Miscellaneous

000033 - Comparing the Effectiveness of Weight-Based versus Fixed Dose Enoxaparin Regimens to achieve Target Thromboprophylaxis Anti-Factor Xa Level in Patients with Obesity

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Introduction

Obesity is an independent predictor of venous thromboembolism (VTE) in bed bound hospital patients, the occurrence which could be reduced or prevented by the appropriate usage of prophylactic anticoagulation therapy (thromboprophylaxis) with enoxaparin. To date, the established regimens for VTE prophylaxis with enoxaparin are derived from large clinical studies on non-obese patients. In contrast, enoxaparin dose modifications in obese patients tend to be derived from small, non-randomised, research studies. Amongst these, several studies had demonstrated the benefits of higher dosage or weight based dosing. In obesity, the bioavailability of enoxaparin is determined by a balance between increased accumulation due to higher volume of distribution and increased elimination due to more efficient renal clearance. It follows that due to the difference in the fat distribution in Asian populations, the behaviour of enoxaparin may differ in Asian from that of Western studies.

Objectives

The objective of this study was to compare the effectiveness of weight-based versus standard fixed dose enoxaparin regimens, to achieve target thromboprophylaxis anti-factor Xa level in obese patients.

Methods

In this Phase III, prospective, randomised, open labelled study, subjects with body mass indices (BMI) of greater than 30 kg/m2 and weighing more than 90 kg were randomised to receive either standard fixed dose enoxaparin (40 mg/day) or weight-based dosage (0.5 mg/kg/day) based on actual body weight. The study was

conducted in Changi General Hospital in Singapore from April 2015 to September 2018. Each subject received three doses of enoxaparin, followed by a peak anti-factor Xa assay 4 hours after the third dose. The primary endpoint was the percentage of patients within range of the target anti-factor Xa level of 0.20 to 0.40 iu/mL in each treatment group. The secondary endpoint was to assess the incident of VTE, major and minor haemorrhages, and other treatment-related adverse effects.

Results

A total of 109 patients were screened for study eligibility. Of these, 40 subjects were randomly assigned 1:1 to the two treatment groups. The full treatment regime was completed in 32 subjects (80%), 16 from each group. Of the 32 subjects who completed the study treatment, 15 (47%) achieved the target anti-factor Xa levels of between 0.20 to 0.40 iu/mL. Subjects who received the weight based regime were more likely to achieve therapeutic anti-factor Xa level (56.2% vs. 37.5%). Of the fixed dosed group, there was a greater proportion who achieved subtherapeutic level of less than 0.2 iu/mL (43.8% vs. 6.2%), indicating underdosing for VTE prophylaxis. The treatment groups did not differ significantly in bleeding complications, with only one patient discontinuing treatment due to thrombocytopenia. No subject developed symptomatic VTE in the course of treatment.

Conclusion

This study demonstrated that using a weight based dosing regimen resulted in a greater proportion of obese patients achieving adequate thromboprophylaxis with no increased bleeding risks. In contrast, using standard dosing of 40mg/day may result in obese patients being at higher risk of VTE due to inadequate thromboprophylaxis.

000043 - Efficiency of endoscopic hemostasis for diverticular bleeding with extravasation on contrast-enhanced CT: A single-center retrospective cohort study

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Introduction

Diverticular bleeding is a common cause of lower gastrointestinal hemorrhage. Patients who have experienced diverticular bleeding have an appreciable risk of rebleeding, so treating the bleeding site is crucial. Active bleeding or stigmata of diverticular hemorrhage are identified in only 10-20% of colonoscopies. However, the endoscopic detection rate of the bleeding point from diverticula is reported in 60-78% of patients in whom extravasation was detected using contrast-enhanced CT (CECT). Bleeding that shows extravasation on CECT is thought to be active, because in such cases, the bleeding rate exceeds0.3-0.5mL/min. It is unknown whether endoscopic hemostasis is the best method to stop active bleeding.

Objectives

The purpose of this study is to examine the efficacy of endoscopic hemostasis for stopping bleeding with extravasation visualized using CECT.

Methods

Endoscopic hemostasis (clip method) is performed initially to stop diverticular bleeding in our hospital. Patients included in the study were those who experienced hematochezia or melena, underwent a colonoscopy within 48 hours from the last event, were diagnosed with diverticular bleeding, and were admitted to our hospital between November 2016 and September 2018. Patients younger than 18 years, who did not undergo a CECT, or who needed treatments for conditions other than diverticular bleeding were excluded. The major outcomes of this study were the detection rate of bleeding diverticula using colonoscopy, treatment rate, and rebleeding rate.

