Effects of an intrathecal drug delivery system connected to a subcutaneous port on pain, mood and quality of life in end stage cancer patients: an observational study

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Background: In cancer patients with limited life expectancy, an implant of an intrathecal (IT) drug delivery system connected to a subcutaneous port (IDDS-SP) has been recently proposed as a successful strategy, but conflicting results are reported on its effects on quality of life (QoL). The suffering of the whole person is the most important feature of cancer-related pain (12). In these patients, pain shows the same symptom pattern as depression. A strong association between pain severity and distress symptoms such as anxiety and depression in cancer patients has been described. Moreover, the prevalence of insomnia in cancer patients is almost 50%. Cancer patients with insomnia had significantly higher rates of pain, nausea, dyspnea, and anxiety. Patients with moderate to severe pain and anxiety had 2-3 times higher rates of insomnia. The aim of this observational study is to report the effects on pain, mood and QoL of IT combination therapy delivered by an IDDS-SP in malignant refractory pain.

Methods: Adult patients in which IT therapy was recommended because of inefficacy or intolerance to strong systemic opioid treatment were recruited. An IT combination therapy with morphine and levobupivacaine was started: VASPI score, depression and anxiety (evaluated by the Edmonton Symptom Assessment System -ESAS-), the Pittsburgh Sleep Quality Index (PSQI), the 5-level EuroQol 5D version (EQ-5D-5L) and the requirements of breakthrough cancer pain (BTcP) medications were registered, together with adverse events rate and the satisfaction of patients scored as Patient Global Impression of Change (PGIC). VASPI score, ESAS, EQ-5D-5L were evaluated at pre-implant and post-implant at 14 days (T14) and at 28 days (T28), together with systemic medications used to control BTCP and basal pain. Post implant PGIC and AEs were also registered. Finally, PSQI was calculated at pre-implant and at T28. PGIC is a 7-points scale depicting patient's rating of overall improvement. Patients rated their change as "very much improved (3)," "much improved (2)," "minimally improved (1)," "no change (0)," "minimally worse (-1)," "much worse (-2)," or "very much worse (-3).

Results: 55 patients were considered potentially eligible. Of these, 5 were excluded (3 for inadequately treated infection, 2 for brain metastases). In total, 50 patients, (16 F/ 34 M) were enrolled (age 63±12). All had advanced cancer with metastasis. The median daily VASPI score was 75. The median depression score in ESAS was 6, and the median anxiety score was 4, median PSQI was 16. At 28 days, a significant reduction in VASPI score was registered (35 mm, p< 0,05) as well as depression item of the ESAS (median 4, p<0,05) and the anxiety item (median 3, p<0,05). Also, PSQI decreased significantly (median value 12, p<0,05). The EQ-5D-5L showed a significant improvement in all components at 14 and 28 days. PGIC scores showed high level of satisfaction.
All patients stopped their previous systemic opioid therapy. 70% of patients reported a sporadic intake of 30 mg of short acting oral morphine, 30% of patients continued to intake only acetaminophen as needed. Eight patients reported they sporadically took transmucosal fentanyl to control BTcP out of 42 patients pre-implant (see table 2). During the entire follow up, 2 patients (4%) experienced confusion, 4 (8%) reported difficulty to void in the first 24 hours, 3 (6%) nausea and 2 (4%) vomiting. Nor infection neither complication related to the IDDS-SP refill were registered.

Discussion: The current study suggests that an IT therapy with IDDS-SP is a successful strategy in patients with malignant pain refractory to high doses of systemic opioids. It allows stable control of pain, as demonstrated by the significant reduction of VASPI score and the reduction of systemic opioids requirements for BTcP and also a better control of depression and anxiety as well as a significant improvement in sleep quality. Moreover, even if more invasive than systemic therapy, the IDDS-SP led to a significant improvement in QoL and high levels of satisfaction.
In the present trial, almost 50% of patients referred an improvement of mobility self-care and ADL, even with an external device. Although doubts and fears about wearing an external device and the consequent reduced mobility, the significant improvements on pain and on other cancer related symptoms, together with the increasing quality of sleep and the reduced incidence of AEs, the reduced need of rescue medication to control BTcP, could all explain our results. These beneficial effects in turn explain the very high levels of patient satisfaction. Surprisingly, also patients with presence of psychological distress or aberrant behaviours reported high levels of pain control and satisfaction with an external device.

