HUNTER
PAIN CLINIC

Marc's Musing JAN-DEC 2012

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Comment – this pooled data from three RCTs really is the clincher to suggest that this is an appropriate treatment strategy to augment non-response in patients with depression prescribed anti-depressants. The dose of Aripiprazole used is usually low (≤ 10mg) and thus has a low side effect profile. Once remission has been achieved, one can subsequently consider reducing or eliminating the Aripiprazole. This is indeed a landmark study having significant offence on prescribing and treatment recommendations.

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Comment: It is good to see a randomised controlled trial in this area. Whilst the evidence base now shows that the local anaesthetic block should have steroid added to it, what we don't know is whether there are additional benefits at six or twelve months from a single injection or whether the block needs to be repeated and if there is additional benefit from doing so. Although we have no evidence, I would suggest that common sense would suggest that if there is no benfit from the block, there's little point in repeating it.

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9. Switching Methadone: A Ten Year Experience of 345 Patients in an Acute Palliative Care Unit, Mercadante, Pain Medicine Vol 13 No 3, 2012 pp 399-405

This is from Prof. Mercadante who is very experienced in this area and he showed a 77% success rate in switching patients from opioid non-responsive doses to methadone using 1/5 the morphine equivalent dose split up as a tds dosing scheduled and then titrating up or down from there. It shows on a clinically empirical basis, that this is a highly effective strategy in the palliative care unit.

Long Term Effect of Pulsed Radiofrequency Neurotomy on Chronic Cervical Radicular Pain Refractory to Repeated Transforaminal Epidural Steroid Injections. Choioi et al. Pain Medicine Vol 13 No 3, 2012 pp 368 – 75

This study looks at 21 patients who had stopped responding to transforaminal epidural steroid injections and underwent pulsed RF of the relevant dorsal root ganglion. 74% had a positive clinical outcome at twelve months and global happiness for treatment was a similar figure at 75%.

Comment: This is supportive evidence of the efficacy of this technique although it must be stated that this is a retrospective study and not a randomised controlled trial. However, it's certainly consonant that somewhere in the order of 2/3 of patients will respond positively to the procedure with 1/3 being unresponsive. This certainly is consonant with the experience in the Pain Clinic.

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This study is from Australia's own Andrew Zacest, an Adelaide based Neurosurgeon, whilst he was working with Kim Burchiel in the United States. They looked at patients with spontaneous onset of constant facial pain and if they had evidence of neurovascular conflict on 3 Tesla MRI imaging, with 3D reconstruction, then they underwent a microvascular decompression procedure. What they found was that one in four patients did not benefit from this, but three out of four patients did. Typically, in patients who did benefit, what they found was that the episodic component of their pain was resolved with the operation and in half the cases, the constant pain resolved as well, but in half the cases, the constant pain continued.

Comment: This study opens up the possibility that some patients may be able to be helped with a microvascular decompression specifically where there is evidence of neurovascular conflict on 3D reconstruction MRI imaging. The results of such surgery are likely to be incomplete pain relief, but nevertheless may be considered in the appropriate overall multidisciplinary care of the facial pain patient.

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12. Epidural administration of spinal nerves with the tumour necrosis factor alpha inhibitor, etanercept, compared with dexamethasone for treatment of sciatica in patients with lumbar spinal stenosis. Spine VOl 37, No 6, pp 439 – 44 Ohtori etal

This study from Tubek University in Japan looked at 80 patients in a prospective randomised trial of 3.3mg of dexamethasone with lignocaine vs. 10mg of etanercept with lignocaine in root sleeve injections for patients with radicular leg pain. There was a statistically and clinically significant improved reduction in leg pain in the etanercept group at four weeks, with the dexamethasone group going from a VAS of 7.5 to 5.2, and the etanercept group going from a VAS of 7.9 to 3.5 (p=0.026).

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This paper looked at 62 patients prescribed opioids who were enrolled in a randomised controlled trial to improve prescription opioid medication compliance in the United States. They showed that even in patients who were at low risk for opioid misuse, there was still a sizeable minority (15%) who had identifiable cravings for taking the opioid that they did not act upon. This figure was much higher in those patients at high risk of opioid misuse as one would expect.

