Management of chronic pain in children

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It is one of the “Rights of the Child” not to have to endure pain. In the past there was little knowledge or understanding of pain in children. Many of us were taught that babies do not feel pain. Minor operations such as circumcision were often performed on neonates with no analgesia. We now know this to be a cruel misconception and in fact neonates have an enhanced, more global response to pain. Sensitisation of the nervous system by trauma at such an early age can lead to different pain behaviour in later life. This better understanding of paediatric pain has led to a revolution in pain management for acute and perioperative pain in children. Most children’s hospitals now have a well established “pain team” who ensure that protocols are followed and that pain is adequately assessed and treated. It is from this initiative that the problem of chronic pain in children came to be recognised, and there are now several chronic pain clinics around the country. The Pain Society has a special interest group for paediatric pain management.

In my own institution the chronic pain clinic had its origins as an extension of the acute pain service. It has developed into a multidisciplinary unit allowing an integrated pain management programme. Pain clinics tend to be the last resort in the management of pain, when initial treatments have failed. Most chronic pain is amenable to treatment with simple measures; however, for the intractable or resistant chronic pain, a multidisciplinary approach is essential. Chronic pain leads to devastating life changes for the child and family and these must be addressed as well as attempts to control the pain itself.

DEFINITIONS AND CONCEPTS

What do we mean by “chronic pain”? The most widely accepted definition is that of Bonica. He defined chronic pain as: “Pain which persists a month beyond the usual course of an acute disease or reasonable time for an injury to heal or is associated with a chronological pathological process which causes continuous pain or pain which recurs at intervals for months or years”.

Pain is an adaptive mechanism. Pain is a sensation and a reaction to that sensation. It helps us to avoid noxious stimuli in our environment and protect any injury while healing takes place. Pain is incorporated in our body image, localised and then changes our behaviour. Our body image and pain behaviour develop throughout childhood. For example, a child under 5 years of age may describe any pain as “tummy ache”. The pain may be somatic, visceral or both, each type of pain having a different effect on the child. Somatic pain is easier to incorporate into the body image. A cut or broken arm can be seen—it is part of the body, outside of “self”. Visceral pain, on the other hand, is more difficult to visualise. It is mediated mainly by C fibre pathways with anatomical connections into the limbic system. This is more frightening and has a greater emotional response. It is also harder to localise. We do not have a well developed internal body image. A good example of this is appendicitis, which presents as a central abdominal pain until our nervous system works it all out.

So, pain may be useful and protective, and this is easier to bear, and usually time limited. Chronic pain can be thought of as “useless” pain. This can lead to more suffering. Suffering is a global concept, associated with negative feeling and impaired quality of life. This type of pain needs a different approach and this is what is provided by pain clinics in their pain management programmes.

The last few years have seen a considerable development in our understanding of pain mechanisms. Laboratory and clinical studies have demonstrated increased spontaneous activity involving both mechanosensitivity and chemosensitivity in damaged peripheral nerves. The consequent increased neural activity effects changes in both the dorsal root ganglion and the dorsal horn of the spinal cord. This is the well known phenomenon of dorsal horn windup. Abolition of spontaneous activity from damaged nociceptors or nerves may allow remodelling of the dorsal horn, and other areas of the central nervous system, resulting in prolonged pain relief.

This is an example of how the nervous system adapts to a chronic stimulus. The nervous system “learns” and tends to facilitate chronic stimulation. This has led to the concept of the plasticity of...
the nervous system which is now well established.\textsuperscript{9–11} Understanding of the way in which the nervous system adapts to chronic pain inputs has led to a range of techniques and specific drug treatments for the control of chronic pain.\textsuperscript{12} This “learning” takes place throughout the nervous system all the way through to how the body image is mapped into higher centres and hence to consciousness.\textsuperscript{13}

Thus the pain may become “neuropathic” (from the Greek \textit{neuro}, meaning nerves, and \textit{pathy}, meaning abnormality). This is pain either originating from abnormal firing of nerve cells, or abnormal propagation of sensory input so that non-noxious sensations are perceived as painful. This type of pain relies on different transmitters within the nervous system, notably the \textit{n}-methyl \textit{d}-aspartate (NMDA), \textit{\gamma} amino butyric acid (GABA), and \textit{\alpha}-amino-3-hydroxy-5-methyl-4-isoxazolepropionate (AMPA) systems.\textsuperscript{14–15} Neuropathic pain does not usually respond to conventional analgesic regimens and is opiate resistant.