Results

A total of 51 patients were included in the analysis. The detection rate of bleeding diverticula using colonoscopy in the extravasation-positive group (E group) was 92.3% (12/13), while in the extravasation-negative group (non-E group), it was 32.4% (14/38) ($p<0.001$). All (12/12) of the E group patients and 92.9% (13/14) of the non-E group patients that displayed bleeding diverticula were treated by endoscopic clips. The acute rebleeding rate was significantly higher (58.2% [7/12]) in the E group ($p=0.041$) compared with 15.4% (2/13) in the non-E group. Among the seven patients in the E group who experienced rebleeding, all underwent re-colonoscopy with endoscopic hemostasis. Of the seven patients, 71.4% (5/7) were treated successfully with additional clips, one patient needed an operation, and one patient received transcatheter arterial embolization, and was transferred to another hospital for further management.

Conclusion

The detection rate of the origin of diverticular bleeding when using colonoscopy was higher in the E group than in the non-E group. However, the rebleeding rate was higher in the E group than in the non-E group, because the bleeding, which showed extravasation on CECT, was thought to be more active. Disregarding the high

bleeding rate, most patients who experienced rebleeding could be treated by re-colonoscopy with endoscopic hemostasis without transcatheter arterial embolization and operation.

000045 - The Role of Early Laparoscopy in Critical Corrosive Injury of Esophagus and Stomach Patients

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Introduction

Strong alkaloid or acid agents are usually applied as industry materials, which are dangerous to the human body due to their corrosive specialty. Ingestion of these agents usually induces severe chemical burn to the upper gastro-intestine tract.

Objectives

For early removal of these corrosive agents, this study designs a method using a laparoscope for early drainage. We hope this method could decrease the rate of esophageal and gastric strictures.

Methods

All patients had a history of ingesting strong acid or strong alkaloid agents. These patients were initially admitted into the emergency department for primary and secondary survey, and management of these patients was conducted according to patients' abdominal conditions. The most dangerous condition is the appearance of peritoneal signs, meaning that emergent DCS were indicated. The other patients who had abdomen tenderness without peritoneal signs were included in this study. These patients were admitted into ICU for close observation. If the abdomen was tender, and became more severe with peritoneal signs, emergent operations were performed. Patients who had early laparoscopy within 24 hours after the accidents to manage these patients, who were categorized as Group 1. The other patients who received close observation were enrolled as Group2. The Group 1 patients received a laparoscopy in the operating room with general anesthesia, and the organs in the abdominal cavity were inspected under laparoscope vision.

Results

14 patients received emergent laparoscopy within 24 hours after their accidents, and were collected as Group 1. The other 51 patients received close observations as Group 2. The basic demographic characteristics included gender and age between two groups, which were equal without significant differences. A total of 20 patients received DCS with total gastrectomy and subtotal esophagectomy due to the trans-mural necrosis of the abdominal esophagus and fundus of the stomach. Among these patients, two patients belonged to Group 1, while the remaining 18 patients belonged to Group 2. In Group 1, 12 patients received gastrostomy and feeding jejunostomy, as the walls of the stomach and esophagus only had mild swelling without necrosis; while 33 patients in Group 2 received medical treatment successfully without any surgical intervention during the study period. After discharge, both groups received regular out-patient clinic for follow up. There were17 patients with stenosis of the esophageal stricture and stomach contracture at three months after their accidents. Only one patient belonged to Group 1, while the other patients belonged to Group 2. The rates of post-trauma stenosis were much higher in Group 2 (8.3% vs. 48.5%, p=0.014).The overall mortality rate in this study was 12.3%. Although Group 1 had no mortalities, there were no statistical differences between the two groups (0 vs. 15.7%, p=0.114).

Conclusion

Early laparoscopy is a good diagnostic tool in corrosive injury patients without obvious peritoneal signs at the acute stage, as this method could detect trans-mural necrosis early. Early laparoscopy could also perform gastrostomy for adequate drainage, which could prevent esophageal and gastric stricture.

000067 - Endocrine impact of acute organophosphate poisoning after suicidal attempt

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Introduction

Suicide is still one of the most frequent causes of death worldwide1, over 80% of attempts being due to self-poisoning1. Pesticide self-poisoning accounts as a high percentage in suicidal attempts, especially in agricultural countries2. Although many of the systemic effects of organophosphate exposure have been extensively studied, endocrine consequences are still unclear3.

Methods

In order to assess the effects of acute organophosphate poisoning on endocrine system, we performed a prospective, observational and cross-sectional study on 13 patients admitted in the Intensive Care–Toxicology Department after self-ingestion of pesticides. Patients with documented pre-existing endocrine dysfunction or in treatment with acetyl-cholinesterase inhibitors were excluded. The final study group included seven patients in whom we determined levels of acetyl-cholinesterase, cortisol, free triiodothyronine (fT3), free thyroxin (fT4), thyroid-stimulating hormone (TSH) and prolactin on admission and after 24 hours. Results were statistically analyzed using t-test and correlations, setting a standardized significant P value of 0.05.

