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Anna-Clara Rullander, J Pain Relief 2016, 5:5(Suppl)
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Adolescent's experiences of undergoing scoliosis surgery: Psychological aspects and patterns of pain

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Scoliosis surgery is one of the most extensive elective pediatric surgical procedures performed today. The surgery is known to cause severe and excruciating pain and requires advanced pain management and nursing skills. Until now, scoliosis surgery has mainly been studied in terms of corrective surgical outcomes, techniques for surgery and pain management. Adolescents' narratives and experiences of recovery after scoliosis surgery, as well as psychological aspects in correlation to postoperative pain have seldom been studied. In four studies with qualitative, quantitative and mixed methods approach it has been shown that adolescent patients are experiencing high levels of stress before surgery and severe postoperative pain. Preoperative stress showed to correlate significantly with postoperative pain, and postoperative pain showed to correlate with levels of stress six months after surgery. During recovery they have to struggle with persistent pain, constipation, nausea, lack of energy, loss of control over the body and they have to struggle back to the normal life. Nightmares concerning the perioperative experiences were appearing up to two years after surgery and some of the studied adolescents showed post-traumatic stress symptoms. With targeted interventions aiming at identifying levels of preoperative stress, promotion of coping techniques, improved postoperative pain management and active nursing follow up after hospital discharge it is possible to improve perioperative care among adolescents going through scoliosis surgery.

Biography

Anna-Clara Rullander has completed her PhD from Umeå University in Sweden, and defended her thesis in December 2015. She is now planning to pursue her Post-doctoral studies in the area of Scoliosis Surgery and Interventions aimed at Optimizing Perioperative Care. She has published four articles and presented her research at five international conferences.

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The impact of chronic musculoskeletal pain on male reproductive hormones and sperm quality

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The association between reproductive hormones (FSH, LH, testosterone and prolactin) and human semen parameters has long been established. Previous studies have recognized that increase in cortisol levels under chronic pain conditions can potentially lead to testosterone deficiency in chronic pain patients, possibly posing a negative effect on sperm quality and eventually affecting male fertility potential. However, other studies reporting no significant difference in testosterone, LH and cortisol levels in men with chronic musculoskeletal pain making it a controversial topic that calls for further investigation. Blood samples from 10 chronic musculoskeletal pain patients and 10 healthy matched controls were collected to assess serum reproductive hormone levels at Aalborg University Hospital. Sperm samples were also collected by masturbation in accordance with the WHO semen sampling guidelines and analyzed for sperm concentration, motility and kinematic parameters using the Sperm Class Analyzer (SCA®) computer aided sperm analysis system. Serum levels of reproductive hormones and sperm DNA fragmentation did not show any significant difference between the test and control groups. However, significantly lower percentage of static and non-progressive motile sperm ($P<0.05$) was observed in the chronic pain patients; while the control group demonstrated significantly higher sperm concentration, progressive motility and percentage of hyper-activated sperm ($P<0.01$). Chronic musculoskeletal pain patients differ from matched healthy controls in several sperm quality parameters but no significant difference exists between the two groups in terms of reproductive hormone levels. These findings highlight the importance of other factors involved in sperm quality decline in chronic pain patients, which needs further investigation.

Biography

Fereshteh Dardmeh has completed her Doctor of Veterinary Medicine (DVM) from Urmia University, Iran in 2011. She then joined the Laboratory of Reproductive Biomedicine and Center for Sensory-Motor Interaction (SMI) in the Department of Health, Science and Technology of Aalborg University, Denmark as a PhD student in 2013. She has since been actively involved in teaching and research in the area of Reproductive Health and Medicine with her current studies focusing on "Probiotic supplements as a novel strategy in pain management and translational investigations of possible associations between pain, obesity and fertility".

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ADX-102, a novel aldehyde trap, reduces nociceptive behavior in mouse models of carrageenan and CFA induced pain

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A variety of aldehyde species have been shown to activate ion channels, such as TRPA1 and TRPV1, involved in mediating pain. Furthermore, aldehyde dehydrogenase 2 which diminishes aldehyde loads by oxidizing aldehydes to acids has been shown to modulate acute inflammatory pain in animal models. Thus, aldehyde signaling represents a novel therapeutic target for the treatment of pain. ADX-102 is a novel small molecule that covalently binds aldehydes including malondialdehyde and 4-hydroxynonenal, which have been shown to mediate inflammatory pain. For that reason, the effect of ADX-102 on acute inflammatory pain was tested in the carrageenan-induced and Complete Freund's Adjuvant (CFA)-induced models in mice. ADX-102 was administered intraperitoneally prior to and after pain induction, at different doses and schedules (30 mg/kg twice daily [BID], 100 mg/kg once daily [QD], or 100 mg/kg BID). Thermal hypersensitivity, mechanical hypersensitivity and paw swelling were assessed at various times to explore the effect of modulating aldehyde signaling on different molecular mechanisms underlying pain. Diclofenac was used as a positive control and vehicle was used as a negative control. ADX-102 mediated dose-dependent reductions in nociceptive behavior in both models of acute pain. In the CFA model, treatment with 100 mg/kg QD or 100 mg/kg BID ADX-102 resulted in statistically significant reductions in thermal hypersensitivity, but reduced mechanical hypersensitivity only after treatment with 100 mg/kg ADX-102 BID. In the carrageenan model, ADX-102 treatment resulted in statistically significant reductions in thermal hypersensitivity at ADX-102 doses of 30 mg/kg BID and 100 mg/kg BID, but did not affect mechanical hypersensitivity. Minor effects on paw swelling were observed in both models. The data imply that ADX-102 may differentially affect thermal and mechanical pain pathways. Overall, the results support the role of aldehyde signaling in pain and suggest that aldehyde traps represent a novel approach for the treatment of pain.