Conclusion: IT combination therapy of morphine and levobupivacaine delivered by an IDDS-SP should be considered for cancer patients with severe pain. It can assure adequate pain relief and reduce other cancer related symptoms, such as depression, anxiety and sleep disturbance.

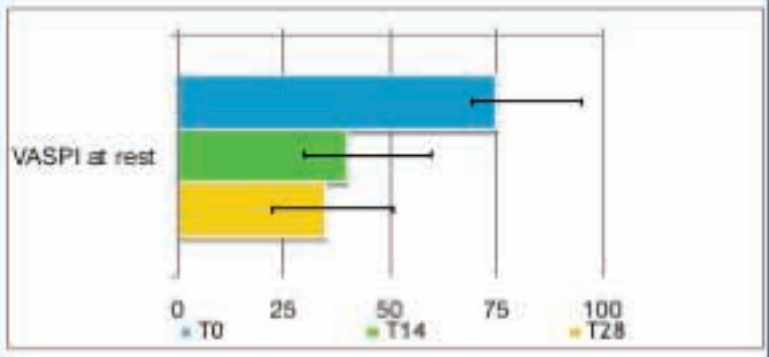

Figure 1: The reduction of VASPI score (median) over time * indicates p< 0,05. (T0=day of IT catheter placement, T14=14 days T28= 28 days).

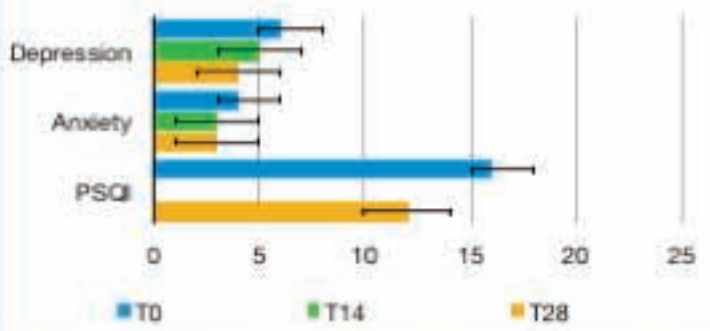

Figure 2: The reduction of VASPI score (median) over time * indicates p< 0,05. (T0=day of IT catheter placement, T14=14 days T28= 28 days).

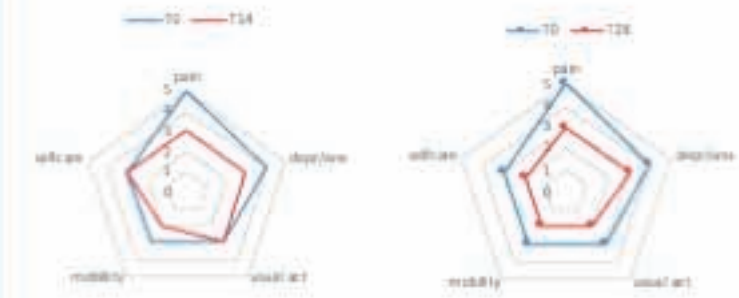

Figure 3: The change of 5-level EuroQol 5D version (EQ-5D-5L) in the overall score as well as in every component (i.e. change in usual activities, mobility, pain, self-care, anxiety/depression) at T14 (14 days after implant, on the left) and at T28 (28 days after implant, on the right).

Figure 4: The PGIC (Patient Global Impression of Change) at 14 days post implant (T14) and at 28 days post implant (T28).

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