Results

All patients in the study group survived after adequate treatment was administered. Acetyl-cholinesterase level was significantly lower on admission indicating an acute organophosphate intoxication status (mean difference between determinations 1312 U/L, $p = 0.0034$). Cortisol level was significantly lower on the second measurement with a mean difference of 25 ng/ml ($p = 0.011$). Levels of fT3, fT4 and TSH were also significantly lower at 24 hours post-exposure ($p=0.001$). Increase of fT3 correlated with increase of fT4 on admission with a $p = 0.053$. Moreover, increase of fT4 on admission was proportional with the increase of cortisol levels ($p= 0.04$). Prolactin levels registered no statistically significant changes.

Conclusion

The present study demonstrates that acute organophosphate poisoning can induce an endocrine dysfunction. High levels of cortisol can be induced by the accumulation of acetylcholine as well as by the direct effects of organophosphate compound. Therefore, normalizing acetyl-cholinesterase levels can solve the adrenal dysfunction. This study identified changes in thyroid hormone levels, suggesting the possibility of a non-thyroidal illness in these patients.

000130 - Mechanistic studies of a halogenated hydrocarbon, 2-

chloroethanol, in the pathogenesis of steatosis

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Introduction

2-chloroethanol (2CE) is a halogenated hydrocarbon used in a number of specialized applications in the industry. [1] It is also a major metabolite of 1,2-dichloroethane and vinyl chloride, which causing steatosis and life-threatening issues in many countries. [2-4] Currently, the mechanism of 2CE intoxication is still not clear, however, the lack of knowledge about it leads to treatment failure in acutely intoxicated patients.[5] Therefore, we investigate the mechanism of 2CE intoxication and establish the potential link to toxicant associated steatosis hepatitis (TASH).

Objectives

Evaluate the mechanism of 2CE intoxication by lipidomic and metabolomic approach.

Methods

ICR mice were randomly divided to control vs. 2CE (135 mg/ kg i.p.) groups. After 24 hours, all mice were sacrificed and (a) liver histopathology and serum biochemistry were performed; (b) 24-hour target urinary organic acid analyzed by GC-MS; (c) comprehensive lipidomic profiling in liver tissue by LC-MS; (d) further access the mitochondrial function with rat hepatic cell lines.

Results

The liver weight and the ratio of liver weight to body weight for 2CE groups were significantly higher than that in the control group ($p<0.001$). 2CE group showed significant hepatic steatosis and profound hypoglycemia. Second, the 24-hour urinary excretion of citrate acid and isocitrate were significantly increased in 2CE-treated mice ($p<0.01$ and $p<0.001$ vs. control) and impaired oxygen consumption rate, indicating the derangement of mitochondrial function. Third, lipidomic profiling revealed significant increasing of triacylglycerols (TG) and phosphatidic acids (PA) with concomitant decrease of other phospholipids species indicating either the inhibition of CDP-diacylglycerol synthase pathway or aberrant PA synthesis, both of which could lead to the formation of giant lipid droplets [6].

Conclusion

We proved the mechanistic insight of 2CE toxicity that leading to steatosis. Further investigation is needed to evaluate the role of 2CE related chemicals in the derangement of phospholipid metabolism and mitochondrial function in TASH.

000021 - Diagnosis of Acute Myocardial Infarction after Coronary Artery Bypass Graft (CABG) Surgery: A Systematic Review

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Introduction

Myocardial infarction after coronary artery bypass grafting is a serious complication and one of the most common causes of perioperative morbidity and mortality. Multiple mechanisms have been proposed to explain myocardial injury after CABG. Diagnosis will be established according to creatine kinase (CK) values more than five times the 99th percentile of the normal reference range during the first 72 hours following CABG, (or Troponin or CKMB more than ten time increase) when associated with the appearance of new pathological Q-waves or new left bundle-branch block (LBBB), or angiographically documented new graft or native coronary artery occlusion, or imaging evidence of new loss of viable myocardium, should be considered as diagnostic of a CABG related MI.

Objectives

: to identify the methods of diagnosis of post coronary artery bypass graft (CABG) acute myocardial infarction.

Methods

Data sources: MEDLLINE (PubMed), EMBASE, Google Scholar and the Cochrane Library and all materials available in the internet till 2017.

Study selection: this search presented 23 eligible studies which studied the diagnostic methods for acute myocardial infarction after coronary artery bypass graft (CABG) surgery.

Data extraction: if the studies did not fulfill the inclusion criteria, they were excluded. The methodological quality of included studies was assessed using an adjusted QUADAS-tool.