\textbf{TREATMENT PRINCIPLES}

These patients have often been seen by many other specialists. Somewhere along the line someone will have told them that it is all in their head or they are merely attention seeking. Tensions within the family will be running high. There is usually a great deal of guilt both in the child, and in the parents who have a child in pain which is not being adequately treated. The approach must be to obtain adequate information from all concerned. Referral letters can often be unhelpful, emphasising the impression that this is an imagined problem. Our practice is to send the child a detailed questionnaire to be filled in before the first clinic appointment. This deals with all aspects of the pain. It sends the message that we are taking them seriously, brings the family together to fill in the form, and provides a basis for the first clinical assessment. The approach is then that we know you have pain and that the treatment will be planned and progressive. There is no “magic wand”. The emphasis is always that we will help you deal with the pain and get on with your life, as well as specific measures to treat it.

The next step is to try to gain control and break the cycle of pain. Patient controlled methods are preferable as they give some control to the child. They have something they can do. This can also help allay the fear that the pain may crescendo and become completely uncontrollable. Children often fear what the pain may be like rather than deal with what it is. Anyone who has performed a venepuncture on a child will know this well! A transcutaneous nerve stimulation device is extremely useful here and is often our first line of approach. For visceral pain we have found a TSE (transcutaneous spinal electroanalgesia) machine extremely useful.

Careful enquiry must be made as to the effect of the pain on the child’s sleep pattern. If the child is kept awake or woken by pain, the whole family will be woken and lose sleep. This has a detrimental effect on everyone’s mood and ability to cope. Pain relief must be first directed to give the child a good night’s sleep. Melatonin is extremely useful for re-establishing normal sleep patterns.

\textbf{MEDICAL TREATMENT}

Having gained some control and hopefully the confidence of the child and family, the next step is to explore the impact of the pain on the school and family life. This brings in other members of the team. Adjunctive treatments can be explored at this stage. Drug therapies are introduced as part of the programme and the concept introduced of starting with simple and non-invasive treatments (table 1) and escalating as necessary.

There is still a place for conventional analgesia regimens. Many children will respond and not progress to the more intractable pain picture. Care must be taken to give adequate \textit{analgesic} doses of these drugs and to make full use of the synergism between different drug groups. A good example of this is to combine paracetamol with non-steroidal anti-inflammatory drugs (NSAIDs).

More specific agents are now available for neuropathic pain (table 2) and their mechanisms of action are better understood.\textsuperscript{16,17} Our first line treatment for somatic neuropathic pain is gabapentin, lamotrigine being preferred for visceral pain. Nerve blocking techniques are useful, and may be peripheral or central. Local anaesthetic administered by subcutaneous infiltration or directly to specific nerves can produce long lasting pain relief for a variety of chronic painful conditions.\textsuperscript{18} Pain relief will often last for months and can be permanent. Abnormal activity within the sympathetic nervous system can lead to specific \textit{sympathetically mediated} pain syndromes such as reflex sympathetic dystrophy (RSD).\textsuperscript{19–21} RSD is also known more properly as complex regional pain syndrome type 1. We have, in our unit, a particular interest in sympathetic block for RSD and coeliac plexus block for upper abdominal pain in complex needs children.

Epidural block is a useful treatment in chronic pain and is often a technique of last resort. The catheter can be tunnelled to allow for long term use. This can be particularly useful in palliative management in terminal illness. There are difficulties involved in managing a patient with a long-term epidural catheter, but these can be overcome with careful monitoring. There are more drug preparations now available for administration by the epidural or caudal route as well as techniques for modification of neuronal function at this level.\textsuperscript{22}

Many treatments, despite involving short term modification of the neural pathways, nevertheless have long term effects—for example, injecting local anaesthetic drugs. We are manipulating the plasticity of the nervous system. I like to think of this as re-booting the system so that the normal programme can run. In this computer age children relate well to this analogy.

