1st International Conference

TRANSLATIONAL AND CLINICAL MEDICINE

Faculty of Medicine

Ivane Javakhishvili Tbilisi State University

5-7 May, 2022

Tbilisi, Georgia

Conference is financed by Shota Rustaveli National Foundation of Georgia

Contents

Open SurgicalRremoval of Firmly Impacted Pancreatic Duct Stent: Two Case Report

Merab Kiladze, Malkhaz Mizandari, George Kherodinashvili, Otar Kepuladze

Abstract

***Background*: Pancreatic stents are used for a variety of different pancreatic disorders: pancreatic duct stones, chronic pancreatitis, pancreatic strictures, unresectable pancreatic cancer, preventing POPF and post-ERCP pancreatitis, papillary adenoma. Conventionally the pancreatic duct stents placement is done by endoscopic transpapillary procedure, but recently there are increasingly more reports of feasibility of percutaneous image-guided pancreatic duct (PD) drainage and stenting, which appears to be a safe and effective procedures, but it should be noted that these procedures also are not without any complications and may have some adverse events. The potential complications and adverse events of pancreatic stents placement, exchange and removal are: stents migration and dislocation; stent-induced strictures; stents fragmentation during removal; obstruction and dysfunction due to mucosal hyperplasia; stents clogging and impaction and at last even the bowel perforation.**

***Aim*: To choose the optimal surgical management**

***Material and Methods*: Two cases of firmly impacted pancreatic stents removal recently observed in our institution led us to report our experience of successful management of these particular cases.**

***Results*: The postoperative course was uneventful; the patients were discharged from the hospital at 5-th p/o day and pancreatic duct drainage catheters were removed at 3-4 weeks after surgery.**

***Conclusion*: Open transduodenal stents removal with lateral pancreaticojejunostomy to prevent the pancreatic duct restenosis seems to be the most optimal and effective surgical procedure of removal the firmly impacted pancreatic duct stents in these difficult cases, which therefore could be considered like a real alternative approach and "parachute" option after failed attempts of stents removal by endoscopic and radiological procedures.**

Image Guided Percutaneous Pancreatic Duct Drainage: What for and How?

Malkhaz Mizandari

Abstract

Background

Various non-malignant and malignant pathologies of pancreas, duodenum, major papilla and retroperitoneal space, associated with pancreatic duct obstruction may lead to initiation of pancreatitis and also to either initiation, or rapid advancement of existing diabetes.

Aim

To present the rationale and technique of image guided percutaneous pancreatic duct drainage (PPDD) for treating pancreatic duct (PD) obstruction.

Material & Methods

In total, 73 patients underwent PPDD. All procedures were performed under moderate sedation and local anesthesia.

Three types of imaging guidance were used, including combined US and fluoroscopy guidance (n = 40), combined CT and fluoroscopy guidance (n = 26), and CT guidance only (n = 7). The patients were categorized into 2 groups based on the type of diagnosis: patients without malignancy (n = 26) with PD obstruction due to acute and chronic pancreatitis (n = 25) or postoperative stricture (n = 1) and patients with malignancy (n = 47) with pancreatic

head tumors (n = 42) and ampullary tumors (n = 5).

Results

Image-guided PPDD was attempted with an overall technical success rate of 98.6% (72/73). In 66 of 73 (90.4%) patients, PD drainage was accomplished in a single procedure; 5 (6.8%) and 2 (2.7%) patients required 2 and 3

attempts, respectively. A total of 94 procedures were performed on 73 patients, with a mean of 1.2 procedures per patient.

In 13 of 73 (17.8%) patients in whom the PD tail segment was accessed through the posterior approach, only the abdominal wall and retroperitoneal fat were traversed. Retroperitoneal hydro - or air dissection for

secure passage tract creation was performed to 5 (6.8%) patients and 1 (1.4%) patient, respectively. The anterior approach was employed in 60 (82.2%) patients. In 5 patients, a 14-gauge needle steering was used to

avoid traversing the stomach and colon. In 35 (50%) patients, only the abdominal wall was traversed. Transhepatic and transgastric routes were used in 13 (17.8%) and 12 (16.4%) patients, respectively.