Biography

Susan Macdonald received her PhD from the University of Massachusetts Medical School and did Post-doctoral work at Onyx Pharmaceuticals. She has extensive experience in Research and Development in the biopharmaceutical industry and is currently Vice President of Research and Development at Aldeyra Therapeutics, a biotechnology company developing a proprietary family of aldehyde traps, which sequester and allow for the degradation of toxic aldehydes, and thus have broad therapeutic potential. She has published numerous articles and book chapters.

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Drug and non-drug conciliation with patient-course process in chronic pain consultation

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Background: In order to implement a prevention of the iatrogenic risk associated with analgesic and ensure a continuity of the course of care in the management of pain, experience in drug and non-drug conciliation was initiated at the consultations pain chronic of the Centre Hospitalier de Narbonne (France) by a pharmacist, a doctor and a nurse. Conciliation is an interactive and multi-professional approach which, in addition to secure the requirements by preventing errors, promotes the transfer of information between health actors and opportunity to strengthen the city-hospital link.

Objectives: Four objectives were investigated: secure drug and non-drug pain management in chronic pain consultations until home, coordinate hospital and city professionals, educate patient and evaluate conciliation by indicators.

Methodology: Prospective monocentric study was performed by proactive conciliation of drug and non-drug prescriptions including clinical pharmacist, doctor, the pain-nurse at the hospital; doctor and pharmacist, in the city.

Results: 25 adult patients were included for two months. Conciliation and intentional divergences were assessed by nine indicators: CM1: eligible patients/total patients (25/25); CM2: patients with serious medication error/conciliated patients (1/25); CM3: non-observant patients/conciliated patients (14/25); CM4: patients with adverse drug reactions/conciliated patients (13/25); CM5: patients with drug treatment optimization (9/25). CM6: patients with non-drug treatment optimization (20/25); CM7: opioids information/concerned patients (7/7). CM8: satisfied patients/conciliated patients (25/25); and CM9: information/city pharmacist (9/9).

Conclusion: Objectives were achieved, and new components emerged: non-drug conciliation, major role of nurse pain, interactive process of continuity of pain treatment between admission in consultation and return to home. This first drug and non-drug conciliation increased pain management security and city/hospital links expansion (physiotherapist, sophrologist, psychotherapist, etc.).

Biography

Alibaud Régine is working as a Pharmacist in Hospital Narbonne, France. He pursed his Diploma in 1979. In 1980, he completed Diploma of Advanced Studies in Pollutants Toxicology. He obtained State Doctorate degree in Pharmaceutical Sciences in 1983.

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The incidence of operated children with meningocele/myelomeningocele

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Background: Meningocele/myelomeningocele is the most common malformation of medulla spinalis. When people talk for spina bifida, often they refer to it as myelomeningocele, which is known as the most serious form.

Research Objectives: Our research is the creation of some statistics for the incidence of children operated with meningocele/myelomeningocele, gender, age, place of residence, and the incidence of complicated cases in Hydrocephaly, in the period from April 2010 to April 2014.

Hypothesis: Hypothesis 1 (H1): The incidence of children operated with meningocele/myelomeningocele and H2: Complications of meningocele/myelomeningocele with Hydrocephaly.

Purpose: The aim of this study is to raise health commitment, public attention for patients affected by meningocele/myelomeningocele, to analyze the incidence of these children who have been operated in our hospital, also treatment and postoperative complications.

Material & Methods: In this study, we have used information from the protocol of neurosurgical operative hall in UCCK in Pristina. This is a retrospective study of the incidence of operated children with meningocele/myelomeningocele. We have analyzed all the clinical data in a retrospective form. The samples considered are 75 children operated with meningocele/myelomeningocele in the hall of Neurosurgery at UCCK in Pristina, during the period from April 2010 to April 2014.

Results: The general number of children being born with defects and different pathologies of neural tube from April 2010 to April 2014 was 133. The incidence of operated children with meningocele/myelomeningocele, in the period from April 2010 to April 2014 in the hall of neurosurgery at UCCK in Pristina was 75 cases, of which 48 (64%) were diagnosed with meningocele (DS=5.31), 27 (36%) were diagnosed with myelomeningocele (DS=1.94). From these cases, 31 (38%) were registered from urban areas (r=.371, p<0.01), 44 (62%) were registered from rural areas (r=.536, p<0.01), 48 (67%) cases were females, while 27 (33%) were males. Out of the 75 children operated with meningocele/myelomeningocele 10 (14%) cases have suffered complications accompanied with hydrocephaly (DS=1.22). The average age of operated children was 4-5 days. By making correlation analysis, a significant report in the structure of operated children with meningocele/myelomeningocele, and the incidence of children with complications with hydrocephaly was found.