Comment: This shows that there is probably a continuum of symptoms where patients may have feelings of taking the next dose or looking forward to the next dose or craving without necessarily acting upon them and having any evidence of opioid misuse. Therefore, rather than a black and white concept, we should think of this as a continuum and that opioids can induce craving even when effectively producing analgesia.

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38. A Prospective Randomised FDA Trial Comparing Cortoss with PMMA for Vertebroplasty Spine Vol 37 No 7 2012 pp 544-550 Bae et al,

This FDA randomised controlled prospective trial examined 256 patients who had vertebroplasty performed for painful osteoporotic vertebral compression fractures who had pain of at least 5/10 and at least 30% disability on the Oswestry Disability Index. The incidence of serious device related adverse events was 4.3% in both groups. There was better maintenance or improvement in ODI at 24 months in the Cortoss group. There was significantly better pain relief at 3 months in the Cortoss group (both statistically significant). This demonstrates that Cortoss has better results for pain reduction at 3 months and for function at 24 months and should be the preferred injectate material for vertebroplasty.

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39. Predictive Factors for Post Herpetic Neuralgia Using Ordered Logistic Regression Analysis, Clinical Journal of Pain, Vol 00, No 00 2011 Kanbayashi et al

This paper from Kyoto looked at 73 patients with acute herpes zoster and factors predicting going on to develop post herpetic neuralgia were documented. It was found that age greater than 75 years had an odds ratio of 2.8 and the presence of deep pain had an odds ratio of 4.2.

Comment: This is probably the best data to date that patients aged 75 or more or patients who present with deep pain, rather than superficial skin pain, should receive aggressive multimodal treatment of their acute zoster pain to try and prevent the development of a post herpetic neuralgia state. The presence of both of these factors would put the patient at extremely high risk of developing post herpetic neuralgia. I think it would be reasonable for general practitioners to use the presence of either of these two risk factors as criteria for referral to a Pain Clinic for further assessment and treatment.

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40. Cravings for Prescription Opioids in Patients with Chronic Pain: A Longitudinal Outcomes Trial, Wasan et al, Journal of Pain Vol 13 No 2, 2012 pp146-54

This paper looked at 62 patients prescribed opioids who were enrolled in a randomised controlled trial to improve prescription opioid medication compliance in the United States. They showed that even in patients who were at low risk for opioid misuse, there was still a sizeable minority (15%) who had identifiable cravings for taking the opioid that they did not act upon. This figure was much higher in those patients at high risk of opioid misuse as one would expect.

Comment: This shows that there is probably a continuum of symptoms where patients may have feelings of taking the next dose or looking forward to the next dose or craving without necessarily acting upon them and having any evidence of opoid misuse. Therefore, rather than a black and white concept, we should think of this as a continuum and that opioids can induce craving even when effectively producing analgesia.

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43. This paper from Shiga University in Japan showed a decrease in the visual analogue scale from 6.5 to 1.9 in the group treated with saline injection and a reduction in pain from 8.1 to 1.7 in the discectomy group.

Comment: On the face of it, it would suggest that this is a reasonable conservative treatment option for patients with radicular pain. However, the fact that there is no basic science research to even suggest this would be a worthwhile technique combined with the fact that patients self-chose whether to undergo discectomy or saline injection, combined with the fact that there are only three month data outcomes, strongly indicates that this is a procedure to be deployed in clinical practice and, at the very least, proper randomised outcomes, measured at one year, need to be conducted in a clinical trial to ascertain whether this is an efficacious and, in particular, a safe technique. Injecting 20ml of fluid into a disc is a very non-physiological event and this paper needs to be interpreted with much caution.

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44. Predictive Factors for Post-Herpetic Neuralgia using ordered logistic Regression Analysis, Clinical Journal of Pain Olv 00, No 00 2011 Kambayashi et al

This paper looked at 73 patients with acute herpes zoster and looked at what factors predicted the patients going on to have post herpetic neuralgia. The factors that predicted this was age greater than 70 or the pain characterised as a deep pain, rather than a superficial pain. Either of these, and especially both, have predicted the subsequently development of post-herpetic neuralgia.