In all cases, external catheters were maintained until recanalization or surgery was performed. The mean drainage fluid output after PD was 630 mL/d ± 279, which progressively increased over 1 week.

All patients improved gradually. Thirteen (17.8%) patients presented with new-onset DM, of whom 8 had pancreatic cancer, 2 had recurrent chronic pancreatitis, and 3 had PD stones. A significant decrease in blood glucose levels was observed in these patients between 2 and 5 weeks after PD drainage. Three (4.1%) patients had a long history of chronic DM, and they did not show an improved glycemic control after PPDD.

Four (5.5%) asymptomatic patients underwent PPDD before pancreaticoduodenectomy at the surgeon's request and had drainage catheters left in place for 2–3 weeks after surgery to maintain access to the pancreaticojejunal anastomosis in case adjunctive procedures were needed.

Conclusion

image-guided PPDD is a feasible and valuable therapeutic procedure in a large cohort of patients with various malignant and nonmalignant pathologies.

3D Bioprinting for Enteroatmospheric Fistulae

Javier Padillo

Abstract

Background: Enteroatmospheric fistulae are challenging clinical conditions that require surgical expertise and that can result in chronic debilitating conditions placing the patient in a vicious cycle characterized by non healing wounds and malnutrition. They are a complex entity that presents great variability depending on the number, shape, and size of the fistulous orifices, their debit, and the dimensions of the wound.

This means that, at present, there is no device that adapts to the anatomical characteristics of each patient and manages to control the spillage of intestinal effluvium from the wound.

Aim: The aim of this study is to describe the manufacturing technique and to assess the preliminary results of a custom

Method: Four patients were included in the proof of concept study. Device designed through bioscanner imaging and manufactured using 3D printing for use with negative pressure wound therapy (NPWT) in the management of enteroatmospheric fistula. A proof of concept is given, and the design of the device is presented for the first time. After obtaining images of each fistula with a bioscanner, a personalised device was designed for each patient by 3D printing shape of a prism and a hollow base, taking into account the dimensions of the fistulous area in order to perform a floating ostomy to isolate the wound from the debit enteric. The polycaprolactone (PCL) device was placed including inside the fistulous surface and surrounding it with the NPWT system in order to accelerate wound healing.

Results: pain ($p<0.002$) pruritus ($p<0.006$) and the number of wound cures ($p<0.001$) decreased significlantly. All patients could be closed the abdominal wall.

Conclusion: The personalized device designed with bioscanner and 3D printing it is useful for patients with Enteroatmospheric fistulae.

Liver Transplantation in Acute Liver Failure

Oleg Rummo

Abstract

Acute liver failure – one of the most difficult diseases of hepatology. The complexity of this problem can be explained not only in the extremely bad condition of a patient but also in the rapid development of the life threatening complications, that may be resolved only by liver transplantation. There is the whole range of criteria that helps to determine indications for liver transplantation within acute liver failure, among which King's college and Clichy criteria are most frequently used. The main factor for successful treatment of patients with acute liver failure is high development of organ donation. In this aspect the Republic of Belarus is among the world's leaders. According to preliminary data for 2021 we are on the 9th place in the world. This fact allows us perform about 90 liver transplants every year. For 14 years of the existence of liver transplantation program we performed more than 900 surgeries. It takes us to the 20th place in the world in terms of the number of transplants per 1 million inhabitants. Among these 900 liver transplantations, 75 cases or 8.5 percent were performed upon acute or acute-on- chronic liver failure. Acute liver failure mainly caused by poisoning with amanita phalloides. The results of liver transplantation suggest that the patients with acute liver failure had a higher MELD score before transplantation and were younger. After the surgery patients were more likely to have acute antibody-mediated rejection and ischemic type biliary lesions. The group of patients who needed a salvage re-transplantation had to undergo hemodialysis more often and in 83 percent of cases they had infectious complications, therefore hospital mortality was in 2 times higher than in ALF group. The most common cause of death of these patients was sepsis. This fact confirms that in some cases of liver failure transplantation is not applicable because the patient is too sick for the surgery.