Conclusion: Out of the 75 operated children with meningocele/myelomeningocele, 10 cases have suffered complications accompanied with Hydrocephaly; time of intervention was after 7-20 days. 3 (30%) cases were from urban areas, 7 (70%) cases were from rural areas. 7 (70%) cases were females and 3 (30%) were males. By making a correlation analysis and standard deviation, we have reached the following values: The incidence of operated children with Meningocele: DS=5.31; The incidence of operated children: DS=1.94; The incidence with complications in Hydrocephaly: DS=1.22, r=0.961, p=0.009 (p<0.01); Complications according to residence: DS=0.707; Village: DS=1.14, r=0.539, p<0.0.01;City: DS=0.894, r=0.371, p<0.01; and complications according to gender: r=0.920, p<0.01. Based on this statistical analysis we see that the correlation of this data is significant.

Biography

Florije Flora Gjonbalaj is working as a Nurse Anesthetist at University Clinical Center of Kosovo, Pristina. She has completed BSc of Pedagogy in Health Sciences, in the field of Nursing and MSc in Health Management. She had published 3 papers in reputed journals and attended 6 workshops.

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Practical incorporation of psychosocial and focused physical assessments for spine-related pain disorders: A practical hands-on workshop

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Overview: Reliance upon the biomedical model and fractured specialty-based care have contributed to a dysfunctional management paradigm for spine-related pain disorders (SRDs), low back and neck pain. In this dynamic, interactive 90 minute workshop, a blend of didactic and practical instruction will teach attendees how to incorporate biopsychosocial assessment questionnaires and learn focused, evidence-based physical examination procedures. Those attending will learn how differently trained and licensed healthcare practitioners can implement an integrative, evidence-informed clinical process for managing SRDs by incorporating an efficient and practical assessment process. Specific attention will be given to psychosocial assessments including the STarT back screening tool, SCP neck screening tool and patient-specific functional scale. Focused examination procedures with high specificity and sensitivity will be described, demonstrated and practiced. Sample case presentations will be used to make clinical decisions and prescribe management focusing on patient self-care.

Rationale: Spine-related pain disorders (SRDs), low back and neck pain, are the first and fourth leading causes of disability in the world, respectively, with enormous global economic impact. Increasing expenditures have not resulted in improved clinical outcomes. Patients and clinical practitioners are faced with a wide array of differing approaches and treatment options yet few have documented success in the majority of patients. There is evidence supporting a clinical model based on relationship-centered care that incorporates the psychosocial needs of patients concurrently with evidence-informed physical evaluation and management strategies.

Objectives: The objectives of this study are to: Understand the global scope, magnitude and economic consequences of spine-related pain and disability; Recognize factors that have contributed to the current dysfunctional state of spine care, with consideration of the biomedical model of disease; Recognize how academic and professional silos and healthcare policies have created barriers to effective care; and Learn how to employ emerging strategies that emphasize patient self-efficacy and offer the potential for improved value.

Topic Areas: The workshop incorporates evidence-based themes into a framework suitable for differently licensed practitioners to apply standardized spine care management by incorporating practical psychosocial and physical assessments and treatments strategies.

Session/Method Outlines: The two speakers will team teach in a conversational and interactive format. Topics are: (1) Economics and epidemiology of SRDs; (2) Factors leading to the current dysfunctional state of spine care; (3) Psychosocial assessment questionnaires - [3a] Introduced; [3b] Instruction in scoring, interpretation and application in patient management; [3c] Scoring and Decision-making exercise; (4) Patient Interviewing - a structured approach to stratify care and referrals; (5) Physical Assessment - [5a] Specificity and Sensitivity of examination procedures- Why it matters [5b] Demonstration and practice of select physical assessment techniques; (6) Diagnosis-based clinical decisions- [6a] Stratification [6b] Management sub-classifications; [6c] Practical decision-making exercise;

(7) Chronic and refractory cases - a consideration of perpetuating factors; and (8) Putting it all together

Materials: Resources used in practical exercises will include: (1) STarT back screening tool; (2) Spine care partners neck screening tool; (3) Patient-specific functional scale; (4) Selected physical assessment descriptions; (5) Pain drawings with case-presentations; and (6) Links for online references.

Equipment: One examination or therapy table for demonstration and practice of physical assessment procedures.

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Novel mechanism-based targets for pain treatment

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Mast cells are tissue resident granulocytes known for their role in itch and anaphylaxis. We examined the contribution of mast cell activation in chronic and acute pain. We used homozygous BERK sickle mice that have constitutive chronic pain and hypoxia/re-oxygenation evoked acute pain. These mice mimic the features of clinical sickle cell disease (SCD), which is accompanied by severe chronic pain and recurrent episodes of acute pain. We found that mast cell degranulation/activation is significantly higher in the skin of sickle mice as compared to controls. This increased mast cell activation contributes to promoting neurogenic inflammation and nociceptor activation via the release of tryptase and substance P in the skin and dorsal root ganglion. Inhibition of mast cells with imatinib *in vivo*, led to a significant decrease in the release of cytokines from skin biopsies *ex-vivo*. Importantly, it led to a correlative decrease between GMCSF and white blood cell counts in sickle mice. Mast cell deletion in sickle mice as well as pharmacologic treatment with imatinib led to a decrease in tonic and hypoxia/re-oxygenation evoked acute hyperalgesia in sickle mice. Mast cell stabilizer cromolyn sodium reduced chronic hyperalgesia and improved the outcome of relatively lower dose of morphine, which is otherwise ineffective. We conclude that mast cells provide a druggable target to ameliorate sickle pathophysiology and pain.