Data synthesis: comparisons was made by structured review with the results tabulated.

Results

Troponin I and T can both be used to indicate myocardial damage, with the level correlating well with the level of injury. However until issues such as a ‘gold standard’ for peri-operative MI are addressed, one single cut-off point cannot be recommended for either test.

Conclusion

Troponin I and T can both be used to indicate myocardial damage, with the level correlating well with the level of injury. However until issues such as a ‘gold standard’ for peri-operative MI are addressed, one single cut-off point cannot be recommended for either test.

000054 - Increasing Incidence of The Coronary Artery Disease in Blood Group A In The Taiwan Population

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Introduction

This study was aimed to investigate the association between the ABO blood groups and the risk of mortality in the coronary artery disease (CAD) patients admitted to our ICU after coronary angiography.

Methods

From Jan. 2014 to Dec. 2018, we retrospectively collected 2269 patients (1760 men and 509 women) who underwent coronary angiography with the diagnosis of CAD in our hospital. Their ABO blood groups were tested during admission using standard agglutination techniques. The primary outcome was the patient’s 30-day in-hospital mortality.

Results

When compared to the Taiwan population (O, 44.07%; A, 26.00%; B, 23.91%, AB, 6.02%, respectively), patients with CAD showed a significantly different blood group distribution (O, 30.1%; A 39.7%; B, 26.5%; AB, 3.7%). Standardized incidence ratios of the blood groups were O, 0.68; A, 1.41; B, 1.10; AB, 0.61. There were no statistical differences of mortality and hospital length of stay between the blood groups.

Conclusion

We found that the CAD is higher in the blood group A population in Taiwan. However, the outcomes of the patients were no statistical differences in the mortality and length of hospital stay.

000065 - Activation of Wnt/β-Catenin-p130/E2F4 Promotes Differentiation of Bone Marrow-Derived Mesenchymal Stem Cells into Type II Alveolar Epithelial Cells in vitro

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Introduction

Our previous study has demonstrated that activating the Wnt/β-Catenin pathway increased the expression of type II alveolar epithelial cell (AT II) markers on MSCs in a co-culturing system *in vitro*. Besides, it was also previously published by Cai et al that activation of Wnt/β-Catenin pathway could promote the differentiation of mouse mMSCs (mMSCs) into AT II in LPS-induced ARDS mice. However, the downstream molecular mechanism of canonical Wnt signaling pathway in regulating the differentiation of MSCs into AT II during mitosis remains unclear. It has been found that activation of the Wnt/β-catenin pathway in mMSCs was associated with accumulation of β-catenin and retinoblastoma protein (pRb) family members during MSCs cycle progression. Also, our previous study found that overexpressing p130 (a member of pRb family) or E2F4 (transcriptional repressor in conjunction with p130) inmMSCs could further improve the injured structure and function of epithelial cells in the lungs of acute respiratory distress syndrome (ARDS) mice as a result of improved differentiation of mMSCs into AT II. Therefore, it is speculated that activation of canonical Wnt/β-Catenin signaling pathway in MSCs can affect the

p130/E2F4 pathway by regulating cell cycle and participate in the differentiation into AT II.

Methods

mMSCs with p130 or E2F4 overexpression were constructed using lentiviral vectors as previously described in our work. And a modified co-culture system with murine lung epithelial-12 (MLE-12) cells and small airway growth media (SAGM) for 7-14d was used to efficiently drive mMSCs differentiation into AT II. The differentiation efficiency was detected for surfactant protein C (SP-C) by immunofluorescence and Western blot assay as well as typical lamellar body-like structures by transmission electron microscopy. To detect the relationship between the canonical Wnt pathway and p130/E2F4, 4 mmol/L LiCl or 200 ng/ml DKK-1 was also added in the co-culture system as previously described in our work. And the protein level of p-p130, p130 and E2F4 were also detected by Western blot assay. Cell cycle of mMSCs after differentiation was evaluated by flow cytometry.

Results

The SP-C protein expression was significantly higher in MSC-p130 (overexpression of p130) and MSC-E2F4 (overexpression of E2F4) groups after induced differentiation into AT II ($p<0.05$). Similar results for SP-C protein expression and lamellar body-like structures the in immunofluorescence analysis and electron microscopy. The levels of p-p130, p130 and E2F4 were also increased in mMSCs when LiCl was added to the co-culture system to activate Wnt/β-catenin signaling pathway ($p<0.05$), while depressed to some extent by inhibiting the pathway with addition of DKK-1 ($p<0.05$). As for cell cycle detection, G1+S phases was evaluated when activating Wnt pathway ($p<0.0001$) while decreased when inhibiting it ($p<0.0001$). However, G1 phase was significantly delayed after differentiation of mMSCs overexpressing p130 or E2F4 ($p<0.0001$).