Conclusion. Treatment of patients with ALF should be carried out at the transplant centers. Conservative methods, including extracorporeal detoxification methods (MARS, Prometheus, plasmapheresis), can be used as a "bridge" to liver transplantation and to correct severe early postoperative liver graft dysfunction. The decision on LT should be based on a comprehensive assessment of both the metabolic and synthetic functions of the liver the degree of encephalopathy, and the possibility of receiving a donor organ in the shortest possible time.

International Multi-centric Minimally Invasive Liver Resection for Colo-Rectal Liver Metastases (SIMMILR-CRLM)

Andrew A. Gumbs, Eric Lorenz, Tzu-Jung Tsai, Lee Starker, Joe Flanagan, Andrea Benedetti Cacciaguerra, Ng Jing Yu, Melinda Bajul, Elie Chouillard, Roland Croner, Mohammad Abu Hilal

Abstract

Background: The Study: of International Multi-centered Minimally Invasive Liver Resection (SIMMILR) is a study of ColoRectal Liver Metstases (CRLM) from 6 international centers.

Materials and Methods: Resections were divided by the approach used: Open liver resection (OLR), Laparoscopic liver resection (LLR) and Robotic liver resection (RLR). Patients with ≥ 3 tumors measuring ≥ 5cm were excluded, and any remaining heterogeneity found was further analyzed after propensity score matching (PSM) to decrease any potential bias.

Results: A total of 1,064 hepatectomies were done at 6 centers. After exclusion criteria and PSM, 142 patients were in each arm of the OLR vs. LLR group and 22 in the OLR vs. RLR and 21 in the LLR vs. RLR groups. Blood loss, hospital stay, and morbidity rates were all highly statistically significantly increased in the OLR group, 636mL vs. 353mL, 9 vs. 5 days and 25% vs. 6%, respectively ($p<0.001$). Only blood loss was significantly decreased when RLR was compared to OLR and LLR, 250mL vs 597mL, and 778 mL vs. 224 mL, $p<0.008$ and $p<0.04$, respectively. Overall survival (OS) and recurrence free survival (RFS) was not statistically different regardless of operative approach.

Conclusion: LLR seems to result in decreased blood loss, hospital stay and morbidity rates when compared to OLR. RLR has decreased blood loss without an increase in operative times when compared to both OLR and LLR. This Study on an International Multi-centric cohort of Minimally Invasive Liver Resection (SIMMILR) indicates that minimally invasive approaches for CRLM that follow the Milan Criteria may have short term advantages that do not appear to significantly change overall and recurrence free survival, but larger studies comparing robotic resections to both OLR and LLR are still needed.

Urine Supravesical Derivation by Using the Intestine

Nino Gabunia, Teimuraz Dochviri

Abstract

Abstract

Background: Urine derivation after cystectomy or bladder functional impairment more than century is a very actual problem. During this time many oparating tecniques are provided after cystectomy due to bladder cancer and non-cancerous diseases. Some of which have been completely abandoned, others are still being adopted. However, the widespread interventions are far from perfect and their results can not satisfy both surgeons and patients expactations. Advanced urological thought has always tried to create such methods of urine derivation, which ensure human life activity, as close as possible to physiological, wich does not lead to psycho-emotional discomfort of the patient and provide high "quality of life".

Aim: The article describes development of different tecniques of supravesical derivation and cystoplastic issues after cystectomy in Georgia from 1929 until now

Materials and Methods: 72 patients with different bladder damage. Pre-operative preparation that includes: diet one week before the operation, the medicine are prescribed for intestinal microflora, checked Cardiovascular, Respiratory system and urinary systems. Patients with specific diseases (for example TB) anti-TB therapy.

for augmentation we need 40-50 cm of ileum intestine. Which we get it from ileocecal angle 20-30 cm away. The integrity of the intestinal tract is restored by applying an anastomosis between the proximal and distal ends of the intestine. The isolated intestinal segment on the vascular pedicle is detubulated and reconfigured in the form of Latin U or W. The medial side of the detobuled intestinal loop is anastomosis with spatulate ureters with 6-8 nodal Vicryl 4.0 sutures. With Vicryl 3.0 continuous stitches, the opposite sides of the detubulated loop of the intestines are sutured and formed " apron ". Only then does the reservoir are formed.