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G-RMPP: Gait retraining as management for patellofemoral pain syndrome

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Gait retraining is a newly researched method for management of patellofemoral pain (PFP). Patellofemoral pain, more commonly known as anterior knee pain, is a common running ailment that typically affects more women than men. Although it affects many individuals, the cause is relatively unclear. Researchers agree that the cause is likely multifactorial with several perturbations leading to the development of PFP. Of those, it appears that patellofemoral joint stress (PFS) has a strong association with PFP. Therefore, a reduction in PFS is thought to lead to reduced PFP. Several interventions have been investigated with their ability to reduce PFP. Most of this research focused on hip kinetics and kinematics, showing some success in reducing PFP. However, a recent study indicated that perturbations at the hip may be a compensatory mechanism that individuals develop to manage the pain and symptoms. New research on foot strike patterns have shown that rear-foot strike running is associated with greater PFS compared to forefoot strike running. Subsequently, it was demonstrated that a significant reduction in PFP occurs as a result of switching foot strike patterns in runners affected by PFP. Specifically, changing from rear-foot strike running to fore-foot strike running has led to reductions in PFS, patellofemoral contact force, knee abduction and PFP, suggesting that it is an effective intervention for management of PFP. It is worth noting that the change in foot strike pattern increased Achilles tendon force, which potentially increases the risk of injury at the ankle.

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Postoperative analgesia after electroacupuncture in inguinal hernia surgery with mesh

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Introduction: Post-operative pain after inguinal hernia surgery is attributed to surgical manipulation or placement of the preperitoneal mesh. Perioperative use of acupuncture can probably be a useful adjunct for postoperative analgesia.

Aim: The aim of this study was to evaluate the effect of EA in mesh inguinal hernia open repair using pain scales, anxiety questionnaire and the evaluation of pain with an algometer and measurements of stress hormones.

Methods & Participants: 54 male patients were included in the study (23 inguinal left and 31 with inguinal right, classification in ASA I-II) submitted in programmed mesh inguinal hernia open repair with the technique Lichtenstein. Investigation parameters included: 1) Pain scales (VAS, PPI, VRS, SS and FS) and the anxiety questionnaire at 30′, 90′, 10 hours and 24 hours postoperatively; 2) Pain threshold and tolerance were evaluated preoperatively, before and after electroacupuncture, and postoperatively at 30′, 90′, 10 hours and 24 hours after surgery; and 3) Blood levels of stress hormones cortisol, corticotropin and prolactin were measured at the same time points (excluding 24 hours). The frequency of complications of opiates was recorded. Patients were randomly allocated in 3 treatment groups of 18 patients. The three groups were: Group 1: placebo EA, Group 2: preoperative (40′) and postoperative (60′) EA, Group 3: preoperative, intraoperative and postoperative EA. The trial used low frequency EA of 2 Hz and frequency scanning mode. Needles were placed bilaterally at points of great analgesic effect. Electroacupuncture was applied to the points in pairs SP6-ST36; LI4–PC6; Shen-Men 55-Thalamus 26a. If the pain VAS score was greater than or equal to 3 cm within 90 minutes after surgery, an intravenous bolus dose of 5 mg pethidine was given and continuous intravenous infusion pump of pethidine at a rate of 10 mg/h was administered for 12 hours. If the levels of analgesia were not satisfactory, parecoxib at a dose of 40 mg was administered. Data were processed in SPSS 17.0 and appropriate statistical tests.

Results: Electroacupuncture groups showed lower scores on scales VAS, VRS and biggest decline in stress hormone levels as compared to the placebo group at 30′, 90′ and 10 hours postoperatively. There were no statistically significant differences between groups 2 and 3. In the left-operated, the evaluation with algometer showed higher pain threshold and tolerance to EA groups compared to the placebo group. Similarly, for right-operated statistically significant differences were observed at 30′, 90′, 10 hours and 24 hours postoperatively. In anxiety scale, the groups of real EA had less anxiety compared to the placebo group at 90′ and 10 hours postoperatively. PPI questionnaire showed statistical differences at 10 hours; Faces scale at 30′ and 90′ postoperatively and satisfaction scale at all-time points, as the EA groups had a better analgesic effect.

Conclusion: Low frequency EA for post-operative pain following mesh inguinal hernia repair significantly reduced postoperative pain compared to placebo. Respectively, there was a decrease in stress hormones levels and anxiety. The acupuncture could be implemented into the clinical routine as a complementary method in the perioperative setting.

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Methadone for pain: What to do when the oral route is not available?

Philippa Hawley
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Methadone has a unique and valuable role in chronic pain management and palliative care. When patients are dying, they often become unable to swallow. In many places methadone is only available in oral formulations, and may be discontinued towards end of life if prescribers are unaware of the alternative routes available for administration. This presentation will describe alternative routes of administration of methadone: rectal, transmucosal and transdermal, while emphasizing that good pain control achieved with methadone can be maintained until the time of death.