Conclusion

Canonical Wnt signaling pathway can affect the differentiation of MSCs into AT II by regulating downstream p130/E2F4, and the mechanism of which may be related to G1 phase extension in the cell cycle of MSCs.

000107 - Is the ratio of SnO_2 to TOI as measured by near infrared spectroscopy feasible for predicting

the return of spontaneous circulation during resuscitation?

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Introduction

Predicting the return of spontaneous circulation (ROSC) in patients in cardiac arrest undergoing resuscitation is difficult. Near infrared spectroscopy (NIRS) has become an attractive research topic as a new method of assessment for predicting ROSC. This method can be used to measure the local oxygen saturation of hemoglobin in specific tissue. Sensors are attached to the forehead at cardiopulmonary resuscitation, and the oxygenation of the brain is evaluated. The oxygen saturation of brain tissue is reported to increase as a result of ROSC, which is thought to improve the pulmonary circulation, thus increasing oxygenation of the entire body, including the brain.

The NIRO-200NX monitor (Hamamatsu Photonics Co., Ltd.) has a function called NIRO Pulse, which is attracting attention because it can measure the local oxygen saturation of the pulse wave components (SnO_2 : variation of oxygenated hemoglobin / variation of total hemoglobin) in tissue. The tissue oxygen index (TOI) reflects the total oxygen saturation of hemoglobin in the local arteries, veins and capillaries of a specific tissue; whereas SnO_2 reflects the oxygen saturation of their pulse wave components, although it is thought that SnO_2 reflects more of the arterial components. Under normal conditions, SnO_2 generally shows a higher value than the TOI. On the other hand, in patients with cardiac arrest, even when cardiopulmonary resuscitation is performed, oxygenation of the brain is poor and the values of both TOI and SnO_2 are low. Therefore, we focused on the ratio of SnO_2 and TOI measured in a patient in cardiac arrest on arrival at the hospital, and evaluated if the ratio could be used as a measure of the possibility of ROSC.

Methods

Among patients with cardiac arrest on arrival at Yamagata University Hospital from October 2017 to March 2018, 24 were selected for the study. They were measured by the NIRO Pulse function of the NIRO-200NX monitor during resuscitation. Immediately upon arrival, we attached monitors to each side of the forehead and measured the mean SnO_2 and TOI values for 1 minute after the start of the measurement.

Results

The median patient age was 83.5 years, and the proportion of patients with witnesses was 11/24 (41.6%). The median initial SnO_2 value was significantly higher for the patients with ROSC [n = 6; 41.2%, interquartile range (IQR) 33.7-69.7] than the median initial value in the patients without ROSC (n = 18; 31.0%, IQR 15.2-38.7; p=0.005), but differences between the initial TOI values of the 2 groups was not significant. The median values of SnO_2/TOI in the ROSC and non-ROSC patients were 0.993 (IQR 0.917-1.457) and 0.879 (IQR 0.571-1.459), respectively (p = 0.403, Wilcoxon test).

Conclusion

The value of SnO_2/TOI on arrival was not related to the resuscitation rate. However, evaluating the values of SnO_2 at the time of arrival might be useful for estimating the possibility of ROSC.

000116 - Benefits of induced pluripotent stem cell-derived exosome therapy for rat models of pulmonary artery hypertension

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Introduction

Abnormal proliferation of vascular smooth muscle cells, inflammation and pulmonary vascular remodeling are prominent features of pulmonary arterial hypertension (PAH). Recent studieshave demonstrated that both hypoxia-induced factors-1 (HIF-1) and p21-activated kinase-1 (PAK-1) are involved in the regulation of cell growth, leading to vascular remodeling.Our previous study showed that intraperitoneal administration ofinduced pluripotent stem cells (iPSCs) improves the function of hemodynamics in lung of monorcotaline (MCT) or hypoxia-induced PAH rats. In recent years, therapeutic benefit of iPSCs may be mediated by a paracrine effect of exosomes.However,the underlying mechanisms mediating these protective effects remain to be characterized.

Objectives

To determine whether iPSC-derived exosomes (iPSC-Exos) treatment can improve chronic hypoxia-induced PAHand vascular remodeling in rats, as well as to identify the mechanisms underlying these effects.

Methods

iPSC-Exos were intraperitoneal injected daily to a chronic hypoxia-induced PAH rat model which under 10% Oxygen concentration for 8 weeks. The protocol of iPSC-Exos were designated as (i) prevention by the provision of iPSC-Exos treatments on same time with under hypoxia condition, or (ii) reversal by administration of iPSC-Exos treatments after hypoxia situation for 4 weeks. The phenomenon of vascular remodelingwere assessed by immunohistochemical and Elastic Van Gieson staining.Hypoxia-induced HIF-1a and PAK1 expression were determined by Western blotting and qPCR.Furthermore, MTT assay and BrdU staining, and TUNEL assay were used to analyze hypoxia-induced pulmonary smooth muscle cells (PASMCs) proliferation and apoptosis, respectively.