Anastomosis of the ureters is performed in the lower part of the intestinal area. Finally, after the formation of the " low-pressure small intestine reservoir'', the implanted ureters are topographically aligned with the Lieto triangle, with appropriate physiology, and this is also the most fixed place in the reservoir.

Results:

After operations:

- **Lethal accident was not detected**
- **All patients were continental**
- **Patients with neurogenic bladder patients were all on self-catheterization**
- **Four men had urinary retention due to prostate hyperplasia; prostate TUR was done**
- **Six patients formed stones in the reservoirs, optical cystolithotripsy was done**

• No clinically significant reflux was observed in any patient.

Conclusions:

- **We got an anti-reflux effect.**
- **After the surgery we had not anastomosis stenosis and reflux.**

- **The method is technically simple and can be widely used in urology, does not require specific equipment**
- **The risk anastomosis stenosis is quite low.**

Since the end of eighties almost every congress of urologic association had been published Georgian urologists publications and reports. Prof. L. Managadze and Prof. T.Chigogidze has been leading the open meeting of sessions and this was the indicator of recognition Georgian urology.

Less-known anatomical structure of the Liver - An anatomical substrate for intrahepatic portacaval shunting

Givi Koberidze, Revaz Otarashvili, Ilia Chanukvadze

Abstract

There are little known anatomical details within human liver formed through the confluence of fibrous sheathes of the portal canals and those of the hepatic veins in some areas where these structures come into contact and interdigitate.

The perivascular fibrous capsule, a layer of connective tissue enveloping the intrahepatic portion of the portal triad, extends from the portal tracts to the hepatic vein walls, ensheathing this latter vessel as the fourth element in addition to the portal triad. We have suggested the term "porta-caval fibrous connections" (PCFC) for the anatomical structures formed through the confluence of fibrous envelopes of the intrahepatic bile ducts and those of the hepatic veins. In order to reveal the porta-caval fibrous con¬nec¬tions, 101 normal livers taken at autopsy from adult patients were studied. The following forms of the intrahepatic porta-caval fibrous connections can be distinguished based on the area of fusion of fibrous sheathes of the portal tracts and the hepatic veins:

Complete fusion - This type of connections can principally be seen within the segments II and III.

Tangential connection. The partial fusion, or tangential intrahepatic porta-caval fibrous connections, are mostly found within the hepatic segments II, III, VI, and VII.

The fan-shaped This peculiar type of IHPCFC is permanently present within the hepatic segment I.

Laminar forms of intrahepatic porta-caval fibrous connections are found in 9.3% of cases and are formed through a fibrous lamina between the perivascular fibrous capsule and the hepatic vein sheath.

Thread-like intrahepatic porta-caval fibrous connections are found in 4.7% of cases.The thread-like IHPCFC are found in the he¬patic segments II, III, VI, and VII.

The relationship of the individual elements of portal triad – with the hepatic veins within the intrahepatic porta-caval fibrous connections is less variable. The hepatic vein is most frequently bordered by a bile duct (78.2%). Moreover, it is frequently the only structure to have contact with the hepatic vein (49.4%) The direct relationship of the hepatic veins with the bile ducts and their mucous glands within the IHPCFC can help inflammation to spread from the bile ducts to the hepatic veins. The close anatomical relationship between the portal and the hepatic veins within the intrahepatic porta-caval fibrous connections is of great practical importance for surgical intrahepatic portacaval shunting for which it provides a favorable condition. Thus, the fibrous sheathes of the portal tracts and those of the hepatic veins, at some of points of their crossing, form a fibrous connection as a distinct anatomical detail through which the hepatic vein is in direct interaction with the portal complex and can be viewed as its part. This anatomical relationship between the portal tracts and hepatic veins is a normal occurrence in human liver. We deem that the hepatic porta-caval fibrous connections deserve an appropriate place in anatomical nomenclature.