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Dealing with metastatic bone disease in lung cancer and prevention of SREs and pain

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Metastatic bone disease occurs in patients with lung cancer, in 30-40% of patients at the time of diagnosis and as the patients live longer, incidence of bone metastases increases. Bone metastases have debilitating consequences called skeletal related events (SREs), i.e. fractures, surgery and radiation to bone, spinal cord compression and hypercalcemia, which then result in significant comorbidities, pain, loss of autonomy, reduced quality of life and increased healthcare costs. In randomized phase III trials in patients with solid tumors, 40-50% of patients developed SREs, 2.71 SREs per patient per year. Mechanism of action of nitrogen containing bisphosphonates and RANKL inhibitor and their efficacy in patients with lung cancer will be discussed. Trial of zoledronic acid (ZA) in patients with bone metastases from non-small cell lung cancer (NSCLC) and other solid tumors versus placebo will be described, including the impact of the reduction of SREs on survival pain and cost of managing lung cancer patients. A phase III trial of denosumab vs. ZA in the treatment of bone metastases in patients with advanced cancers (excluding breast and prostate cancer) or multiple myeloma, SREs and pain outcomes, analgesic use will be described. The proportion of patients with no or mild pain at baseline reporting moderate or severe pain by visit, pointing out that denosumab delayed the moderate or severe pain more effectively than ZA and how many patients in each arm shifted to strong opioid use. The conclusion of this trial was that a better pain control was achieved with denosumab compared to ZA. New bone targeted agents, i.e. dasatinib, sotatercept, cabozantinib and RAD 223 are under investigation.

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Nurse led fascia iliaca compartment block service for fractured neck of femur

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This was a service set up to be run by the pain nurses for the initial administration of pain relief to elderly patients with fractured neck of femur. This service was the first of its kind in the UK and Europe. In fact, we are not aware of the existence of a similar service anywhere else in the world as of the time. However, it has to be said that since then various modifications of the service have been reported. It is noteworthy that fascia iliaca compartment block (FICB) is not in itself new but it is a rather underused technique of pain relief. However, nurse administered FICB was a pioneering service. Our team was made up of 2 anesthetists and 2 pain nurses. After obtaining the Hospital Guidelines Committee approval which rigorously scrutinized the service proposal, the 2 pain nurses were trained by the 2 anesthetists. The training consisted of ensuring the appropriate patient selection, the performance and management of possible complications of fascia iliaca compartment block. Prior to rolling out the service and an initial audit was carried out. Patients were recruited into audit following the designed protocol. The outcome of the audit has been presented and published. My talk will cover how the service was set up, the initial challenges faced and how they overcame and the recent developments.

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Pulmonary endarterectomy with deep hypothermic circulatory arrest: Acute pain management

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Aim: To assess postoperative pain intensity and the analgesic requirements in the postoperative period, in patients undergoing sternotomy for pulmonary endarterectomy involving deep hypothermic circulatory arrest compared to valvular cardiac surgery not involving deep hypothermic circulatory arrest.

Design & Setting: Retrospective cohort study, single-hospital center study.

Participants: Patients 18 years and older undergoing sternotomy for cardiac surgery between August 2012 and August 2014 were considered for the study.

Interventions: No modification to usual clinical practice.

Measurements & Results: Intraoperative opioid and steroid administration, Intensive Care Unit pain scores and analgesic administration in the first 48 hours after the admission to the Unit were recorded. Postoperative pain was evaluated by means of a categorical verbal scale from no pain (0) to severe pain (3) as this is the routine analgesic scale used in our Intensive Care Unit. A total of 300 consecutive sternotomy patients were included: 200 undergoing pulmonary endarterectomy (PTE group) and a control group of 100 valvular cardiac surgical procedures (non-PTE group). No patient in the PTE group received morphine during surgery while all patients in non-PTE group did ($p<0.001$). Mean (standard deviation) post-operative pain intensity score at 24 hours was 0, 30 (0, 54) in PTE group and 0, 22 (0, 41) in non-PTE group ($p=0.193$). Postoperative morphine was administered in 39% patients in PTE-group and in 47% in non-PTE group 2 ($p= 0.185$).

Conclusion: The total analgesic requirements of patients undergoing sternotomy for pulmonary endarterectomy was lower compared to patients undergoing conventional valvular cardiac surgery. No differences in pain score was found at 24 hours after surgery.

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Development and validation of analytical method for simultaneous estimation of paracetamol and thiocolchicoside by RP-HPLC in bulk and pharmaceutical dosage form

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A simple, precise and accurate HPLC method has been developed and validated for assay of combined dosage form of paracetamol and thiocolchicoside in commercial pharmaceutical dosage form. Reversed-Phase High Performance Liquid Chromatographic (RP-HPLC) analysis was performed on a BDS Hypersil C18, 250 mm×4.6 mm, 5 µ (particle size) and Thermo Scientific column using potassium di-hydrogen phosphate: methanol (40:60, v/v) as eluent. The flow rate of the mobile phase was adjusted to 1.0 ml/min and the injection volume was 20 µl. Detection performed at 247 nm. The retention time of paracetamol and thiocolchicoside were found to be 3.27 and 5.50 respectively. The method was validated for linearity, precision, accuracy and robustness. Response was a linear function of drug concentration in the range with 250-750 µg/ml for paracetamol and 1-3 µg/ml for thiocolchicoside. Intra-day and inter-day precision were determined. Accuracy of paracetamol and thiocolchicoside was found between 99-100%. All analytical validation parameters were determined by following the ICH guidelines and its limit. The developed method proclaimed to be precise and robust for the estimation of paracetamol and thiocolchicoside in their combined dosage form.

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Ozone therapy as an alternative treatment to the pain in the temporomandibular disorder

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Introduction: The temporomandibular disorder is very frequent, existed few studies reflect the effectiveness of the ozone (intra-articular gas) application in the region of temporomandibular joint.

