(408) Screening of several N-acyl amides for antinociceptive properties against pain induced by Levantine viper venom

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Searching for the drugs with lower health risks is one the most important issues in pain medicine. Viper venoms, which have significant destructive action on victim's organism, also cause strong pain sensations connected with tissue injury and development of inflammatory processes both in the site of injection and in whole body afterwards. It is well known that TRPV (transient receptor potential vanilloid) channels are involved in pain information transduction by nociceptive afferents. Cannabinoid receptors (CB) modulate nociceptive information. Endogenous lipid derivatives – N-acyl amides are believed to be the potential modulators of pain and inflammation.We have tested several N-acyl amides, with agonistic activity on TRPV and CB channels, against Levantine viper (Macrovipera lebetina obtusa, MLO) venom induced pain. Levantine viper venom was injected subcutaneously into mice hind paw to induce nociceptive behavior. The liking/bitings of injected paw were counted during 45 min. The following N-acyl amides were tested: N-arachidonoyl taurine (AA-Tau, TRPV1, TRPV4 agonist), N-oleoyl taurine (OL-Tau, TRPV1, TRPV4 agonist), N-arachidonoyl vanillin (Arvanil, CB1, CB2 and TRPV1 agonist). According to our results all 3 tested N-acyl amides inhibited venom induced changes in nociception. The mean number of paw lickings during 45 min for groups were: 33.6$\pm$2 (MLO+N-acyl amide buffer), 26.0$\pm$0.8 (MLO+OL-Tau), 23.0$\pm$6.0 (MLO+AA-Tau) and 9.5$\pm$1.9 (MLO+Arvanil). So, the Arvanil had the highest percent of inhibition: Arvanil (71.73%) > OL-Tau (31.55%) > AA-Tau (22.6%). Above mentioned results allow us to conclude that tested N-acyl amides may be used as analgesics in the treatment of viper venom induced pain and other similar inflammatory events.

(409) Chromocell's Compounds A: a novel, orally active, selective NaV1.7 inhibitor

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Compound A is a novel, orally bioavailable, peripherally restrictive, selective inhibitor of NaV1.7 that is 1000x selective for the inactivated state of the channel over the resting state. Compound A is active in numerous rat and mouse models of pain and itch including the formalin model of induced pain, acetic acid writhing model, complete Freund's adjuvant model, chronic constriction injury model, partial sciatic nerve ligation model, streptozotocin induced diabetic neuropathy model and histamine and serotonin induced itch models. Overall, Compound A has an attractive in vitro profile with broad selectivity at 10 uM including 1000x selectivity over hERG and NaV1.5 with no cytotoxicity up to 300 uM. The compound is soluble and stable in solution and is metabolically stable. Compound A has a broad safety window of at least 25x based on both Cmax and AUC in rats. Compound A is a promising preclinical candidate that is progressing toward first in man. The in vitro and in vivo properties of this compound will be presented.

(410) Ketamine infusion for refractory pain in Dercum's Disease (Adiposis dolorosa): a novel treatment approach

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Dercum's disease (Adiposis dolorosa) is a rare disorder characterized by multiple, tender subcutaneous nodules on the trunk and extremities. There is a higher incidence in obese, postmenopausal women. The exact mechanism is unknown, but it is hypothesized to be due to abnormal blood flow or circulatory dysfunction. Treatment is extremely challenging and is often times resistant to numerous modalities. We present the case of a 47 year-old female with a 2-year history of Dercum's disease. The patient had seen numerous physicians and tried multiple treatment modalities, all with little success. After initial consultation, the decision was made to proceed with 2 four-hour trials of IV Ketamine infusions in the ICU. Patient reported approximately 60% relief of her pain immediately after her infusions and states that the relief lasted through her follow up four weeks later. Dercum's disease remains a devastating diagnosis for many patients. It is extremely challenging to treat and has a significant adverse effect on patients' quality of life. Ketamine infusions should be considered after conservative methods of treatment have failed and prior to proceeding to invasive treatment solutions such as liposuction.

F15 Opioids in Acute Pain

(411) An open label study introducing post-op tonsillectomy as a new pain model for clinical research in young children

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Clinical trials in young children are very challenging. It is therefore important to find a new model to allow such studies. The treatment of pain after tonsillectomy is introduced as a new model for pain research in young children (2 < 6 years). The Pharmacokinetics (PK), safety and efficacy of a single dose tapentadol oral solution on children (n=17) were explored in an open label study. Healthy male or female patients weighing between 12.7-19.5 kg with an ASA status I-II and pain levels requiring opioid treatment post-surgery were enrolled. Children were alert, able to follow commands and able to tolerate the oral medication. The treatment and evaluation period was 15 hours post-dosing. Serum concentrations of tapentadol and tapentadol-O-glucuronide were measured. Pain assessments consisted of FPS-R and FLACC. Safety lab parameters, vital signs, pulse oximetry, and ECGs were summarized with changes from baseline and frequency tabulations of abnormalities. All subjects who received trial medication were included in the safety analysis that included a description and incidence of adverse events, their outcomes, and relationship to tapentadol. The safety profile was consistent with the known safety profile for tapentadol. There were no discontinuations due to AEs. The incidence of TEAEs was 35%. The most common TEAEs were headache and cough (11.8% each). Pain intensities decreased post-treatment however meaningful conclusions about efficacy could not be drawn due to confounding factors (i.e. allowed concomitant medication, single-dose administration). Overall, serum tapentadol concentrations observed in the trial population were within the range observed in adults after administration of 50-100 mg oral tapentadol. Serum concentrations of the metabolite (tapentadol-O-glucuronide) were generally lower when compared to adult data. The actual recruitment time for this population in a single center was 6 months. We therefore consider this new pain model very successful to study new pain medications in young children.