Epidermal growth factor receptor – inhibition (EGFR-I) in the treatment of neuropathic pain

Reference: Kersten, C., Cameron, M.G., Laird, B., Mjaland, S. British Journal of Anesthesia, 115 (5), 761–7, 2015
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Abstract: Background: Neurobiological work has demonstrated that expression of mitogen-activated protein kinases (MAPK) is up regulated on neurons and glial cells after nerve damage. Furthermore, the epidermal growth factor receptor (EGFR) has been identified as having a key role in this process and subsequent interruption of this using EGFR-Inhibitors (EGFR-I), may improve neuropathic pain. The aim of this report was to explore if EGFR-I attenuated neuropathic pain in humans.
Methods: A selection of patients with neuropathic pain was treated off-label with one of four EGFR-Is, approved for the treatment of cancer. All patients had chronic and severe neuropathic pain (as defined by diagnostic criteria). Pain intensity, interference with function, and adverse events were prospectively registered.
Results: Twenty patients were treated. Eighteen patients experienced clinically significant pain relief after treatment with EGFR-I. Median observed pain reduction for all patients was 8.5 (IQR=5–9.5) points on a 0–10 numeric rating scale. Neuropathic pain spike duration and frequency also improved. Pain relief was most often achieved within 24 h and was more rapid in cases of i.v. than oral administration. All four EGFR-I that were tested were of equal efficacy. The duration of pain relief was consistent with the individual drugs' half-lives. No cases of drug-tolerance were observed. Side effects were predominantly skin reactions. One grade 3 adverse event was registered. Median follow-up for responders was 7 months (Range 1–37).
Conclusions: EGFR-I improves neuropathic pain and this is in keeping with basic science work. Controlled clinical trials are now eagerly awaited to assess this further.

Strengths:

- Large proportion (90%) of patients experiencing significant pain reduction.
- Long duration of treatment and follow-up regarding effectiveness of EGFR inhibitors.
- 7 of the 20 patients had neuropathic pain related to their cancer and had pain relief to a rating of 0(originally scores were 8-10) within the first 24 hours.
- Minimal adverse events with the most common being skin changes, which is a known side affect of EGFR inhibitors.

Weaknesses:

- Exact mechanism of EGFR inhibitors is not entirely understood.
- No other trials to confirm findings of study.
- Small number of patient participants.
- Pain scale used for study was self-reported by patients.
- Study design was not randomized or concealed potential for bias or placebo effect.
- Cost of medication (25 mg tablet ~$2800 USD)

Relevance to Palliative Care:

Neuropathic pain is difficult to manage in cancer patients. Opioids such as methadone can be effective in treating neuropathic pain, but have several side affects. EGFR inhibitors may be a potential alternative to opioids to manage neuropathic pain. Larger RCT's are needed determine their effectiveness. Cost may be a barrier for there use.