Letters to the editor

‘Melatonin as a sedation substitute for diagnostic procedures: MRI and EEG’

SIR–We read with interest the experience of Espezel and colleagues1 with the use of melatonin for Auditory Brainstem Response Threshold (ABR) testing. We too have used melatonin as a sedation substitute for diagnostic procedures.

Espezel et al. report disappointing results. Only three of six children had successful ABRs. Although five of the six children fell asleep, none of the children stayed asleep during the test.

We have used melatonin for EEGs in 30 children2. Twenty-four fell asleep after a mean of 21 minutes and an EEG was obtained in 28 children.

We have also used melatonin as a sedative substitute for brain MRI in 27 children. This was less successful. Only 16 of 27 children fell asleep after a mean of 31 minutes and a satisfactory MRI was obtained in 12 children. Seven of the 16 children woke up during the procedure.

The main difference between the EEG and MRI settings is the noisy environment of the MRI. Another difference is that during MRI the child is moved onto the scanner bed (although only three of 16 sleeping children woke up with movement).

Like Espezel et al. we hypothesize that melatonin may not sufficiently mask environment disrupters of sleep. Noise disrupts normal sleep. Although melatonin induces sleep it cannot be relied upon to maintain sleep in a noisy environment.

We agree with Espezel et al. that melatonin can be useful for diagnostic procedures as a sleep inducer, but is less useful in noisy environments.

E Wassmera
M Fogartyb
A Pageb
K Johnsonb
E Quinc
S Seric
W Whitehousea

Birmingham Children’s Hospital
Neurologya, Radiologyb and Neurophysiologyc Departments
Steelhouse Lane
Birmingham B4 6NH
United Kingdom

References

‘Dramatic improvement of severe acute disseminated encephalomyelitis after treatment with intravenous immunoglobulin in a three-year-old boy’

SIR–For more than two decades acute disseminated encephalomyelitis (ADEM), also called postinfectious encephalitis, has been treated with glucocorticoids with apparent success in the majority of patients1. Some patients, however, do not respond to this treatment. Plasmapheresis has been used successfully in a few adult patients with fulminant ADEM2.

In recent years, two children with ADEM treated with high-dose intravenous immunoglobulin (IVIG) with apparent success, have been described in the literature3,4. We recently treated a third child with IVIG5. Unlike the two previous cases, she suffered from severe ADEM with unconsciousness and stayed on high-dose methylprednisolone (that had been without initial effect) while treated with IVIG.

This child was a three-year-old boy admitted to the pediatric department on suspicion of meningitis. There was no history of fever or other signs of infection or of vaccination in the weeks preceding the admission, at which time she was passive, reacted weakly to stimuli, and was without visual contact.

Lumbar puncture revealed clear CSF with slightly elevated cell count (117 x 10^6/l) with a predominance of mononuclear cells and normal sugar and protein content. Acute CT of the brain was normal. Blood samples showed elevated C-reactive protein (720 nmol/l) and mild leukocytosis (19,0 x 10^9/l) and neutrophilia (16 x 10^9/l). Herpes encephalitis was suspected and treatment with intravenous acyclovir commenced.

The following day the boy was still stuporous without auditory and visual contact and only a weak reaction to
pain stimuli and skin touch. He had reduced power, tone, and mobility, particularly in the left-sided extremities, hyperactive patella reflexes, bilateral ankle clonus, and Babinski’s responses.

EEG was severely abnormal showing diffuse low-frequency activity with mild right-sided predominance, consistent with encephalitis. MRI of the brain showed patchy and confluent changes in the white matter of the cerebral hemispheres, the basal ganglia, the mesencephalon, and the pons (Fig. 1a). The changes were compatible with ADEM, and intravenous methylprednisolone 2 mg/kg/day was added to the treatment.

During the following two days the child’s condition worsened with unconsciousness, lack of reactions to external stimuli, total paralysis, and signs of increased intracranial pressure, i.e. hyperventilation and bradycardia. Acute MRI of the brain revealed significant deterioration (Fig. 1b). The changes now covered two-thirds of the right hemisphere and a great part of the left. New changes were seen in the cerebral cortex and the medulla oblongata. The child was treated with IVIG 1 g/kg/day for seven days. Twelve hours after the addition of IVIG spontaneous movements were seen and the child became responsive. During the following week the patient’s condition gradually improved, and after 14 days he had recovered, except for slightly reduced power in the left-sided extremities.

Prednisolone was then gradually tapered over three weeks. At outpatient follow-up, six weeks after the first appearance of symptoms, the boy had entirely recovered apart from mildly reduced motor control of the left arm. MRI of the brain 11 months after the first appearance of symptoms showed almost complete regression of the above mentioned changes (Fig. 1c). Persistent high intensity areas were seen in the subcortical white matter of both parietal regions. There was no suspicion of loss of substance. At this time the boy was entirely well, and neurological examination was normal.