Machine Perfusion Based Sub-normothermic Preservation of the Organs In-situ, in Block and Ex-vivo

Nodar Khodeli, Zurab Chkhaidze, Nino Inauri

Abstract

Introduction

Organ transplantation is multi-component treatment method. It has no alternative in irreversible diseases. Its accompanied by many important issues, but the most discussed is - Organ Preservation . There are known a lot of methods of organs preservation were used.

The increasing demand for donor organs is forcing transplantologists to search for alternative approaches. Machine perfusion can be considered as one such approach.

At the Institute of Morphology, a number of perfusion machine models have been undergoing development since 2000. Representing miniature compact, portable versions of the heart-lung bypass machine. A cycle of experimental studies has been carried out with the presented machine:

1. In the model of the animal with the cardiac arrest artificial heart-lung bypass was conducted in order to resuscitation.

2. In case of liver autotransplantation, veno-venous shunting for hemodynamic protection of the recipient during the Ahepatic phase.

The aim of the study

To assess the morphological state of liver after 7 –hour "in-situ" machine perfusion with pulsatile flow. To test the possibility of "ex vivo" preservation of hepato-renal block using machine perfusion with maintenance of physiological parameters.

Material and Methods

"In situ" preservation of liver was performed in 10 experimental animals. In all cases, the cardiac arrest was remodeled, keeping the same duration of warm ischemia period. Duration of perfusion in this group was defined for 7 hours. Preservation was conducted under the systemic perfusion by constant and pulsatile flow (by own-desined pulsator).

In "ex-vivo" case the liver and kidney were removed together with the aorta and caudal vena cava on a common vascular pedicle. The perfusion was done through the aorta and portal vein.

Results

Morphology study results of "in situ" liver preservation .

Under non-pulsatile flow, after 7 hours of perfusion, the sd-MaS is diffuse. Ld-MaS is observed in 18% of liver tissue, singular necrotic areas.

Pulsatile flow mode after 7 hours, Sd- MaS in 5%. Ld-MaS in 5% .

The results of 6-hour "ex-vivo" preservation : The dilatation of renal tubules and the wall thickness of several arteries were found. Mild mixed ld-MaS and sd-MaS were found in less than 10% of the hepatocytes.

These data are higher than at the perfusion starting but they continue to remain in the frame of standards suggested for the donor organs.

Conclusion

Thus, as a result of experiments, a portable perfusion device was developed, which provides optimal perfusion of an organ during systemic preservation with oxygenated blood, both for pulsatile arterial flow and for splanchnic flow in portal vein, as well as in situ multi-organ preservation in the donor organism.

Morphologic study results demonstrate the systemic sub-normothermic perfusion with perfusion machine successfully provides the liver preservation by continuous and pulsatile flow.

Liver is valid for transplantation. Pulsatile flow is confidently better.

The results of ex-vivo experiment of isolated liver and kidney indicate the possibility of further increase in duration of perfusion.

Restoration of Cortical Network after Ischemic Stroke

Zaal Kokaia

Abstract

Background: Transplanted neurons derived from stem cells have been proposed to improve function in animal models of human disease by various mechanisms such as neuronal replacement. Stem cell transplantation can improve behavioral recovery after stroke in animal models but whether stem cell-derived neurons become functionally integrated into stroke-injured brain circuitry by receiving functional synaptic inputs from the recipient's brain and establishing efferent synaptic connections with host neural circuitry is unknown.

Aim: The main aim of the study was to investigate the synaptic inputs from the host brain to grafted cortical neurons derived from human induced pluripotent stem cells (iPSCs) after transplantation into stroke-injured rat cerebral cortex. Also, we explored whether grafted neurons also send widespread axonal projections to the host brain.

Materials and Methods: We used rat model of focal cortical stroke induced by occlusion of distal branch of middle cerebral artery. The rabies virus-based trans-synaptic tracing method and immunoelectron microscopy was used to identify afferent and efferent synaptic connections of grafted neurons. Electrophysiological in vivo recordings and patch-clamp recordings from acute brain slices were used to study electrical activity and network connections of grafted reprogrammed neurons. For the behavioral assessment the of a sensorimotor function we used cylinder test.

