



VII HIGHER EDUCATION COURSE IN PAIN MANAGEMENT : "ACUTE AND CHRONIC PAIN, FROM RESEARCH TO THE CLINIC" CAPRI (11-13) OCTOBER 2017

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Summary – Over the past years, the importance of the multidisciplinary approach to chronic pain, through a direct involvement of professionals from all branches of medicine who are confronted daily with pain patients, has emerged. Advances in pain management, have been achieved through pre-clinical and clinical studies conducted by researchers and clinicians. The treatments normally used for managing pain usually lack of efficacy, thus new strategies have been developed so far. To date new researches have been focused on: a) the pre-operative analgesia; b) the illicit and pain; c) cancer pain management; d) the application of nanotechnologies in treatment of chronic pain. Here, we reported the most relevant discussion presented by speakers in the conference "Personalized medicine in the VII Higher Education Course in Pain Management: "Acute and Chronic Pain, from research to the clinic" held in Capri (11-13) October 2017 (Figure 1).



KEYWORDS: Pain management, Conference scene, Acute and chronic pain, Cancer pain.



SESSION: I DON'T HAVE THE STRENGTH TO COMPLAIN

Dr. **Francesca Bifulco** introduced the “BACK TO THE FUTURE 2: NSAIDS AND OPIOIDS”.

More than 80% of surgical patients experience postoperative pain and 40% experience are severe to extreme postoperative pain. The concurrent use of more than one class of analgesic drug or technique to target different mechanisms of analgesia has been advocated to improve analgesia while reducing opioid-induced side effect. Multimodal analgesic regimen is an essential component of ERAS program. Recent researches highlight the role that perioperative NSAIDs have on modulating nociception and their benefits in multimodal analgesia. In the recent American Pain Society guidelines, the panel recommends that clinicians provide adults and children with NSAIDs as part of multimodal analgesia for the management of postoperative pain in patients without contraindications¹. Indeed experts recommend to consider giving a preoperative dose of oral celecoxib in patients without contraindications, as it is associated with reduced opioid requirements after surgery and some studies reported lower postoperative pain scores. Recent researches indicate that, in addition to peripheral blockade of prostaglandin (PG) synthesis, centrally NSAIDs act in spinal dorsal horn to inhibit PGE2 production via COX 2 and in the brain activating medullary and cortical regions involved in descending inhibitory pathways².

Notwithstanding opioids use is essential in multimodal analgesia, the panel recommends against routine basal infusion of opioids with IV patient-controlled analgesia (PCA) in opioid-naïve adults, because basal infusion does not improve analgesia when compared with PCA without basal infusion¹. A new therapeutic option for postoperative pain management is parenteral administration of oxycodone, that can have advantages vs. other iv opioids. Oxycodone has a rapid onset time that may be very helpful in immediate postoperative hours³.

SESSION: WHAT WOMEN SAY

Dr. **Rym Bednarova** introduced the “Pharmacological approach in multi drug's market”.

The difference in gender is of growing importance and interest in relation to pain experience. Men and women differ in their responses to pain, with increased pain sensitivity for clinical pain commonly observed among women as well as response to pharmacological and non pharmacological pain interventions. Women have more than twice higher prevalence in painful disorders compared to men. The putative mechanisms underlying sex differences in pain include multiple biological and psychosocial processes. Emerging evi-

dence suggests that genotype and endogenous opioid functioning play a causal role in sex disparities, and considerable literature implicates sex hormones as factors influencing pain sensitivity. The psychosocial processes such as pain coping and early life exposure to stress, stereotypical gender roles also explain differences in pain expression and its management. In Italy there is a growing attention to chronic pain conditions in women as vulvodynia that often is a result of episiotomy practice. Vulvodynia is defined as dysfunctional sensory processing in the central and peripheral pain generators similarly observed in other common painful conditions in women as fibromyalgia. Nevertheless, the taxonomy and classification of these pain conditions and whether they might be considered neuropathic are not yet clear due to heterogeneous diagnostic criteria. Literature shows how this situation together with the already difficult interception of pain conditions in women and their variable response to therapy requires major research and attention.

SESSION: THE NUMBERS OF PAIN

Dr. **Luca Miceli** proceeded to examine: “When numbers speak, Italian data”.

In this relation the arguments treated are:

- Distribution of Italian patients that are in chronic therapy with opioids.
- How much opioid in morphine equivalent dose is used in Italy;
- Trends in (Rapid Onset Opioids) ROOs use;

General practitioners (GPs) and patients with chronic pain, how many chronic pain patients does each GP treat?

