

3A GENERAL SURGERY 1

O67 PEROXISOME PROLIFERATOR ACTIVATED RECEPTORS (PPARS) MODULATE TRANSLOCATION ACROSS HUMAN EPITHELIAL MONOLAYERS

E Theophilidou, J Lund, SE O'Sullivan

Division of Medical Sciences, School of Medicine Royal Derby Hospital, University of Nottingham

Introduction: PPARs are ligand-activated transcription factors belonging to the nuclear hormone receptor family and exert beneficial effects during inflammation. Intestinal permeability (IP) plays a key role for the development of sepsis and colitis. The ability of PPAR to modulate IP in inflammation may be important in therapy and prevention of bacterial translocation and sepsis. The aim is to study the effects of PPARs during inflammatory conditions using a gut inflammation in vitro model.

Method: Caco-2 cell line monolayers were used as a model of intestinal epithelial cells. Inflammation was induced with the addition of the cytokines interferon gamma and tumour necrosis factor alpha. Ligands of PPAR isotypes (α , β/δ and γ) were added for 7 days prior to the induction of inflammation. Permeability was assessed using transepithelial-electrical-resistance (TEER) measurements. FD4 and FD10 dextran probes were used to assess translocation of different molecular sizes across the monolayer through fluorescence.

Result: Basolateral application (mimicking systemic circulation) of the PPAR ligands (α , β/δ and γ) for 7 days prior to the induction of inflammation significantly increased TEER baseline measurements, hence reducing permeability ($p < 0.0001$, $p < 0.05$, $p < 0.001$ respectively). A highly significant decrease in the translocation of FD4 was observed during inflammation ($p < 0.0001$) for PPAR α and γ compared to controls. Translocation of FD10 was greatly reduced 48 to 72 hours after inflammation ($p < 0.0001$) for all PPAR ligands).

Conclusion: PPAR agonists prevent the translocation of different molecular sizes during inflammation in an in vitro model, and could be pharmacologically targeted in preventing the development of sepsis.

Take-home message:

Peroxisome Proliferator-activated receptors exert anti-inflammatory properties in gut inflammation. These receptors could be pharmacologically targeted for the prevention of sepsis.

O68 DEVELOPMENT OF A PHARMACOLOGICAL AGENT TO PREVENT THE PERMEABILITY CHANGES CAUSED BY SEPSIS

DG Couch, E Theophilidou, SE OSullivan, J Lund

Derby Royal Infirmary Teaching Hospital NHS Foundation Trust

Introduction: During episodes of colonic inflammation translocation of fluid, bacteria and lipopolysaccharide across epithelial membranes leads to septic shock. We have previously demonstrated that palmitoylethanolamide (PEA) and cannabidiol (CBD) prevent these permeability changes in the gut, and may act as novel drug therapies in inflammatory bowel disease. In this study we sought to identify their mechanism of action.

Method: Ethics was granted for all experiments by the local research ethics committee. Samples of normal human colon were obtained from consenting adults undergoing right hemicolectomy for malignancy ($n=8$). Tissue was cultured for 24 hours with tumour necrosis factor alpha (TNF α) and interferon gamma (IFN γ) to induce inflammation with or without the addition of PEA or CBD as appropriate. Concentrations of multiple inflammatory cytokines from different aspects of the inflammatory cascade were sampled from culture media using ELISA. Production of intracellular signalling proteins was measured using Multiplex assays. All values were corrected for protein content using bicinchoninic acid assay.

Result: Treatment of tissue with TNF α and IFN γ caused a significant increase in the production of interleukin-8 (IL-8), IL-6, IL-17, granulocyte macrophage colony stimulating factor, monocyte chemoattractant protein-1 and ICAM-1 (intercellular adhesion molecule-1) (all $p < 0.05$). Addition of PEA prevented the production of all measured cytokines ($p < 0.01$), CBD prevented the production of all cytokines except ICAM-1 ($p < 0.05$). PEA prevented the increased production of the intracellular signalling proteins CREB, NF- κ B, STAT-3 and STAT-5 (all $p < 0.05$), whereas CBD did not affect the production of these proteins.

Conclusion: PEA and CBD prevent colonic permeability changes through intracellular immunosuppression of the immune response.

Take-home message:

PEA and CBD may be used as agents to prevent the translocation of fluid and bacteria in sepsis. Their immunosuppressive properties may make them particularly suited to inflammatory bowel disease.

O69 PATIENT REPORTED OUTCOME MEASURES (PROM) FOR GROIN HERNIA OPERATIONS IN ENGLAND: AN ANALYSIS OF PAST FIVE YEARS

A Kanwar, IK Ibrahim, R Thakkar, P Williams, C Wilson, J French, R Charnley, D Talbot, DM Manas, SA White, G Sen

Freeman Hospital

Introduction: Patient Reported Outcome Measures (PROMs) is a Department of Health initiative, aiming to measure effectiveness of care as perceived by patients. Patients are invited to complete

questionnaires, both before and after an operation (sent after at least three months). We aimed to assess national trends from groin hernia PROMs data for last 5 years.

