Most of the information we have about chronic opioid use comes from studying drug addicts who have been maintained on methadone for years. Whilst studies have shown that there are biochemical and physiological changes associated with chronic opioid use, there are minimal side effects of any clinical significance.

Toxicity is rare.

However, the term "Opiate-induced neurotoxicity" has been used by authors such as Daeninck and Bruera ( [i] ) They refer to the syndrome of delirium, hallucinosis (hallucinations), myoclonus (muscle jerks)/seizures and hyperalgesia (increased pain) which may occur at higher doses.

Myoclonus may be seen with high dose opioid therapy. Myoclonic jerks are brief, involuntary jerks which may be severe enough to be painful. They are not the same as muscle spasms, which tend to be more sustained.

Animal studies have suggested that myoclonus and hyperalgesia (heightened response to pain) and indeed, allodynia (pain felt from non-painful stimuli) may be due to accumulation of one of the metabolites of opioids: the 3-glucuronide metabolite.

Opioid rotation/switching may be helpful to manage these problems. This is simply exchanging one opiate for a different one, when the side-effects of the original opiate have become intolerable for the patient.

Paradoxical pain may be actually reduced by *decreasing* the opiate dose. I know of one man who had escalating pain levels that could not be controlled by increasing doses of opiates: but once the doses were significantly decreased, he actually improved considerably.

[i] Daeninck, Bruera *Acta Anaesthesiol Scand* 1999 Oct;43(9):924-38 Opioid use in Cancer pain. Is a more liberal approach enhancing toxicity?