anesthesia, it follows that an exaggerated fear response to auditory stimuli may be a potential trigger for emergence delirium. The connection between auditory stimulation and increased activity within the amygdala has been demonstrated to such an extent that in some institutions the primary method used to gain the attention of a patient during emergence is to rub their feet rather than to use verbal commands (Kain et al., 2006). Interestingly, hyperactivity of the amygdala has also been connected to increased levels of impulsiveness, aggression and violence in response to provocative stimuli in the general human population (Siever, 2008). It has further been shown that a patient's level of impulsivity correlates strongly with increases in emergence delirium (Mountain et al., 2011). Hyperactivity of the amygdala is more likely to lead to this type of behavior, particularly when there is diminished cortical regulation as occurs during a state of anesthesia. As the cerebral cortex is primarily responsible for regulation and inhibition of

lesser order brain functions, it is logical to conclude that any inhibition of a fear response will not take place until these higher order functional areas of the central nervous system have recovered from the effects of general anesthesia (Dahmani, Delvit, & Hilly, 2014).

Another area postulated to be involved in emergence delirium is the locus coeruleus. This is an area within the pons of the brainstem that is involved in the physiologic response to stress. The locus coeruleus sends excitatory signals to various target areas within the central nervous system by way of the neurotransmitter norepinephrine, and as such it plays a role in controlling the overall activity level of the brain (Miller, 2011). Lending credence to this area being important to our understanding of emergence delirium is the finding by Yasui, Masaki, and Kato (2007), who showed that blocking norepinephrine release within the locus coeruleus, by the administration of the alpha-2 agonist dexmedetomidine, was useful in preventing emergence delirium. Furthermore, these researchers found that the order of inhalation anesthetics in activating excitatory changes within the locus coeruleus is in accord with the rate at which each inhalation agent appears to be implicated in causing emergence delirium.

Since the brain does not fully develop until well into the late teenage years, there are significant physiological differences between the brains of children and adults, and these differences clearly play a role in the increased incidence of emergence delirium among pediatric patients. Interestingly, similarities have been found between the electroencephalogram (EEG) patterns seen during emergence delirium and those that occur during night terrors in children (Dahmani, Delivet, & Hilly, 2014). Sevoflurane, as well as desflurane and isoflurane, all induce EEG changes that are similar to one another and markedly different from those produced by halothane, an agent associated with a

much lower incidence of emergence delirium. This suggests that some degree of interference in the balance between synaptic inhibition and excitement may be at play (Vlajkovic & Sindjelic, 2007).

Due to the finding that adults with PTSD have rates of emergence delirium roughly equal to those exhibited by children - nearly 29% in a study done by Wilson (2013) - it makes sense to examine the effect of pharmacological agents used in the treatment of PTSD on the incidence of emergence delirium. One of the more commonly prescribed classes of drugs for the treatment of PTSD are SSRIs, or selective serotonin reuptake inhibitors. These drugs have been shown to dramatically decrease the incidence of emergence delirium, suggesting involvement of serotonergic processes in the etiology of both PTSD and emergence delirium (Lankinen, Avela, & Tarkkila, 2006). Serotonin has been found to enhance cortical function in areas known to modulate and suppress aggressive behaviors, and SSRIs have been found to reduce impulsive aggression and decrease noradrenergic activity (Siever, 2008). The primary limiting factor for the use of these agents in the general surgical population is that they tend to take upwards of six weeks to take effect (Lovestrand, Phipps, & Lovestrand, 2013). The fact that sevoflurane and other inhalation anesthetics often lead to emergence delirium may be due in large part to the finding that in low doses these agents exhibit a degree of EEG activation, followed at higher doses by EEG suppression (Bennett et al., 2009). Thus, when volatile agent concentrations are low, as occurs during emergence, there is actually an increase in brain activity. The fact that only certain individuals experience emergence delirium may be due in part to the finding that there is both genetic variation,

as well as age-based variation in the makeup of the different subtypes of GABA receptors (Kim, 2011).

Of course no study of the phenomena of emergence delirium would be complete without addressing the means by which anesthetists can attempt to decrease the incidence of this adverse response to anesthesia. Numerous studies have investigated the effect that agents such as opioids and benzodiazapines have upon the development of emergence delirium. It makes sense that researchers would have examined these agents, as both pain and anxiety have been strongly implicated in the development of emergence delirium. While studies have been mixed with regards to the effect of benzodiazepines - specifically midazolam - studies examining the effect of opioids have demonstrated very strong results. Interestingly, while midazolam has had mixed results in terms of its effect on emergence delirium, with a recent meta-analysis by Dahmani et al. (2010) demonstrating that it is not effective in preventing emergence delirium, it has been shown to consistently reduce preoperative anxiety. While it may seem surprising, then, that midazolam has not been found to be effective in decreasing the incidence of emergence delirium there are several factors that may help to explain this finding. First of all, providers generally are more apt to give midazolam preoperatively to individuals with increased levels of anxiety, the very individuals who have been found to have the greatest risk of developing agitation in the first place. Despite the strong link between preoperative anxiety and emergence delirium, the lack of an effect from preoperative midazolam may be due to the fact that it often does not last through to the recovery period (Mountain, Smithson, Cramolini, Wyatt, & Newman, 2011). In addition, midazolam has been found to produce paradoxical effects of anxiety and agitation in