Objectives: To identify the signs and symptoms of temporomandibular disorder; to determine the remission time of the pain in the temporomandibular joint; and to evaluate the disappearance of the upset signs of temporomandibular disorder in the studies after the ozone therapy application.

Material & Methods: An intervention study was realized in patients of International Centre of Investigations of Ozone. Ozone was applied intra-joint for 10 sections 3 mg/L for a volume of 3 ml equivalent to 0.03 mg in one bilateral section, plus rectal application.

Results: The pain subsided before the fourth application of ozone (100%). The mouth opening limitation referred in (100%) followed to a lesser degree of deflection and mandibular deviation.

Conclusions: The intra-articular and rectal ozone is a safe method for the pain relief in the temporomandibular disorder and remitted before the fourth treatment session.

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Continuous intra-articular and periarticular of levobupivacaine for management of pain relief after total knee arthroplasty: A prospective randomized, double-blind pilot study

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Background: Total knee arthroplasty (TKA) can result in major postoperative pain which can impact on the recovery and rehabilitation of patients and for this reason the use of a pain-control infusion pumps (PCIP) enhances analgesia for TKA.

Purpose: To investigate whether a PCIP of levobupivacaine would reduce pain in patients following TKA.

Methods: This was a prospective, randomized, controlled study conducted in 57 patients. Criteria for participation were unilateral TKA for osteoarthritis, and no allergies to levobupivacaine. The primary outcomes measured were postoperative pain intensity on visual analogue scale (VAS) score measured at 24 hours and 48 hours. Other measures included amount of narcotics, presence of adverse events and length of hospital stay.

Results: PCIP-treated patients (n=28) showed significant reductions in VAS score at any time versus control ($p<0.01$). Amount of narcotics, presence of adverse events, length of hospital stay were significantly less with the PCIP versus control (each $p<0.01$).

Conclusion: The use of a mix of levobupivacaine, ketorolac-trometamina and adrenalin provides a safe and effective means by post-operative pain relief in patients undergoing TKA.

Level of Evidence: Level II therapeutic study.

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Subclinical neck pain impairs cognitive ability which can be improved by chiropractic treatment: A four week longitudinal study with a healthy control group comparison

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The research objective was to determine if the cognitive effects of neck pain could be reduce significantly with the chiropractic treatment. The research methods included the recruitment of 42 right handed subjects between ages of 18 and 45 years. 28 of these subjects had neck pain, and 14 subjects were without neck pain and were used as healthy controls. The neck pain group was split into two groups which were the "treatment" and "control" groups. Each subject completed 3 different cognitive tests which were the intra/extra dimensional test (IED), rapid visual processing (RVP) test and the spatial span (SSP) test using Cambridge Cognition software. Subjects were tested before and after 4 weeks. During those 4 weeks the neck pain treatment group received chiropractic treatment. The research outcomes were a significant difference between the healthy subject's baseline and the neck pain subject's baseline (neck pain control and treatment groups) during the RVP test. There was a significant difference between the neck pain control group and the neck pain treatment group in the RVP and IED findings. For the SSP findings, there was a significant difference between the healthy subject's baseline and the neck pain subject's baseline. The interpretation is at baseline that the subclinical neck pain individuals performed worse than the healthy controls on the RVP, IED and the SSP tests of cognitive function. The working population can have reduced cognitive processing due to low grade neck pain which can increase workplace errors, affecting the safety and productivity.

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Multimodal therapy to manage elder patients with persistent pain

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Introduction & Aim: Chronic pain in geriatric patients represents a very common complaint in our daily clinical routine. The geriatric day hospital at the Nuremberg Medical Center developed a novel therapeutic concept particularly designed for the treatment of the elderly multimorbid patient (average 75 years) with chronic pain. In the multimodal targeted therapy program principally non-pharmacological measures are used to treat chronic pain i.e. a newly conceived pain education. Evaluation of initial results will be examined to find out how geriatric patients suffering from chronic pain can exert a positive influence on their well-being and activity by helping themselves.

Methods: Checks at the beginning and end of the procedure will be undertaken and evaluated in a geriatric assessment i.e. psychological (hospital anxiety depression scale (HADS)) and physical parameters (short physical performance battery (SPPB) and Tinetti-test).

Results: The program helped for the first time to visibly increase the wellbeing of the 166 patients with chronic pain and also their daily activities by teaching those methods to help them. At the beginning the higher values of anxiety, depression, inactivity and tendency to fall were at the end clearly improved.

Discussion: This investigation should stimulate the discussion on which medical parameters for persistent pain in geriatric patients can be applied for assessment, diagnosis, follow-up, and treatment.

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Efficacy of paravertebral block analgesia for post-thoracotomy pain control

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Paravertebral block (PVB) is an effective analgesic technique for post-thoracotomy pain, whereas there is no clear proof on how it can be more effective. We aimed to assess if the pleural integrity has a significant effect on thoracic PVB analgesia. Data of patients who underwent thoracotomy and paravertebral catheterization at the Menoufia University Hospitals, between November 2010 and December 2014 were retrospectively collected. Patients were classified into two groups; Group A, where the parietal pleura was disrupted, and Group B, where there was no pleural tear. Pain scores and pulmonary functions were compared between both groups. Also, the frequency of PVB analgesia and the need for supplementary drugs taken as well as the use of rescue pain medications were assessed in both groups. 132 patients were analyzed; group A (n=68) patients with pleural disruption and group B (n=64) patients with intact pleural. There was no statistical significant difference regarding age, sex, body mass index, American society of anesthesiologists score (ASA), diagnosis, and operative details. Pain scores were significantly lower in Group B, where no there was no pleural tear. Pulmonary functions significantly improved among intact pleura group. Significant increase in the frequency of PVB analgesia, supplementary drugs taken in postoperative period and in the use of rescue drugs were observed in patients with pleural disruption. Complications were higher in pleural disruption group. Preservation of integrity of the parietal pleura is essential for the quality thoracic PVB.