Method: We interrogated the online database(www.digital.nhs.uk) on PROMs for groin hernia surgery performed between April 2011 and December 2015. 2 validated questionnaires are used; the EQ(Euroqol)-5D and EQ-VAS(visual analogue score). EQ-5D is scored between 1 and -0.594(1 = full health state). EQ-VAS is a simple visual analogue scale from 1-100(100 = best health state possible).

Result: A total of 337,689 groin hernias were done in the specified period. Overall 210,326(59.5%) patients participated. 127,100 patients eventually had both pre- and post-operative response. Average pre-operative EQ-5D score was 0.79, increasing to 0.87 post-operatively(health gain of 0.084). Of total 117,406 patients, 58,238(49.5%) reported improved health on EQ-5D score post-op; 37,581(31.9%) had no changes; and 21,263(18%) reported worsening health status. Average pre-operative EQ-VAS score was 80.2, decreasing to 79.4 post-operatively (health gain of -7.9). Of 119,406 patients, 45,125(37.7%) reported improving health on EQ-VAS scale; 22,242 (18.8%) had no changes; and 52,039(43.5%) reported worsened health.

Conclusion: A large proportion of patients noticed either no change or were worse after their surgery. This provides a valuable insight into patients' perception and certainly does not match traditional supposed benefits of groin hernia surgery. A better selection criteria for surgery may be required.

Take-home message:

better patient selection criteria is required for groin hernia operations.

070 CROSS-LINKED COLLAGEN IMPLANT MATERIALS ARE NOT INERT, WITH IMPLICATIONS FOR INFLAMMATION AFTER ABDOMINAL WALL RECONSTRUCTION

S Pengelly, JEA Berry, SE Herrick, GL Carlson
University of Manchester

Introduction: A variety of implanted materials are used for abdominal wall reconstruction. These materials are said to have differing clinical profiles, some of which have been attributed to the development of local inflammatory responses. The aim of this study was to test the hypothesis that implant materials are able to influence the local proinflammatory cytokine environment, independently of interaction with host tissue.

Method: Discs of various implant materials were incubated for 18 hours in DMEM supplemented with IL-1 β , IL-6 and TNF- α , at concentrations previously shown to be produced ex vivo by human peritoneum. Supernatant cytokine concentration was then measured by ELISA and compared to control (without implants). Concentration changes in cytokines were expressed as percentages of control. Statistical analysis was performed by ANOVA, $p < 0.05$.

Result: Strattice™ (non-crosslinked porcine dermal collagen) resulted in a significant reduction in TNF- α concentration (52%, $p = 0.0001$) but not IL-1 β or IL-6, compared with control. Similar reductions in TNF- α concentration (45%, $p = 0.0001$) but not IL-1 β or IL-6, were observed with Biodesign™ (non-crosslinked porcine intestinal collagen). Crosslinked collagen, Polyglactin or Polypropylene, were not associated with a significant change in any the supernatant concentration of any cytokine.

Conclusion: Non-crosslinked collagen is associated with reduced TNF- α concentrations. This effect appears to be implant and cytokine-specific. It is unclear if this is due to adsorption, enhanced cytokine degradation or altered immunogenicity. These novel findings suggest, however, that non-cross linked collagen is not inert, and that chemical properties of implants should be taken into consideration when evaluating biological effects of these materials.

Take-home message:

Different implants may be manipulating the local cytokine environment, affecting the healing process.

071 NOT PRESENTING

072 ADAPTATION OF THE BOWEL OCCURS EARLY AFTER RESTORING BOWEL CONTINUITY IN PATIENTS WITH A SHORT BOWEL

F Adaba, J Warusavitarne, JMD Nightingale
St Mark's Hospital, London

Introduction: Glycogen like peptide 2 (GLP-2) and peptide YY (P-YY) may be involved in the adaptation of the short bowel. Citrulline can act as an indicator of bowel adaption. The aim of this study is to investigate when bowel adaption starts after restoring bowel continuity.

Method: This is a prospective controlled study. Patients were identified and recruited consecutively via the Intestinal Failure Unit. Serum levels of P-YY, GLP-2 and citrulline were analysed at pre-restoration and 1 and 6 months post restoration.