certain individuals and benzodiazapines have also been shown to decrease the pain threshold, and thus may result in pain that is not adequately controlled by a standard dose of narcotic. It may be this pain that individuals are responding to, as pain itself has been linked to increased rates of emergence delirium.

When a patient does develop emergence delirium, treatment typically consists of giving fentanyl, or in some institutions dexmedetomidine. In a study by Stamper et al. (2014) the use of these medications was found to effectively treat emergence delirium in over 60% of individuals. Fortunately for those individuals for whom treatment was not effective, emergence delirium is a self-limiting phenomena, generally resolving within 15 to 30 minutes. Interestingly, one of the most effective treatments appears to be parental presence during recovery from anesthesia and may even work faster than pharmacological agents (Arai et al., 2007; Vlajkovic & Sindjelic, 2007).

When one considers the typical physiological factors that come into play during surgery, one of the first things to be considered is the effect of stimulation upon the sympathetic nervous system. This is the system responsible for the fight or flight phenomena that is commonly discussed in regards to the stress response. In this stress response the body releases catecholamines, primarily norepinephrine, which travels to target tissues to activate specific adrenergic receptors. In the peripheral circulation the activation of these receptors results in vasoconstriction and other target organ directed effects, while in the central nervous system the effect is to increase alertness and create a state of hypervigilance. It would seem reasonable, therefore, to predict that blocking the effect of norepinephrine within the central nervous system may be an effective means of inducing a quieting or suppressing of arousal and consciousness. A couple of

medications that work in this function have gained a great deal of attention in terms of their effects on diminishing the frequency of emergence delirium. These drugs are the alpha-2 receptor agonists, clonidine and dexmedetomidine. As alpha-2 agonists they cause a negative feedback inhibition of alpha-1 receptors, the same receptors primarily stimulated by norepinephrine during periods of sympathetic stimulation. Clonidine is frequently prescribed for its antihypertensive effect, however it has been found to have sedating and analgesic properties by virtue of its central nervous system effects as well (Kulka, Bressemer, & Tryba, 2001). A study by Tazeroualti, De Groote and De Hert, (2007), found that oral clonidine administered prior to the induction of general anesthesia resulted in a significant decrease in the incidence of emergence delirium, while a study by Bock, Kunz and Schreckenberger (2002) showed that intraoperative administration of clonidine reduced emergence delirium to just 5%, with no delay in discharge as can occur when more sedating medication is given.

A more novel anesthetic agent, dexmedetomidine, has eight times the affinity of clonidine for the alpha-2 receptor (Guler et al., 2005) and has received a great deal of attention in the prevention of emergence delirium. While dexmedetomidine is most frequently given by infusion, a study by Ibache, Munoz, Brandes, and Morales (2004) found that a bolus administration of 0.3 mcg/kg at the end of anesthesia reduced the incidence of emergence delirium from 47% to just 5%. In addition, dexmedetomidine has an advantage in that it has been shown to decrease the frequency of airway problems resulting from laryngeal stimulation during extubation (Gulen et al., 2005; Shukry et al., 2005). Another study by Guler et al. (2005) showed that a bolus administration of dexmedetomidine as high as 0.5 mcg/kg was similarly effective, and even at this higher

dose did not result in either hypotension or bradycardia, two of the most common adverse effects of this medication. Although not FDA approved for oral use, a study by Zub, Berkenbosch and Tobias (2005) showed that oral doses of 3 mcg/kg of dexmedetomidine given preoperatively were effective in reducing emergence delirium and there were no complaints about palatability or bitter taste as is the case with oral midazolam. The main disadvantage of dexmedetomidine is that it remains quite expensive. For this reason the much less costly alpha-2 agonist, clonidine, may be the most practical agent to use to blunt the noradrenergic response of centrally mediated sympathetic stimulation and resultant emergence delirium.