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The trends and challenges of pain management in the Neonatal Intensive Care Unit

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Critically ill immature preterm infants experience multiple noxious stimuli while receiving care in the Neonatal Intensive Care Unit (NICU). These noxious stimuli include, but are not limited to: venipuncture; insertion of intravenous and arterial catheters; suctioning of the nose, mouth and oropharynx; endotracheal intubation for mechanical ventilation; insertion of chest drains; and repositioning and other types of patient manipulation. The delivery of optimal doses of analgesics for these noxious stimuli is a major challenge due to the lack of knowledge about drug disposition and its effects in this population. Beyond the lack of knowledge for dose selection and response prediction, it is also relevant to consider the clinical importance of new consequences of analgesic use such as opioid-induced tolerance, hyperalgesia drug related toxicities and neonatal drug discontinuation syndrome, which challenge the current paradigm for pain management in the newborn infant population. In addition, the impact of pain in the neurodevelopment aligned to fast development of the immature brain increase the complexity in the evaluation of nociception/pain. The drug therapy used in pain management relies on an adequate pain assessment of the preterm neonate. The development of computational algorithms to measure nociception/pain in real-time constitutes the next step for pain management in the NICU. An efficient evaluation system may decrease the uncertainty on drug dosage, increase patient safety and improve pain management addressing the impact of pain in the immature brain and explain the neurologic pathway of pain in preterm infants.

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Spinal 5-HT1A receptor plays a major role in directing serotonergic modulation toward inhibition on mechanical allodynia of carrageenan inflammation

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Introduction: Descending serotonergic projections may facilitate or inhibit nociceptive processing in the spinal cord depending on several factors. Unlike other pain states, spinal 5-hydroxytryptamine 3 receptors (5-HT3R) were shown to play a limited role in nociceptive transmission of carrageenan-induced inflammatory pain. Instead, a facilitatory role of 5-HT1AR and 5-HT1BR in spinal nociceptive processing was observed during early-phase of carrageenan model. Although, the maximum release of 5-HT in spinal cord reaches the maximum 2-3 hours after carrageenan injection (early-phase), its release returns to baseline 8 hours.

Aim: To identify the role of Spinal 5-HT1A receptor in directing serotonergic modulation toward inhibition on mechanical allodynia of carrageenan inflammation.

Methods: Effects of intrathecal (i.t.) nonspecific 5-HTR agonist, subtype agonist or antagonists (5-HT1AR, 5-HT1BR, 5-HT3R), and 5,7-dihydroxytryptamine (5,7-DHT, a serotonergic neurotoxin) on mechanical allodynia were tested for early- and late-phase allodynia.

Results: Lesioning spinal serotonergic projections with 5,7-DHT induced a significant increase in the intensity of mechanical allodynia at both early and late-phase. This increase was attenuated by i.t. 5-HT. Also, i.t. 5-HT itself produced a significant antiallodynic effect in late-phase, but not in early-phase. Similarly, i.t. 5-HT1AR agonist (8-OH-DPAT) attenuated the intensity of late-phase allodynia in a dose-dependent manner which was antagonized by 5-HT1AR antagonist (WAY-100635), but produced no effect on the early-phase allodynia. However, other agonists or antagonists of 5-HT1BR and 5-HT3R did not produce any anti or pro-allodynic effects.

Conclusion: Descending serotonergic modulation plays a vital role in inhibition of nociceptive processing during late-phase allodynia, which involves spinal 5-HT1A, but not 5-HT1B or 5-HT3 receptors in carrageenan-induced inflammation. However, the defined role of 5-HT1A and serotonergic inhibition during early-phase remains undetermined.

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Pain management techniques

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In the present study, we hypothesized that listening to music would modulate the effects of allodynia, hyperalgesia and fatigue in patients with fibromyalgia (FM). Due to its emotional effect, we expected that listening to music would have a greater moderating effect on the perception of pain and fatigue than listening to non-musical sounds. To investigate this hypothesis, we carried out a study in which people with FM were given a listening device for four weeks enabling them to listen to either music or environmental sounds when they experienced pain, in either an active (while carrying out a physical activity) or passive (at rest) situation, while measuring changes in levels of pain and fatigue. The results of this study indicate that when people with FM listen to music or environmental sounds when they are at rest, their pain and fatigue decreased after 20 minutes of listening. This physical improvement persists for ten minutes after the end of the listening session. In physical active situations their pain did not decrease but it did not increase. Contrary to our expectations, music and environmental sounds produced the same effect on pain and fatigue, with no extra benefit gained by listening to music rather than environmental sounds.

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Bone healing, hormonal bioassay and growth factors measurement in patients with long bone fractures and concomitant acute traumatic spinal cord injuries

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Aim: The aim of the study was to test the effect of acute traumatic spinal cord injury of quadriplegia or paraplegia on bone healing in patients with associated long bone fractures and to investigate the molecular and cellular events of the underlying mechanism for a possible acceleration.