Results

The *in vivo* study demonstratedthat administration of iPSC-Exos group decreases the hemodynamic values of RVSP and ameliorates the lumen diameter and wall thickening of pulmonary arterioles in hypoxia-induced PAH.Histological examination of lung tissue showed that the levels of HIF-1a and PAK1 was lower in the iPSC-Exos group than the no-treatment group. Administration ofiPSC-Exossignificantly inhibited hypoxia-induced HIF-1a and PAK1 expression inlung tissue lysates revealed by Western blotting and qPCR.Similar to the results observed in vivo,treatment of PASMCs with iPSC-Exossignificantly inhibitedhypoxia-induced HIF-1a and PAK1 protein and mRNA expression.By MTT assay and BrdU staining, the proliferation of PASMCs induced by hypoxia was significantly inhibited by pretreatment with iPSC-Exos. By TUNEL assay, iPSC-Exos promoted PASMCs apoptosis in response to hypoxia stimulation.

Conclusion

Our findings showed that iPSC-Exos exerts a protective effect on pulmonary vascular remodeling in hypoxia-treated PAH model through down-regulation of HIF-1a and PAK1,leading to ameliorate hemodynamic values of RVSP. In PASMCs, iPSC-Exosinhibits hypoxia-induced HIF-1a and PAK1 signaling pathway and blocks excessive cell proliferation. iPSC-Exos also prevents the resistance of PASMCs to apoptosis. These finding may provideuseful information about iPSC-Exos as a new therapeutic strategy for PAH diseases.

000134 - Cardiac and Brain Autophagy Expression in the Post-Resuscitation Diabetic Animal Model

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Introduction

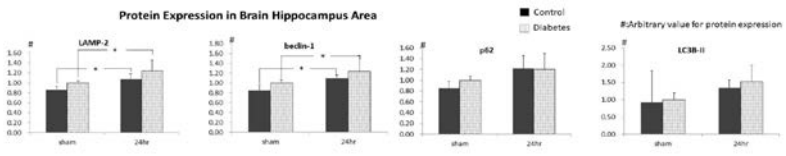
Cardiac and brain injuries keep deteriorating in the post-cardiac arrest period and lead to mortality. Autophagy is recently found as a way to re-cycle the intracellular damaged substance and organelles including mitochondria. Activation the autophagy can reduce the myocardial damage and improve outcome after ischemia-reperfusion injury. Impaired autophagy cascades are noted in metablic diseases including diabetes. Diabetes mellitus and poor glycemic control are associated with poor outcomes for cardiac arrest patients (1). The objective of the study is to investigate the effect of diabetes on regulation of autophagy in the post-cardiac arrest syndrome.

Methods

Adult male rats were treated with streptozotocin at 6 weeks old to induce diabete. We established the asphyxia-induced cardiac arrest rat animal model (2). After 9.5 minutes of asphyxia, epinephrine 0.01 mg/100g is administrated through the venous line and chest compressions are delivered by index finger at a rate 200 beats per minute for all animals. Hemodynamic parameters were recorded for 4 hours after ROSC and body temperature was monitored. Autophagy-related proteins expression were assessed by western blotting. Neurolgical outcome was evaluated by neurological functional scale with a full score of 12.

Results

The survival rate of resuscitated animal was 48.1%(13/27) in diabetic group vs. 60.0% (9/15) in control group at 24th hour after ROSC (P=0.461). Worse neurological score was noted in the diabetic group (5.1±1.8 vs. 7.8±1.5, P<0.001) at 24th hour after ROSC. Cardiac output at 4 hours after ROSC was 70.0±18.6 ml/min in the diabetic group vs. 74.0±21.1 ml/min in the control group without significant difference. The cardiac expression of P62 and LC-3BII were higher in the diabetic group at 24 hours (1.95±0.22 vs. 1.29±0.28, p=0.002 for P62; 1.57±0.64 vs. 0.85±0.14, p=0.026 for LC-3BII). However, the level of LAMP-2 and beclin-1 were not different between diabetic and control groups. The autophagy-related proteins expression in brain were increased at 24 hours after ROSC compared to baseline, but there was no significant difference between the diabetic and control groups (figure 1, *p<0.05).



Conclusion

Autophagy is upregulated in the post-cardiac arrest period with different expression pattern in the heart and brain. Diabetes is associated with worse outcome after ROSC and increased autophagy-related protein expression in heart.