Comment: This suggests that patients with either of these two risk factors should receive early referral to a Pain Clinic for assessment and treatment to prevent chronic post-herpetic neuralgia.

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45. Perceived Injustice: A Risk Factor for Problematic Pain Outcomes: Clinical Journal of Pain VOl 28, No 6, July/August, 2012 Sullivan et al.

This paper from McGill University reviewed the literature on the subject and showed that perceived injustice appears to be associated with problematic health and mental health recovery trajectories after the onset of a pain condition. No studies have been done to date treating this perceived injustice and documenting outcome.

Comment: This is an evolving field but the evidence to date suggests that it may be important to address perceived injustice in pain sufferers to achieve optimal outcome.

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46. No Difference in Nine Year Outcome in Chronic Low Back Pain Patients Randomised Lumbar Fusion vs. Cognitive Behavioural Therapy and Exercise. European Spine Journal, 6th June, 2012 Froholdt et al.

This paper from Oslo looked at a nine year follow up of two randomised controlled trials comparing instrumented lumbar fusion with cognitive intervention and exercises for chronic low back pain. The two studies were merged before the four year follow up. One third of the patients randomised to cognitive intervention exercises had crossed over and been operated on and one third of the patients allocated to lumbar fusion had been re-operated on. On an intention to treat analysis, there was no difference between the two groups. Analysed according to the treatment received, more operated patients used more pain medication and were out of work. The outcome at nine years on the Oswestry Disability Index was not different between the two groups.

Comment: Spine surgery for back pain remains a difficult and enigmatic outcome to achieve over more conservative therapeutic options.

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47. The Change in Deep Cervical Flexor Activity after Training is Associated with the Degree of Pain Reduction in Patients with Chronic Neck Pain: Clinical Journal of Pain Vol 00, No 00, 2011 Falla et al.

This paper looked at fourteen women with chronic neck pain who undertook a six week program of specific training that consisted of a craniocervical flexion exercise performed twice per day for 20 minutes at a time. This targets the deep flexor muscles of the upper cervical region. After training, the activation of the deep cervical flexors increased with the greatest change occurring in patients with the lowest values of deep cervical flexor EMG amplitude at baseline and there was a significant relationship between initial pain intensity and subsequent change in pain level with training and change in EMG amplitude for the deep cervical flexors during craniocervical flexion.

Comment: This shows that this training exercise reduces pain as well as improving the activation of these muscles. This should be considered an important part of treating patients with chronic neck pain.

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48. Demographic and Medical Parameters in the Development of CRPS: A Prospective Study on 596 Patients with a Fracture, Pain Vol 153, pp 1187 – 1192, 2012 Beerthuizen et al.

This prospective Dutch study showed that using the most restrictive criteria of Harden and Bruehl, 7% of patients developed CRPS after a fracture. If one used Veldman's criteria, 21% developed CRPS.

Comment: Clinically, the Bruehl criteria appeared to resonate with what I see in clinical practice. Certainly a rate of 7% mandates prophylactic treatment with Vitamin C 400mg daily which has been shown in an RCT to be an effective preventer of CRPS. Unfortunately, this remains poorly implemented within Emergency Departments as recommended treatment.

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49. Psychological Risk Factors for Chronic Post Surgical Pain after Inguinal Hernia Repair: A Prospective Cohort Study, European Journal of Pain, 2012, April, Vol 16, No 4, pp 600 – 610 Powell et al

This study looked at 135 patients having repair of their inguinal hernia and looked at the outcome at four months. 40% of patients had persistent chronic post-surgical pain at four months and the greatest predictive factor was those patients who had low pre-operative optimism.

Comment – Once again, psychological variables trump others in predicting outcome of persistent pain. It's clear that pre-operative psychological input may be our best bet at altering chronic post-surgical pain.