Nausea is a common symptom of chronic pain associated with renal or hepatic dysfunction, chemotherapy and of course opiates. In children, however, we find that if the dose

\begin{table}
\begin{tabular}{ll}
\hline
\textbf{Table 1} & Simple analgesics: first line treatments for pain \\

\hline
Paracetamol & \begin{tabular}{ll}
60 mg/kg/day in four divided doses (analgesic dose) \\
(maximum 4 g daily)
\end{tabular} \\

Non-steroidal anti inflammatory drugs (NSAIDs) & \\
Caution if bleeding risk, asthma, atopy, renal dysfunction, GI ulceration/ bleeding, on antiocoagulants (avoid if \(<6\) months or weight \(<10\) kg) \\
Diclofenac & \begin{tabular}{ll}
1 mg/kg up to 8 hourly \\
46 kg 20 mg daily
\end{tabular} \\
Ibuprofen & \begin{tabular}{ll}
10 mg/kg up to 6 hourly \\
>5 years old: 10 mg/kg in 2 divided doses \\
(higher doses can be used)
\end{tabular} \\
Naproxen & \begin{tabular}{ll}
\(<5\) years old: not recommended \\
16–25 kg 10 mg daily \\
26–45 kg 15 mg daily \\
\(=46\) kg 20 mg daily
\end{tabular} \\
Piroxicam & \begin{tabular}{ll}
\(<1.5\) kg 5 mg daily \\
16–25 kg 10 mg daily
\end{tabular} \\
\hline
\end{tabular}
\end{table}
Table 2  Neuropathic pain drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabapentin</td>
<td>&gt;50 kg: max dose up to 2400 mg/24 hours</td>
</tr>
<tr>
<td></td>
<td>35–50 kg: max dose up to 1600 mg/24 hours</td>
</tr>
<tr>
<td></td>
<td>25–35 kg: max dose up to 1200 mg/24 hours</td>
</tr>
<tr>
<td></td>
<td>&lt;25 kg: not recommended</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>&gt;50 kg: start 10 mg twice daily (max 40 mg twice daily)</td>
</tr>
<tr>
<td></td>
<td>30–50 kg: start 5 mg twice daily (max 25 mg twice daily)</td>
</tr>
<tr>
<td></td>
<td>&lt;30 kg: not recommended</td>
</tr>
<tr>
<td>Topiramate</td>
<td>&gt;40 kg: 100 mg at night should be effective at this dose</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Tricyclic antidepressants requires hold the sodium channel blockers but if these have been ineffective then it can be useful in the older child</td>
</tr>
</tbody>
</table>

Table 3  For severe chronic pain/palliative care

<table>
<thead>
<tr>
<th>Opioids</th>
<th>Minimum monitoring standard for in-patients. Do not mix opioids or routes of administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine iv loading dose</td>
<td>&gt;3 months old 100 µg/kg</td>
</tr>
<tr>
<td>Titrate to effect</td>
<td>Switch to oral as soon as possible</td>
</tr>
<tr>
<td>Oral opioids</td>
<td></td>
</tr>
<tr>
<td>Morphine sustained</td>
<td>&lt;15 kg: expert use only release tablet: opioid 15–25 mg 5 mg twice daily</td>
</tr>
<tr>
<td></td>
<td>naive child 25–50 kg 10 mg twice daily</td>
</tr>
<tr>
<td></td>
<td>&gt;50 kg: 15–20 mg twice daily</td>
</tr>
<tr>
<td>In addition prescribe</td>
<td>morphine oral solution (oral release morphine sulfate tablets) for breakthrough pain.</td>
</tr>
<tr>
<td></td>
<td>In an opioid naive child, prescribed as one fifth of total morphine sustained release tablet dose every 4–6 hours as needed</td>
</tr>
<tr>
<td></td>
<td>If more than 3 doses per day are needed increase morphine sustained release tablet dose by adding total dose of liquid (or normal tablets) needed to the sustained release tablet dose and divide into 2 equal doses</td>
</tr>
<tr>
<td></td>
<td>Always titrate to effect. Doses may be considerably higher in children who are not opiate naive.</td>
</tr>
<tr>
<td>Oxycodone and oxycodone are alternatives to morphine sustained release tablets and oral morphine liquid solutions</td>
<td></td>
</tr>
</tbody>
</table>