000165 - Protection effect of Remote Ischemic Preconditioning on Lipopolysaccharide Induced Systemic Inflammation model

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Introduction

Remote ischemic preconditioning (RIPC) has a protective effect on ischemic-reperfusion (I/R) injury and septic inflammatory injury. The protective effect has been reported to have a biphasic pattern such as acute and delayed protection in I/R injury. However, it is not yet known whether RIPC has biphasic pattern or not on the protective effects in sepsis.

Objectives

Therefore we investigated whether RIPC has protective effect by biphasic pattern in terms of survival rate, pro-inflammatory cytokines, and NF-κB activation in lipopolysaccharide (LPS)-induced sepsis model.

Methods

The LPS-induced sepsis model was created by injecting 20 mg/kg LPS intraperitoneally (i.p.) in BALB/c mice. RIPC was performed with three cycles of 10 min of ischemia and 10 min of reperfusion of the right hind limbs using a tourniquet

(1, 4, 8, 10, 12, 14, or 24) h prior to the injection of 20 mg/kg LPS. The control group received i.p. normal saline.The 5-day survival rate and serum cytokine levels were measured. We determined the levels of total and phosphorylated AKT, MAPKs (ERK and p38), NF-kB (p65), COX2 from liver tissues.

Results

Survival was significantly increased in mice who received RIPC compared to the LPS group ((80–100) % vs 30 %, $P<0.05$). Levels of interleukin-6 and -12 were significantly decreased in RIPC treatment groups compared to the LPS group (all $P<0.05$). All RIPC/LPS groups showed significantly decreased phosphorylation of ERK, p38, and AKT, nuclear NF-kB binding and COX2 compared to the LPS-only group.

Conclusion

The protective effect of RIPC was not limited to the biphasic time pattern in terms of survival rate and pro-inflammatory cytokines in an LPS-induced sepsis model. RIPC appears to exhibit protective effects by suppressing the activation of MAPKs, AKT, NF-κB activation, and also COX-2.

000169 - Plasma hepatocyte growth factor in sepsis and its association with mortality: A prospective observational study

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Introduction

Sepsis and septic shock are commonly associated with endothelial cell injury. Hepatocyte growth factor (HGF) is a multifunctional protein involved in endothelial cell injury and plays a pivotal role in sepsis. This study assesses its correlation with relevant endothelial cell injury parameters and prognostic value in patients with sepsis.

Methods

A prospective, observational cohort study was conducted in patients with sepsis admitted in the department of critical care medicine at the Zhongda Hospital from

November 2017 to March 2018. The plasma HGF level was collected on the first 24h after admission (day 1) and day 3, then was measured by enzyme-linked immunosorbent assay. The primary endpoint was defined as all-cause 28-day mortality. Furthermore, we analyzed the correlation of HGF with relevant endothelial cell injury markers.

Results

Eighty-six patients admitted with sepsis were included. HGF levels of non-survivors were elevated upon day 1 (1940.62 ± 74.66pg/mL vs. 1635.61 ± 47.49pg/mL; p = 0.002) and day 3 (1824.82 ± 137.52pg/mL vs. 1309.77 ± 83.49pg/mL; p = 0.001) compared with that in survivors, and showed a strong correlation with von Willebrand factor (r = 0.45, p <0.0001), lactate (r = 0.35, p = 0.0011), pulmonary vascular permeability index (r = 0.38, p = 0.0241), first 24h fluid administration (r = 0.38, p <0.0001) and sequential organ failure assessment score (r = 0.40, p = 0.0001). Plasma levels were able to discriminate prognostic significantly on day 1(AUC: 0.72, 95%CI: 0.60-0.84)) and day 3 (AUC: 0.77, 95%CI: 0.63-0.91).

Conclusion

HGF levels are associated with sepsis and are correlated with established markers of endothelial cell injury. Elevated HGF level in sepsis patients is a predictor of mortality.

000205 - PM4.0-induced lung injury could be alleviated by Kefir peptide in luciferase transgenic mice through inhibiting the NF-κB pathway

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Introduction

The human studies demonstrated that exposure to particulate matter (PM) could induce airway inflammation and animal studies also revealed that PM2.5 could induce lug inflammation and fibrosis. Kefir peptides, generated by kefir grain fermentation of milk proteins, showed positive antioxidant effects, lowered blood pressure and modulated the immune response.

Objectives

In this study, kefir peptides were evaluated regarding their anti-inflammatory effects on particulate matter < 4 μm (PM4.0)-induced lung injury in NF-κB-luciferase+/+ transgenic mice.