IVIG has been used in the treatment of a great variety of autoimmune neurological disorders. In some of these disorders, e.g. Guillain-Barré syndrome and chronic inflammatory demyelinating polyneuropathy, which both seem to be pathogenetically closely related to ADEM, the benefit of IVIG has been proven in controlled clinical trials. The mode of action of IVIG on the immune system in these disorders is generally unknown, but the information available suggests, that multiple mechanisms may be involved. These include neutralization of autoantibodies by passive transfer of anti-idiotypic antibodies, down regulation by Fc receptor interactions of antibody production by B cells and of cytokine release and phagocytosis by T cells and macrophages, solubilization of immune complexes, inhibition of complement mediated cytolysis and

![Figure 1b](image1b.jpg) Axial T2 weighted image two days after first MRI. Image shows marked progression in number and extension of hyperintensities, and there is now involvement of cortex cerebri as well. Brain is swollen.

![Figure 1c](image1c.jpg) Axial T2 weighted MRI 11 months after first appearance of symptoms showing persistent high intensity areas in subcortical white matter of both parietal regions. Cortex cerebri now appears normal.
inhibition of superantigen-mediated T-cell activation. 

Recently it has been suggested that the most plausible unifying explanation for the efficacy of IVIG in the treatment of antibody-mediated autoimmune diseases may be the one originally described by Brambell and coworkers in 1964, concerning concentration-dependent elimination of IgG from plasma.

According to this theory, IgG that is picked up from plasma by cells binds to a protective receptor FcRn in endocytotic vesicles and subsequently returns intact to the circulation instead of passing on to the lysosomes to be degraded. When the FcRn receptor is saturated, e.g. with IVIG, IgG is eliminated in direct proportion to its plasma-concentration. In this way IVIG is thought to accelerate the elimination of autoantibodies in autoimmune diseases. Various experimental data support the theory.

Moreover, it has been shown that glucocorticoids down regulate the expression of FcRn messenger RNA. This is compatible with a possible synergistic effect of IVIG and glucocorticoids in some autoimmune diseases, as indicated by a Dutch pilot study of combined IVIG and high-dose glucocorticoids in some autoimmune diseases, as indicated by a Dutch pilot study of combined IVIG and high-dose glucocorticoids versus IVIG therapy alone for Guillain-Barré syndrome. We suggest that this possible synergistic effect may also be a plausible explanation for the dramatic recovery after the supplementation of the steroid treatment with IVIG in our patient with severe ADEM.

Neither treatment with glucocorticoids nor with IVIG in ADEM is evidence based. The final documentation for the therapeutic effect would demand prospective randomized multicenter based studies. However, since ADEM is a potentially dangerous disease and the therapeutic effect of steroids seems empirically documented, such placebo-controlled studies might be problematic from an ethical point of view.

In the light of the above data we recommend treatment of ADEM with IVIG in all patients with a reduced level of consciousness, at least when initial treatment with glucocorticoids has no apparent effect.

Jesper B Andersen MD
Lene H Rasmussen MD
Margrethe Herning MD
Anders Pærregaard MD

aPaediatric Department
H:S Hvidovre University Hospital
bThe Danish Scientific Center for Magnetic Resonance
H:S Hvidovre University Hospital
Copenhagen
Denmark

References

‘Beliefs about pain among professionals working with children with significant neurologic impairment’

SIR—Over the past years there has been a growing interest in pain in non-verbal populations of infants, children, adolescents, and the frail elderly with dementia. The frequent failure to appreciate pain in this context has lead some to the erroneous belief that individuals with cognitive and communication impairment may be indifferent or insensitive to pain. However, there is no reason to believe that preverbal infants, the frail elderly with dementia, or children with communication impairments are spared any of the misery and suffering that is inherent to the human experience. Emerging work is providing substantial evidence of the unique pain experiences among children with a significant neurologic impairment (SNI).

A particularly crucial aspect of this pain experience is the beliefs health care professionals bring to recognizing and managing pain in this setting. Health care professionals’ understanding of pain is integral to providing adequate and timely health care. There is considerable evidence that the recognition and management of pain is influenced by the beliefs and attitudes of health care professionals. In this letter we report on a qualitative survey we undertook to examine beliefs about pain among professionals working with children with SNI.

Given the perceived or real blunted pain response among individuals with SNI and the importance of health care workers’ pain beliefs and attitudes, we sought to learn more about pain in the clinical setting by investigating pain-related beliefs among professionals working with children and adolescents with SNI. A questionnaire was developed using information gathered through a focus group. This focus group of 20 professionals working at Sunny Hill Health Centre for Children, Vancouver, (a tertiary-care provincial facility for children with SNI) helped to examine beliefs about pain among professionals working with children with SNI.

We sought to learn more about pain in the clinical setting by investigating pain-related beliefs among professionals working with children and adolescents with SNI. A questionnaire was developed using information gathered through a focus group. This focus group of 20 professionals working at Sunny Hill Health Centre for Children, Vancouver, helped to define particular areas or themes relating to pain in this population. The hospital’s in-patient population included children with SNI due to a variety of causes including cerebral palsy, acquired brain injuries, and metabolic diseases.
From the results of this focus group, a 24-item questionnaire was developed to probe the professionals’ understanding of pain in this population and their experiences with pain in the week before completing the questionnaire. The questionnaire was divided into four sections to identify information about: (1) the professionals’ practice experience and patients with whom they worked, (2) the pain caregivers thought individuals experienced, (3) the communication of pain, and (4) pain management options.