Results: We demonstrated that the grafted neurons receive direct synaptic inputs from neurons in different host brain areas located in a pattern similar to that of neurons projecting to the corresponding endogenous cortical neurons in the intact brain. The rabies virus–based transsynaptic tracing, showed that host neurons in the contralateral somatosensory cortex receive monosynaptic inputs from grafted neurons. Moreover, immunoelectron microscopy demonstrated myelination of the graft-derived axons in the corpus callosum and that their terminals form excitatory, glutamatergic synapses on host cortical neurons. Electrophysiological *in vivo* recordings from the cortical implants showed that physiological sensory stimuli can activate spontaneous activity in grafted neurons, indicating that at least some of the afferent inputs are functional. In agreement, we found that a portion of grafted neurons respond to photostimulation of virally transfected, channelrhodopsin-2-expressing thalamo-cortical axons in acute brain slices. We showed that the stroke-induced asymmetry in a sensorimotor function is reversed by transplantation. Light-induced inhibition of halorhodopsin-expressing, grafted neurons did not recreate the impairment, indicating that its reversal is not due to neuronal activity in the graft.

Conclusions: The present study demonstrates, for the first time, that the host brain regulates the activity of grafted neurons, providing strong evidence that transplanted human iPSC-derived cortical neurons can become incorporated into injured cortical circuitry. Our data indicate that activity in the grafted neurons, probably mediated through transcallosal connections to the contralateral hemisphere, is involved in maintaining normal motor function. This is an example of functional integration of efferent projections from grafted neurons into the stroke-affected brain's neural circuitry, which raises the possibility that such repair might be achievable also in humans affected by stroke.

Collagenoplasty in ophthalmology

Oleg Golovachovi, Mariam Golovachovi

Abstract

Background: Glaucoma surgical procedures are the most common cause of ocular hypotony, which can occur as a result of bleb leak or overfiltration, use of glaucoma drainage implants, or iatrogenic cyclodialysis cleft. This rare complication may be asymptomatic or lead to visual loss. Glaucoma tube erosion occurs as a late postoperative complication in 2% to 5% of eyes after glaucoma drainage device implantation. Tube exposure can lead to serious complications such as hypotony, ocular inflammation, and endophthalmitis. Therefore, the aim of our study was to evaluate the efficacy and complications of treatment method with collagen implants according to standard surgical technique in glaucoma surgery and in ophthalmic trauma surgery.

Collagen implants combine all benefits that synthetic polimers and tissue transplants have, and devoid of negative aspects as toxicity and carcinogenicity; immunotropic and allergic activity.

Collagen implants have great potential for the treatment of damaged tissues, have hemostatic effect, are able to form complexes with various pharmacological agents and it can be used as a mechanical barrier to prevent post-surgical adhesions.

Aim: Evaluation of collagen Salvecoll use in ophthalmic surgery.

Material and methods: We used collagen Salvecoll soaked with 5FU in glaucoma surgery to prevent postoperative hypotony and bleb scarring. Salvecoll was used for antiglaucomatous surgeries such as: trabeculectomy 24, non-penetrating sclerectomy 26, implantation of mini shunt 16 (Express shunt), implantation of Ahmed valve to prevent stripping of silicone tube – tube was covered by pericard+salvecoll, sizes 6×6 mm 25; cystic bleb surgery 3; bleb fistula surgery 1.

Pericard and Collagen Salvecoll was also used for trauma surgery such as: penetrating injury of sclera 17, perforation of cornea after corneal ulcer 3.

Observation period was from 2nd day to 24 months.

Results: Postoperative condition in glaucoma patients was same to that after operation without salvecoll. There was performed impressive, wide filtration bleb. Postoperative hypotony was in more fewer cases. The range of postoperative IOP was from 10 to 14, 95 patients.

In cases of ocular trauma, healing process went well. The range of postoperative IOP ranged from 10 to 25. In cases of corneal perforation the eye was saved, in several cases we got vision about 0.3.

We have operated 115 patient, 115 eyes: 95 glaucoma, 17 trauma, 3 perforation of cornea.