Methods

Homozygous transgenic mice (NF-κB-luciferase+/+) were randomly assigned to a control group or groups receiving low (10 mg/kg) or high (20 mg/kg) doses of PM4.0 for treatment (n = 8). The mice were exposed to PM4.0 by intratracheal instillation once a day for 4 weeks and then examined via bioluminescence images, measurements of the protein expression level of inflammatory factors and histopathological analyses of the lung tissues.

Results

PM4.0-induced lung injury significantly increased the generation of reactive oxygen species (ROS) and inflammatory cytokines; increased the protein expression levels of p-NF-κB, NLRP3, caspase-1, IL-1β, TNF-α, IL-6, IL-4 and α-SMA; and decreased the level of superoxide dismutase (SOD). Alveolar infiltration of neutrophils and macrophages was also observed in the PM4.0-treated lung tissue. The results showed that both the low and high doses of PM4.0 significantly induced inflammatory cell infiltration, oxidative stress and overexpression of inflammatory mediators in lung tissue by activating the NF-κB pathway. Thus, we choose the low dose (10 mg/kg) of PM4.0 for animal trials; the mice were assigned to four treatment groups, including a normal control group and PM4.0 alone group. Two groups, KL (150 mg/kg low-dose kefir peptides) or KH (500 mg/kg high-dose kefir peptides), were fed kefir peptides one hour before the intratracheal administration of PM4.0 or saline (daily, 4 weeks). Data showed that treatment with both doses of kefir peptides obviously decreased the PM4.0-induced inflammatory cell infiltration in bronchoalveolar lavage fluid (BALF) and the expression of the inflammatory mediators IL-lβ, IL-4 and TNF-α in lung tissue by inactivating NF-κB signaling (evaluated by luciferase expression, phosphorylated NF-κB, NLRP3-dependent inflammasome and caspase-1).

Conclusion

Kefir peptides ameliorate PM4.0-induced lung damage by inactivating NF-κB signaling to inhibit the inflammatory response and may have potential for clinical applications involving particulate matter air pollution.

000212 - Acute Cholecystitis as an imitator for Acute Coronary Syndrome. Our experience

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Introduction

Various etiologies have been reported to cause ST segment and T-wave abnormalities that are not related to acute coronary syndromes. Patients with acute cholecystitis rarely present dynamic T-wave abnormalities; however, the incidence and exact mechanism of such ECG changes are still unknown.

Objectives

To describe the characteristics of a fourteen patients cohort admitted to ICU with initial diagnosis of Acute Coronary Syndrome (ACS) that after completing the whole diagnostic-therapeutic process were finally diagnosed as Acute Cholecystitis.

Methods

Descriptive analysis of fourteen patients admitted to ICU with atypical chest pain and diagnosis of suspected ACS at admission and with a finally diagnosis of acute cholecystitis at ICU discharge in a thirty-six month period (1/1/2016 to 1/1/2019) in two different Cardiologic Intensive Care Units in Granada (Hospital Universatario Virgen de las Nieves and Hospital Universitario San Cecilio). Variables analysed: demographic (age and sex), diagnostic (ECG, myocardial and cholestasis biomarkers, echocardiography, cardiac catheterization, abdominal ultrasound), therapeutic (medical and/or surgical treatment) and complications.

Results

From a total of 14 patients in 3 years: 8 (57.1%) were male with a mean age of 68 ± 8.2 years. ECG was pathologic in 10 of them (71.4%): 3 with complete left bundle block (LBB) and 7 with anterior subepicardial ischemia. All of them presented enzymatic typical curve for ischemia (High-sensitivity cardiac troponin I) and in all of them the value at admission was higher than 1500 pg/ml). The study of the hepatobiliary markers was not realized until coronary pathology was excluded, later on, the total bilirrubin was elevated in 100% patients (in between 2.1 and 5.2 mg/dl). The echocardiography performed by the intensivist and echocardiographer at admission was not conclusive. Coronary catheterization was performed in all patients within the first 48 hours of admission and in the 3 cases of complete LBB as a primary PCI revascularizaton. None of them showed significant coronary disease. All

were treated with double antiplatelet therapy (SAA plus a second one, 4 clopidogrel and 8 ticagrelor) and anticoagulation (7 with fondaparinux, 4 with low molecular weigh heparine and 3 non fractioned heparin). The final diagnosis of acute cholecystitis was made by abdominal ultrasound. 10 patients (71.4%) were treated by laparoscopic cholecystectomy, frome these, 2 (14.2%) was converted to open surgery due to hemorrhagic complication. The other 2 patients (25%) were treated only with antibiotics.

Conclusion

The diagnosis of Acute Cholecystitis in some cases can be complex as they might simulate other syndromes, especially like an ACS as in these case-series. These patients experienced diagnostic invasive tests and received medical treatment that might cause complications in the subsequent surgical management of an usually commonplace pathology.