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50. Persistent Post Surgical Pain in a General Population: Prevalence and Predictors in the Tromso Study, Pain, Vol 153, 2012 pp1390 – 1396 Johansen et al

This paper comes from Norway as a population survey of 13,000 people of whom 2,000 patients had had surgery between three months and three years preceding the survey and 18% of these had persistent post-surgical pain. Interestingly, the odds ratio for decreased sensation in the operative area was 2.7 for then leading to persistent pain and the odds ratio was 6.3 if there was heightened sensitivity to sensation in the pain area for leading to persistent pain.

Comment: This gives us a good population grounded response that approximately one in five patients will have persistent post-surgical pain and we know that if there is abnormality of sensory processing, this puts the patient at great risk of subsequent development of post-surgical persistent pain. Clearly, the condition of persistent post-surgical pain is more common than either the population or the medical profession would generally believe or allude to and clearly should be a component of any decision making process and discussion with patients.

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51. Pain, August 2012 Vol 153 No 8 pp 1749 – 1754 Goeslig et al NO ARTICLE NAME

This paper from University of Michigan in the United States looked at 426 patients going through a multidisciplinary pain clinic and examined their pain levels, smoking levels, depression symptoms and a range of other variables. They showed that there was a much higher incidence of severe pain in patients who were smokers compared to former-smokers or non-smokers and the longer a patient had been a former smoker, the lower the average pain level. They showed that this relationship between smoking and pain disappeared when depression was taken into account, indicating that it is not the smoking per se that makes the pain worse, but that the smoking appears to either cause, or is associated with, depression which then makes the pain severity worse.

Comment: This answers the critical question of why smoking appears to be associated with worse pain outcomes and we now have two studies (the Hooten Study was the other study that has shown this mediated effect). Therefore, we can tell patients that if they smoke and develop pain, they are more likely to become depressed and their pain is going to be rated more severely than if they were non-smokers. Therefore, every smoker should attempt to give up.

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Comment: This gives us a good population grounded response that approximately one in five patients will have persistent post-surgical pain and we know that if there is abnormality of sensory processing, this puts the patient at great risk of subsequent development of post-surgical persistent pain. Clearly, the condition of persistent post-surgical pain is more common than either the population or the medical profession would generally believe or allude to and clearly should be a component of any decision making process and discussion with patients.

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Comment: This answers the critical question of why smoking appears to be associated with worse pain outcomes and we now have two studies (the Hooten Study was the other study that has shown this mediated effect). Therefore, we can tell patients that if they smoke and develop pain, they are more likely to become depressed and their pain is going to be rated more severely than if they were non-smokers. Therefore, every smoker should attempt to give up.

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61. Nucleoplasty is effective in reducing both mechanical and Radicular Low Back Pain: A Prospective Study in 87 Patients, Journal of Spinal Disorders and Techniques Vol 25 No 6 August 2012 pp 329-332 Shabat et al

This study showed that there was a 50% reduction in pain at both one and two years in patients who underwent nucleoplasty at the L3/4, L4/5 or L5/S1 discs for disc protrusion in combination with radicular pain, where there was more than a 50% disc height preservation. They additionally received non-steroidal anti-inflammatory agents and a lumbar epidural steroid injection.

Comment: As this is not a randomised controlled trial, it's difficult to know how much additional pain relief nucleoplasty afforded the patients besides simply natural history resolution with pharmacotherapy and epidural steroid injection. Overall, this would be classified as low level evidence of the benefit of nucleoplasty within this situation.

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62. Therapeutic Effects of Lignocaine Patch on Myofascial Pain Syndrome of the Upper Trapezius American Journal of Physical Medicine and Rehabilitation CME Article 2012 No 9.

This study from Taiwan showed a significant reduction in pain for two weeks, but not for four weeks, after application for one week of the Lignocaine patch. Reduction in both the neck disability index, the pain score and the pressure pain threshold.

Comment: This indicates that the Lignocaine patch reduces pain for the duration that it's on and probably for one week afterwards. It possibly may have a place as part of a comprehensive rehabilitation program for patients with persistent myofascial pain, although more work needs to be done in this area.