Result: Nine (2 females, age range 33-85 years) patients with short bowel were recruited. Nineteen (10 females, age range 25-65 years) healthy participants were recruited as controls. Compared to controls, the median P-YY and GLP-2 serum levels at pre- restoration were (182 pg/ml vs 215 pg/ml) and (3.7 ng/ml vs 2.6 ng/ml) respectively. Post restoration, P-YY increased (355 pg/ml and 498 pg/ml at 1 and 6 months respectively) while GLP-2 reduced (3.8 ng/ml and 2.4 ng/ml at 1 and 6 month post respectively). Median values for citrulline increased over time following restoration of bowel continuity. There was a significant correlation between residual small bowel length and citrulline levels at pre-restoration ($p = 0.015$), 1 month ($p = 0.021$) and 6 month ($p = 0.001$).

Conclusion: Adaptation of the bowel occurs as soon as bowel continuity is restored and this process probably continues for a long term.

Take-home message:

Bowel adaptation of the short bowel occurs soon after restoring bowel continuity and Peptide YY plays a role.

073 THYROID NODULE FINE NEEDLE ASPIRATION CYTOLOGY CORRELATED TO FINAL POST-OPERATIVE HISTOLOGY IN A DISTRICT GENERAL HOSPITAL

E Halliday, A Patel

Peterborough City Hospital

Introduction: Fine needle aspiration cytology (FNAC) is used in the assessment of patients with thyroid nodules. Cytology reports include a Thy diagnostic category (Thy1-Thy5); the implied risk of malignancy increases with each category. The aim of this study was to correlate the pre-operative cytology with post-operative histology to assess the accuracy of cytology and calculate the malignancy rates for each Thy category.

Method: Retrospective observational study of all patients undergoing any thyroid excision surgery in a five year period. Patients were included if they underwent FNAC in the six months prior to surgery. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated considering Thy2/2c as true-negative and Thy3f/Thy4/Thy5 as true-positive.

Result: 351 patients underwent 494 FNAC procedures. The overall malignancy rate was 19.5%. Papillary carcinoma was the most common cancer diagnosis (34.7%). In general, the malignancy rate increased with Thy category: Thy1/1c 9.3%, Thy2/2c 13.6%, Thy3a 26.7%, Thy3f 20.7%, Thy4 75.0%, Thy5 100.0%. The NPV and PPV for the benign (Thy2/2c) and malignant (Thy5) categories were 86.4% and 100.0%, respectively. The sensitivity and specificity were 71.2% and 51.7%, respectively.

Conclusion : This study demonstrates the potential for discordance between thyroid FNAC and final histology: a significant proportion of patients with benign cytology will have a malignancy and many patients with Thy3a/Thy3f cytology will undergo unnecessary diagnostic surgery for a benign nodule. The diagnosis of thyroid cancer requires a multidisciplinary approach to review all clinical, cytological and radiological information; FNAC results cannot be interpreted alone.

Take-home message:

There is the potential for discordance between thyroid fine needle aspiration cytology and final post-operative histology.

074 ASYMPTOMATIC GROIN HERNIA SHOULD NOT BE REPAIRED – A PROM (PATIENT REPORTED OUTCOME MEASURES) PERSPECTIVE

A Kanwar, IK Ibrahim, R Thakkar, P Williams, C Wilson, J French, R Charnley, D Talbot, DM Manas, SA White, G Sen

Freeman Hospital

Introduction: Surgical treatment for asymptomatic groin hernia although reduces the risks of potential complications, but there is serious lack of evidence on quality of life outcomes following surgery. We aimed to analyse the PROMs data to assess the outcomes in patients who underwent a primary groin hernia repair without any pre-operative symptoms.

Method: We interrogated the online database(www.digital.nhs.uk) on PROMs for groin hernia surgery performed in England between April 2010-December 2015. Patients complete validated questionnaires with scoring systems, both pre and at least 3 months post-operatively. 2 questionnaires are used; the EQ(Euroqol)-5D and EQVAS (visual analogue score). EQ-5D is scored between 1 and -0.594(1 = full health state). EQ-VAS is a simple visual number scale from 1-100(100 = best health state). We analysed all patients who had best possible pre-operative scores, i.e asymptomatic, and compared it with their post-operative scores.

Result: Overall, 126,712 patients returned valid questionnaires. Based on EQ-5D scores, 33,299(26.3%) patients were asymptomatic; of those, 6,930(20.8%) patients reported a decline in their post-operative health score. 75% of those affected patients had symptoms of discomfort, 30% reported of problems affecting their daily activity and 22% felt their mobility was worse. 16% reported wound complications and 16% required further surgery. 11% stated fair satisfaction and 4% had poor satisfaction. Based on EQ-VAS scores, post-operatively only 112 patients had the best score of 100, in comparison to 462 patients pre-operatively; a decline of 76%.

Conclusion: For asymptomatic groin hernia, a surgical repair cannot be justified based on these patient reported outcomes.

Take-home message:

Asymptomatic groin hernia should not be operated.