We analyzed all outpatient opioid prescriptions in Italy between 2013 and 2015; after that, we performed a census of all patients in chronic therapy (three or more consecutive months with at least one prescription a month). Around 500 thousand Italians are on chronic opioid therapy being 15% of total Italian patients and they consume 58% of opioids prescribed. Considering the total number of patients that probably suffer chronic non-cancer pain and those with chronic cancer pain, our data showed that in Italy only about 4% of both groups receive opioids. Compared to trends of opioid use in literature, it seems that cancer patients are corresponding to trends of about 80 mg morphine per day, whereas non cancer pain patients are treated with MED less to 60 mg morphine per day. Over 20% of ROOs seem to be used with MED less to the recommended around the clock daily dose. The principal ambulatory procedures include epidural blocks and peripheral nerve blocks that are in diminution over the years. The major part of GP has about from 1 to 20 patients in chronic opioid therapy giving usually the first prescription of opioids.

SESSION: RESEARCH IN PAIN THERAPY

Dr. **Antonio Barbieri** reported a study on "The role of opioids and antagonists in tumor growth".

Morphine is considered a stronger analgesic used to relieve suffering of patients with cancer⁴. It is of note that morphine is able to inhibit or to promote tumor growth, depending on the concentrations used. As regards triple negative breast cancer (TNBC), it has been demonstrated that morphine, at clinical relevant doses, *in vitro* and *in vivo* enhanced the proliferation, inhibited the apoptosis and promoted the neoangiogenesis⁵. Interesting results were obtained by using the same *in vitro* and *in vivo* models for the naloxone, which is a specific opioid antagonist acting at level of opioid receptors (μ , δ , and κ)⁶. Recent data showed that naloxone reduced breast cancer progression without significant effect on tumor angiogenesis⁷. The results obtained from these experiments shed a light on the role of morphine and naloxone in the regulation of breast cancer development and progression. In order to develop novel morphine or naloxone-based therapeutic compounds for breast cancer therapy, more studies will be extremely necessary.

Dr. **Sabrina Bimonte** clarify the important role of "Natural compounds in treatment of neuropathic pain". Neuropathic pain (NP), a chronic disorder caused by lesions or defects of the somatosensory system, is classified in central NP (caused by defects of central nervous system [CNS]); peripheral NP (caused by defects of peripheral nervous system [PNS]), and mixed NP (due to alterations of PNS and CNS)⁸⁻¹⁰. Since NP dramatically affects patient quality of life, many pharmacological approaches to treat NP have been proposed, unfortunately with no encouraging results¹¹. In order to find successful therapies for NP, several pre-clinical studies with natural compounds have been conducted so far. Interesting results were obtained by *in vivo* studies with Epigallocatechin-3-gallate (EGCG), which is able to ameliorate NP and pain from bone metastasis by acting on several signaling pathways¹²⁻¹⁷. To translate the use of EGCG into clinical practice for management of NP, it is necessary to refine experiments identifying the optimum therapeutic dosage of EGCG for intervention trials in patients suffering from NP.

Dr. **Massimiliano Berretta** discussed on "The role of CAM in multidisciplinary pain management". Complementary and Alternative Medicine (CAM) include a wide range of products (herbs, vitamins, minerals, and probiotics) and medical practices, such as acupuncture or magneto-therapy, developed outside of the mainstream Western medicine. Pa-

tients with cancer are more likely to resort to CAM first or then in their disease history for a wide range of reasons. The potential side effects as well as the costs of such practices are largely underestimated. Recently the use of CAM in the treatment of cancer pain obtained a contradictory results. In conclusion, although roughly half of cancer patients recourse to CAM for their disease, the role on the use of CAM is controversial. It is necessary that health professional explore the use of CAM with their cancer patients, educate them about potentially beneficial therapies in light of the limited available evidence of effectiveness, and work towards an integrated model of health-care provision.

CONCLUSIONS AND FUTURE OUTLOOK

Pain management represents a very important issue, since it needs of continuous updates in order to improve the quality of life of patients. Due to the enormous progress obtained in pain diagnosis and the availability of new therapies, we are able to obtain encouraging pre-clinical and clinical results. We believe that the right way to obtain better results is based on a multidisciplinary treatment approach through a direct involvement of professionals from all branches of medicine who are confronted daily with pain patients.

CONFLICT OF INTEREST:

The Authors declare that they have no conflict of interests.

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