Pharmacological interventions for pain in children and adolescents with life-limiting conditions

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Authors' objectives

Background: Pain is one of the most common symptoms in children and young people (CYP) with life-limiting conditions (LLCs) which include a wide range of diagnoses including cancer. The current literature indicates that pain is not well managed, however the evidence base to guide clinicians is limited. There is a clear need for evidence from a systematic review to inform prescribing. Objectives: To evaluate the evidence on the effectiveness of different pharmacological interventions used for pain in CYP with LLCs. Search methods: The following electronic databases were searched up to December 2014: CENTRAL (in the Cochrane Library), MEDLINE, EMBASE, PsycINFO and CINAHL. In addition, we searched conference proceedings and reference lists of included studies. For completeness, we also contacted experts in the field. No language restrictions were applied. Selection criteria: Randomised controlled trials (RCTs), quasi-randomised studies and other studies that included a clearly defined comparator group were included. The studies investigated pharmacological treatments for pain associated with LLCs in CYP. The treatment included those specifically developed to treat pain and those that acted as an adjuvant, where the treatment was not primarily developed to treat pain but has pain relieving properties. The LLC was identified by its inclusion in the Richard Hain Directory of LLCs. Data collection and analysis: Citations were screened by five review authors. Data were extracted by one review author and checked by a second. Two review authors assessed the risk of bias of included studies. A sufficient number of studies using homogeneous outcomes was not identified so a meta-analysis was not possible. Main results: We identified 24,704 citations from our database search. Nine trials with 379 participants fulfilled our inclusion criteria. Participants had cerebral palsy (CP) in five of the studies and osteogenesis imperfecta (OI) in the other four. Participants across the trials ranged in age from 2 to 19 years. All studies, apart from one cross-over trial, were parallel designed RCTs. Three of the trials on CP evaluated intrathecal baclofen (ITB) and two botulinum toxin A (BoNT-A). All of the OI trials evaluated the use of bisphosphonates (two alendronate and one pamidronate). No trials were identified that evaluated a commonly used analgesic in this patient group. Pain was a secondary outcome in five of the eight identified studies. Overall the quality of the trials was mixed. Only one study involved over 100 participants. For the two ITB studies for pain in CP, in the same study population but assessed at different time points in their disease, both found an effect on pain favouring the intervention compared to the control group (standard care or placebo) (mean difference (MD) 4.20, 95% confidence interval (CI) 2.15 to 6.25; MD 26.60, 95% CI 2.61 to 50.59, respectively). In these studies most of the adverse events related to the procedure or device for administration rather than the drug, such as swelling at the pump site. In one trial there were also eight serious adverse effects; these included difficulty swallowing and an epileptic seizure. The trial did not state if these occurred in the intervention group. At follow-up in both BoNT-A trials there was no evidence of a difference in pain between the trial arms among CP participants. The adverse events in the BoNT-A trials mostly involved those who received the intervention drug and involved seizures. Gastrointestinal problems were the most frequent adverse event in those who received alendronate. The trial investigating pamidronate found no evidence of a difference in pain compared to the control group. No adverse events were reported in this trial. Authors' conclusions: Published, controlled evidence on the pharmacological interventions for pain in CYP with LLCs is limited. The evidence that is currently available evaluated pain largely as a secondary outcome and the drugs used were all adjuvants and not always commonly used in general paediatric palliative care for pain. Based on current data this systematic review is unable to determine the effects of pharmacological interventions for pain for CYP with LLCs. Future trials with larger populations should examine the effects of the drugs commonly used as analgesics; with the rising prevalence of many LLCs this becomes more necessary.

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