Methods: Bone healing indicators of long bone fractures, hormonal bioassay for parathyroid hormone, growth hormone, corticosteroids, noradrenaline, adrenaline, leptin hormone, and growth factors measurement for Insulin like growth factor II (IGF-II), platelet- derived growth factor (PDGF), vascular endothelial growth factor (VEGF), Activin-A, and cytokine Interleukin I (I-L-1), in the patients' blood were calculated for 21 patients with spinal cord injuries and associated long bone fractures (Group B) in prospective controlled study and compared to 20 patients with only spinal cord injuries (Group A), and 30 patients with only long bone fractures (Group C).

Results: The study results showed that the mean time of bone union in group B was 6.3, range (3.7-7.5) weeks. There were no cases of non-union of long bones in this group. The mean maximal thickness of union bridging callus as shown in CT scan was 29, range (10-48) mm. The mean healing rate was 4.7, range (2.6-7.5) mm/week, versus 6 (16.7%) went into atrophic non-union, with the mean healing time 22.5, range (14-42) weeks, the mean maximal thickness of union callus 8, range (2-20) mm, and the mean healing rate 0.41, range (0.25-1) mm/week in group C. The study showed statistically higher levels of parathyroid hormone and growth hormone ($p<0.005$) and normal corticosteroids levels. Patients with long bone fractures only showed consistent and statistically significant higher level of noradrenaline and adrenaline hormones compared to patients with spinal cord injury alone or associated with long bone fractures ($p<0.001$). Leptin hormone showed statistically significant consistent decrease in patients with spinal cord injury and concomitant long bone fractures compared to healthy subjects ($p<0.001$). It also showed statistically significant higher levels of growth factors like PDGF, VEGF, Activin-A, and cytokine I-L-1, along the 3 weeks of follow-up ($P>0.005$). I-IGF-II showed statistically significant subnormal level along the whole follow-up period in the same patients ($P>0.005$).

Conclusions: We concluded that long bone fractures in spinal cord injury patients heal more expectedly, faster, and with exuberant and florid callus formation. We can also conclude that bone healing has a central neuronal regulation and a combined neuro- hormonal mechanism with inhibition of the sympathetic nervous system is a possible cause of accelerated healing of long bone fractures in patients with associated spinal cord injury and growth factors like IGF-II, PDGF, VEGF, Activin-A, and cytokine I-L-I have roles as mediators, in molecular events and as byproducts of the aforementioned mechanism.

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Gut-the Trojan horse in remote organs' autoimmunity

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Human beings assemble and maintain a diverse but host-specific gut microbial community along the longitudinal axis of the intestines. Helped by a functional tight junction, the default response to commensal microbes is tolerance, whereas the default response to pathogens is an intricately orchestrated immune response, resulting in pathogen clearance. Nutrients and industrial food additives were suggested to impact the intestinal ecosystem and to breach tight junction integrity, thus, contributing to autoimmunogenesis. Taken together, certain nutritional components, increased intestinal permeability, disease specific dysbiotic pathobionts and their capacity of post translation modification of proteins and their secreted metabolites are luminal events that impact autoimmunity. The current presentation expands on the multi gut originated axes and their relationship to remote organ autoimmune diseases. Brain, joint, bone, endocrine, liver, kidney, heart, lung and skin autoimmune diseases are connected to the intestinal luminal compartmental deregulated events to form the gut-systemic organs axes. Multiple brain functions, sensations, behavior and human mood originate from the intestinal lumen and traffic bi-directionally between the two organs, impacting the gut-brain axis.

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Qualitative phytochemical screening and evaluation of anti-inflammatory, analgesic and antipyretic activities of *Microcos paniculata* barks and fruits

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Methanolic extracts of *Microcos paniculata* bark (BME) and fruit (FME) were qualitatively evaluated for phytochemical constituents, as well as to evaluate their anti-inflammatory, analgesic and antipyretic activities. Phytochemical constituents of BME and FME were determined by different qualitative tests such as Molisch's test, Fehling's test, alkaloid test, frothing test, FeCl3 test, alkali test, Salkowski's test and Baljet test. The anti-inflammatory, analgesic and antipyretic activities of the extracts were evaluated through proteinase-inhibitory assay, xylene-induced ear edema test, cotton pellet-induced granuloma formation in mice, formalin test, acetic acid-induced writhing test, tail immersion test and Brewer's yeast induced pyrexia in mice. *M. paniculata* extracts revealed the presence of carbohydrates, alkaloids, saponins, tannins, flavonoids and triterpenoids. All of the extracts showed significant ($P<0.05$, vs. aspirin group) proteinase inhibitory activity, whereas the highest effect elicited by plant extracts was exhibited by the BME (75.94% proteinase inhibition activity). Each extract at the doses of 200 and 400 mg/kg body weight showed significant ($P<0.05$, vs. control) percentage inhibition of ear edema and granuloma formation. These extracts significantly ($P<0.05$, vs. control) reduced the paw licking and abdominal writhing of mice. In addition, BME 400 mg/kg, and FME at 200 and 400 mg/kg showed significant ($P<0.05$, vs. control) analgesic activities at 60 min in the tail immersion test. Again, the significant ($P<0.05$, vs. control) post-treatment antipyretic activities were found by BME 200 and 400 mg/kg and FME 400 mg/kg, respectively. Study results indicated that *M. paniculata* could be a source of plant compounds with anti-inflammatory, analgesic and antipyretic activities.

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