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63. The Prevention of Chronic Post-surgical Pain using Gabapentin and Pregabalin: A Combined Systematic Review and Meta-analysis, Pain Medicine, August 2012 Vol 115 No 2, pp 428, Clarke et al

This paper from the Pain Research Unit of Toronto General Hospital looked at eleven studies, eight of which could be meta-analysed. Six Gabapentin trials demonstrated a moderate to large reduction in the development of chronic post-surgical pain, odds ratio 0.52 (P=0.04) and two Pregabalin trials showed a large reduction in the development of chronic post-surgical pain, odds ratio 0.09 (P<0.01).

Comment: This shows that Gabapentin and especially Pregabalin can reduce chronic post-surgical pain and are ideally suited to being deployed to prevent this outcome in high risk subjects or high risk surgical settings.

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64. Forefoot Running Improves Pain and Disability Associated with Chronic Exertional Compartment Syndrome American Journal of Sports Medicine 2012 May Vol 40 No 5 pp 1060-7 Diebal et al

This paper from the Keller Army Community Hospital at Westpoint in New York showed ten patients with this condition awaiting surgical decompression who underwent six weeks of forefoot running training and their compartment pressures dropped significantly and their running distance increased from 1.4km to 4.8km and no patient required surgery.

Comment: This case series which is Level evidence IV showed symptoms were greatly reduced for up to one year after a forefoot running program in patients with chronic exertional compartment syndrome.

65.The Long Term Outcome of TENS in the Treatment of Patients with Chronic Pain: A Randomised, Placebo Controlled Trial, Oosterhof et al, Pain Practice, Vol 12, Issue 7 2012 pp 513 – 22

This study from the Netherlands looked at one year outcomes of TENS vs. sham TENS in 165 patients. After one year, 30% of the TENS group and 23% of the sham TENS group were satisfied with the treatment result, experiencing a mean overall improvement of 63%. There was no difference between the two groups.

Comment: On the face of it, this is a negative result but, in fact, what it shows is that for 3/10 patients they will get a 60% reduction in pain from continued use over one year with TENS, but that sham TENS is just as good, indicating that there may be non-specific benefit accruing to applying external treatment. Overall, it remains confusing as to how much of a role TENS should play in chronic pain treatment as there are a number of positive and negative studies in this area.

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66. Risk Factors for New Osteoporotic Vertebral Compression Fractures after Vertebroplasty: A Systematic Review and Meta-Analysis. Journal of Spinal Disorders and Techniques, 2012 28 September Zhang et al.

This paper from Nan Zhing University in China showed that patients with low bone mineral density (therefore at increased risk of osteoporosis), low body mass index (thus not enough muscle to take load and all the load goes onto bone) and intradiscal cement leakage (making a stiff transition point within the bone between osteoporotic bone and solid cement) were risk factors for new vertebral compression fractures after vertebroplasty.

Comment: This makes intuitive sense and provides you with the first step of attempting to reduce the risk for certain patients.

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67. Factors Determining the Success of Radiofrequency Denervation in lumbar Facet Joint Pain: A prospective Study, Streitberger et al, European Spine Journal 2011 Vol 20 pp2160 – 65

This paper comes from University Hospital of Bern where they followed 41 patients. They showed that in an analysis of age, sex, depression, work inability and previous surgery, only depression was a significant factor that adversely affected the clinically effective outcome of 50% or more of pain relief. They showed that in patients who were depressed, only 10% of patients had a 50% or more reduction in pain at six months vs. 40% of patients who had a 50% or more reduction in six months who were not depressed.

Comment This is more evidence (if we needed it) that biologically based therapies do not work in patients with significant mood disorders, in particular depression. On a separate note, it's unclear why their 40% response rate was so poor with response rates up to 87% having been previously achieved. A small gauge

radiofrequency needle was used (20 gauge instead of the more typical 18 gauge) and that may have adversely affected their results, as may have their selection protocol. Nevertheless, the important thing here is that patients with depression should not be offered a radiofrequency procedure because of the lack of efficacy in this subgroup.