Table 4  Antiemetics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Domperidone</td>
<td>200–400 µg/m²/hour patch</td>
</tr>
<tr>
<td></td>
<td>15 kg: quarter patch</td>
</tr>
<tr>
<td></td>
<td>&gt;15 kg: half patch</td>
</tr>
<tr>
<td></td>
<td>&gt;30 kg: not recommended</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>500 µg/kg/day oral or iv</td>
</tr>
<tr>
<td></td>
<td>Also has a prokinetic effect on the upper gastrointestinal tract which may be useful</td>
</tr>
<tr>
<td></td>
<td>Anticholinergic</td>
</tr>
<tr>
<td></td>
<td>Hyoscine topical patch: Dose &gt;35 kg 1 mg patch</td>
</tr>
<tr>
<td></td>
<td>(Scopolam 10% TTS)</td>
</tr>
<tr>
<td></td>
<td>Not recommended &lt;10 years</td>
</tr>
<tr>
<td></td>
<td>A useful drying agent for excess secretions especially in palliative care</td>
</tr>
<tr>
<td></td>
<td>Phenothiazine</td>
</tr>
<tr>
<td></td>
<td>Levomepromazine</td>
</tr>
<tr>
<td></td>
<td>Excellent for intractable nausea/vomiting. Sedative and useful for “terminal agitation” in palliative care</td>
</tr>
<tr>
<td></td>
<td>Initial dose 250 µg/kg/day given in 2 or 3 divided doses. This dosage may be increased gradually until an effective level is reached which should not exceed 40 mg/kg/day for a child less than 12 years of age</td>
</tr>
</tbody>
</table>

of opiates is appropriate for the pain then side effects do not present a significant problem. It is only when the dose is escalated in a futile attempt to control pain that has become opiate resistant, that the unwanted effects emerge. Nausea can be as distressing as the pain itself and should be treated aggressively.

The drugs and doses that we use in our clinic and their indications are listed in tables 1 to 5.

New drugs on the horizon which may be useful for neuropathic pain are levetiracetam, an anti-epileptic with a novel mode of action, and the AMPA blocking agent anatantamide.

ETHICS

Many of these new techniques and methods have resulted in some ethical dilemmas. For example, most of the drugs used are licensed for use in children or are being prescribed for conditions that are “off-label” for that drug.

COMPLEMENTARY THERAPIES

In a pain management programme the input of other health care professionals is essential. Physiotherapy is a major adjunct to successful management of chronic pain and in our unit also provides a forum for the use of other techniques such as acupuncture and aromatherapy.24 Often our treatment merely provides a “pain-free window” for physiotherapy to be effective. Psychologists can help with a cognitive behavioural approach and organise a programme for return to school in association with community health teams. Liaison with the psychiatric unit will help with management of the psychiatric traumas, notably depression, associated with chronic pain.

Acupuncture can be extremely effective and is used extensively in our clinic. This must be carefully introduced and is not of course for the needle phobic! We use both traditional and (more usually) trigger point needling techniques. The complexity of chronic pain presentations
will often mean that some psychological preparation of the child and family will be necessary before therapeutic intervention. The concept is one of preparing the soil for the therapeutic seed.

Families will sometimes consult other complementary therapists. We try to work this in to our programmes where possible. We have a close liaison with the local homeopathic therapists. We have also had children who have been helped by such varied therapies as reflexology, phrenology and Chinese herbal tea.

There are times when the “drugs don’t work”. The focus is then on living with the pain and cognitive behavioural therapy can be very effective here. The pain clinic can act as a centre of support for the child and family and help with the difficult transition through teenage years and then on to adult based pain clinics. Adult services will usually have much longer waiting times and the transition must be carefully managed.

THE FUTURE

There are many promising new developments in the study of chronic pain. We have several new drugs which can be used to modify the method of transmission of chronic pain and research continues in this area. New developments in functional MRI give us a better understanding of the central changes associated with chronic pain and its treatment. Remapping sensory input into consciousness is an exciting possibility.23 There is also increasing evidence of a genetic basis or predisposition to chronic pain syndromes opening up further avenues of treatment.24–28 These advances will help us in our understanding of the effects of our therapies on the pain pathways and central pain perception, and may also guide in the choice of appropriate treatment.

Competing interests: none

Table 5 NMDA (N-methyl-D-aspartic acid) antagonists

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidurally: epidural agents</td>
<td>may be used to test efficacy 1 mg/kg diluted in 5 ml water: split out after 2 mins or if feeling dizzy.</td>
</tr>
<tr>
<td>Intravenous: start at 15 mg/kg in 24 hour period diluted in normal saline to give a dose volume of 2–4 ml/hour. May need up to 25 mg/kg/24 hours.</td>
<td></td>
</tr>
<tr>
<td>Epipodally: 0.6 mg/kg and then 0.8 to 1 mg/kg in 24 hour period Methodone.</td>
<td></td>
</tr>
</tbody>
</table>

References

24. Kemler MA, Rijks CP, De Vet HC. Which patients with chronic reflex sympathetic dystrophy are most likely to benefit from physical therapy? J Manipulative Physiol Ther 2001;24:272–8.