The professionals in our survey were any professional working with our in-patient population of children with SNI during a given 14-day period. The questionnaires were handed out on our ward and adjacent office areas where the professionals worked. Following the first administration of the questionnaire, a reminder plus an additional questionnaire were sent out for additional response a week later. There was equal representation proportional to all disciplines thereby reducing any sampling bias.

Our survey had an 80% response rate (50 out of 70), with a multidisciplinary background. Of the 50 respondents, 16 were nurses, 23 were physio- or occupational therapists, 4 were speech and language therapists, and the remainder came from a variety of other health professionals (n=7). The respondents were an experienced group of professionals, 58% of whom had over six years experience working with children in this setting.

The majority of children with whom they worked were entirely dependent on others for activities of daily living, (ADL) had moderate to severe communication impairments, and over 50% were moderately to severely cognitively impaired.

Pain in this setting has been traditionally thought to be musculoskeletal or surgical in origin and was predominantly disease or anatomy related. Our respondents also provided additional specific painful locations such as joints, skin, mouth, genitourinary, and gastrointestinal tracts.

Seventy-one percent of professionals responded that pain was part of the children’s everyday lives and 84% perceived that pain sometimes interfered with routine ADL. Lying in bed was reported to be associated with daily pain (marked/mild/moderate/mild) by 41% of respondents; sitting, 88%; transfers, 63%; feeding, 47%; and oral care, 66%.

Communication and oral care were recognized as painful, related to concurrent oral disease and the use of communication technology that may involve neck or mouth movements.

The majority of respondents (79%) reported that there was an increased frequency of procedures (gastric tube replacements, blood collection, orthopedic interventions, surgery, injections, or dental treatment) performed on children with SNI compared to a non-impaired pediatric population. Seventy-five per cent reported that the children under their care experienced pain as a consequence of these frequent ‘routine’ procedures. The pain intensity associated with these procedures was thought to be equal to or greater than that of typical children as perceived by 65% of our sample of professionals. Interestingly, 35% responded that they were not sure about the level of pain.

Our sample reported that even with children who they knew well the communication of pain was difficult. Although the presence of pain could be identified (Table I), especially with cry, facial expression, and words when they were available, the specific location or source of pain could only be identified using non-specific behavioral changes (Table I). The commonly used pain signals from changes in vital signs, the use of augmentative communication devices, and standard behavioral or facial scales were not found to be particularly helpful in identifying the presence or location of the pain, though in other pediatric settings these tools are thought to be very useful.

When asked how well children communicated their pain, only approximately 20% of the professionals felt that pain was adequately expressed and/or accurately located. More than two thirds (69%) of individuals reported that they could not often or always perform an accurate assessment of pain when they thought pain was present.

The final area of the questionnaire examined pain management options. The most frequent pharmacologic options used were anti-inflammatory and anti-spasticity medications. Other options used for pain management included ice, hydrotherapy, splinting, and specialized seating systems. Often a practical approach was utilized with 64% reporting that distraction and changes in activity were useful options available for pain relief.

This preliminary survey reports on the understanding of pain among a multidisciplinary sample of experienced health care professionals working with children with moderate to severe neurologic impairment. In general, there was a high level of awareness of pain in the lives of children with SNI. While pain was viewed as a common experience even as a part of ADL, it was recognized as being poorly communicated, localized, and inadequately treated. These findings raise important questions about the pain experience among children with SNI and have material implications for daily care. Even among experienced caregivers, pain was not well appreciated by all. The commonly used pain indicators such as physiologic measures and behavioral and facial scales were not found to be helpful measures of pain for this population. Finally, pain was not easily assessed or thought to be adequately managed even when it was recognized.

Pain clearly plays an important role in the lives of children with SNI and their caregivers. It appears to have an impact on all aspects of the quality of life. The results of this survey illustrate the urgent need for more knowledge regarding the assessment and management of pain in this particular pediatric population.

### Table I. Percentage of respondents identifying utility of behaviors and/or signs that may identify presence and location of pain

<table>
<thead>
<tr>
<th>Presence of pain (%)</th>
<th>Location of pain (%)</th>
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<tbody>
<tr>
<td>Changes in vital signs</td>
<td>55</td>
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<tr>
<td>Behavioral scale</td>
<td>19</td>
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<tr>
<td>Facial rating scale</td>
<td>25</td>
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<tr>
<td>Facial expression</td>
<td>92</td>
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<tr>
<td>Changes in motor function</td>
<td>92</td>
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<tr>
<td>Changes in muscle tone</td>
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<tr>
<td>Communication device</td>
<td>54</td>
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<tr>
<td>Cry/fret</td>
<td>98</td>
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<tr>
<td>Words</td>
<td>85</td>
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</tbody>
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Percentage indicates degree of helpfulness each factor demonstrated.
References