The intravenous induction agent propofol has been studied extensively for its ability to decrease emergence delirium in both children and adults. A study by Abu-Shahwan (2007) showed that doses of propofol of 1 mg/kg just prior to emergence from general anesthesia dramatically reduced the incidence of emergence delirium and was not shown to delay recovery or discharge time. Unlike the effect with dexmedetomidine, the effect of propofol appears to be time sensitive, as only doses given just prior to emergence or by continuous infusion (as in total IV anesthesia) are effective (Uenzono, Goto & Terui, 2000). When propofol is given earlier in a case, it has no effect on the incidence of emergence delirium (Cohen, Finkel & Hannallah, 2002). Another potential agent for the reduction of emergence delirium is lidocaine. In a study by Elgebaly (2013) it was shown that preoperative lidocaine injected into the sub-tenon space for ocular surgery not only reduced airway reflexes and the risk of laryngospasm, but also reduced the incidence of emergence agitation, with no increase in sedation in the recovery room. Rahimzadeh et al. (2014) also examined the effectiveness of lidocaine, but in this case IV

lidocaine was used following mask induction of general anesthesia with sevoflurane. They found a significant decrease in emergence agitation with the use of this medication and an even greater decrease when it was used in combination with propofol. These results led researchers to speculate that lidocaine is effective by way of its ability to diminish the sympathetic response to intubation and noxious stimuli, thereby decreasing activation of the sympathetic nervous system.

Fentanyl has been shown to reduce the incidence of emergence delirium as well, with a recommended dose to achieve this effect of 2.5 mcg/kg intravenously (Ford, 2013). However, other studies have shown that 1 mcg/kg IV given ten minutes prior to the end of surgery is adequate, and will lessen the chances of any adverse side effects (Vlajikov & Sindjelic, 2007). One might speculate that fentanyl's effect is simply due to its analgesic properties, as emergence delirium has long been associated with increases in post-operative pain. However, in studies of pediatric patients undergoing objectively non-painful MRI studies, the use of fentanyl dramatically reduced the frequency of emergence delirium (Bonhomme et al., 2012). One of the major disadvantages of fentanyl over propofol is the increased incidence of nausea and vomiting that occurs with a narcotic-based approach. A study by Kim, Moon, Kim and Lee (2012) found a 26% incidence of PONV when fentanyl was used, as compared to just 6% with the use of propofol.

While practitioners may be concerned about the risk of increased respiratory depression and prolonged recovery from anesthesia when adjunct medications such as propofol and fentanyl are used, these concerns do not appear to justify any routine withholding of such medications for the prevention of emergence delirium during post

anesthesia recovery. There are a variety of nonpharmacological methods that have proven to be effective in reducing the incidence of emergence delirium as well. These consist of a quiet induction environment with decreased sensory stimuli, music therapy, and distraction by way of videos or touch screen games. Interestingly, parental presence at induction has not been found to be consistently effective, although parental presence following emergence is (Dahmani, Delivet, & Hilly, 2014).

Recent literature has devoted a great deal of coverage to concerns over postoperative cognitive dysfunction, although this is not a new phenomena and has been recognized for over a century (Woffard & Vacchiano, 2011). Some have speculated that emergence delirium and postoperative cognitive dysfunction may be somehow linked, or that experiencing emergence delirium puts one at increased risk for postoperative cognitive dysfunction. While both syndromes can be characterized primarily by the presence and severity of apparent confusion and agitation, emergence delirium is transient and has not been linked to any increase in mortality, whereas postoperative cognitive dysfunction is associated with both increases in mortality and can remain quite pervasive in some individuals years after the provoking surgery (Woffard & Vacciano, 2011). Although emergence delirium is transient, it has been found to be associated with postoperative maladaptive behavioral changes, with children who display emergence delirium being seven times more likely to develop postoperative maladaptive behaviors such as night terrors, bed wetting, general anxiety and loss of appetite for up to 2 weeks following surgery (Kain et al., 2004, Kain et al., 2006). Of note, it has been found that children given preoperative midazolam and therefore had lower preoperative anxiety levels had fewer maladaptive behavioral changes following anesthesia even though the

incidence of emergence delirium was unchanged (Kain, Mayes, Caramico, Wang, & Hofstadter, 1999).

Discussion

There has been much progress made in our understanding of emergence delirium since it was first described in the early 1960s. Not only has there been a vast increase in our knowledge of human physiology and pharmacology, but there has also been an explosion of attention paid to all manner of medical conditions. Anesthesia providers now have a wide range of pharmacological agents that can be used to help attenuate reactions to anesthesia such as emergence delirium, and new agents are continually being investigated. Although an understanding of the precise mechanism behind emergence delirium continues to elude us, our improved mapping of the human brain at the neuronal and receptor levels has led to a much better understanding of the functions various brain regions play in both arousal and aggression. As further progress is made in neuroscience we will continue to gain a deeper understanding of complex phenomena such as emergence delirium, and consequently we may be able to target treatment to fully prevent this disturbing and potentially dangerous condition.

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