Conclusions: using of collagen implants and pericard biorepar in ophthalmic surgery increases the efficiency of ocular surgery. Impressive, wide filtration blebs were performed and less postoperative scarring in glaucoma surgery. Additional hermetization of penetrating ocular trauma supports getting better scarring without growing additional proliferative tissues into the eye.

Local Drug Delivery System for the Treatment of Tumor

Zurab Kakabadze, Teona Paresishvili

Abstract

Background. The present study discusses a targeted delivery system based on a nanogel consisting of PEGylated fibrinogen and platinum nanoparticles (Pt NPs) for the destruction of residual cancer cells. Macroporous gelatin microcarrier beads (CultiSpher) were used as a carrier of platinum nanoparticles. The efficacy of nanogel was evaluated in a subcutaneous Ehrlich ascites carcinoma mice model. Material and methods. 60 male mice weighing 20-25 g were subcutaneously inoculated in the back area with Ehrlich carcinoma cells. On the 16th day after inoculation, when the size of the subcutaneous tumor reached 2x2 cm, the animals were divided into three equivalent groups. Animals of the first group were observed without treatment. In the animals of the second group, the wounds were sutured after the removal of 95% of the mass of the tumor. In animals of the third group, after removal of 95% of the mass of the tumor, the wound was filled with nanogel and then sutured. The observation period for animals was 3 months. Results. Studies have shown that the animals of the first group died on days 35-40 after subcutaneous inoculation of Ehrlich's carcinoma cells from tumor progression and invasion in the subcutaneous tissue, muscles, and the abdominal cavity. In animals of the second group, within 30 days after the removal of 95% of the mass of the tumor, a non-healing wound was formed, while a rapid progression of the residual tumor was observed. In animals of the third group, after removing 95% of the tumor mass and covering the wound with nanogel, the wound healed on days 20-25. In animals of this group during the entire period of observation, the progression of the residual tumor was not noted. The nanogel induced apoptosis, inhibited angiogenesis, and suppressed the growth of residual Ehrlich carcinoma cells. Conclusion. Targeted drug delivery system based on nanogel consisting of PEGylated fibrinogen and Pt NPs can be used to destroy residual cancer cells after cancer removal.

Radiofrequency Volume Reduction (RAVOR) of the inferior Nasal Turbinates

Merab Khvadagiani, Giorgi Khvedelidze

Abstract

Introduction: The hyperplasia of the inferior nasal turbinate is a widespread reason for the chronically obstruction of the nasal respiration. A variety of surgical procedures are perfomed for reduction of hyperplastic inferior nasal turbinates. The multitude of methods reflects the challengefor an ideal treatment. RF generator BM-780 for the treatment of concha hyperplasia by Ravor is evaluated clinically.

Material and Methods: 917 patients (age 5-72) who undervent submucosal turbinotomy with RF generator BM780,between 2010-2021,were etamined preoperatively and 1-3-5 weeks postoperatively by endoscopy and rinomanometry. 175 patients were examined also 1-10 years postoperatively. After local anesthesia the "Binner" bipolar needle electrode was inserted (5-9 sec all intensive level 2-2.5) in the submucosal tissue of the inferior turbinate head , body and posterior part.

Results: RF surgery is performed under local anesthesia without postoperative use of nasal tampons. Intra and postoperative pain is extreamely low. A shrinkage of the concha coul already be observed during the coagulation. During 1-3 weeks postoperatively 800 of 917and during 3-5 weekspostoperatively 117 of 117 patients showed a reduction of inferior turbinate volume.

Conclusion: Submucosal Radiofrequency Volume Reduction with the RF generator BM-780 and the "Binner"bipolar needle electrode is an effective method for treating distrubed nasalbreathing with minimal damage of tissue."Ravor"method is an efficient and easy to handle alternative to the known standartmethods as resection and laser coagulation. The adventages can been seen in the safe procedure and the minimal side-effects dueto local anesthesia. Over the 12 year period of treatment there are no recurrenses ,less complications and better results .

Autors: M. Khvadagiani , G. Khvedelidze , K. Arabuli. Iv.Javakhishvili State Univercity Medical Faculty, Department of Clinical Surgery; Medical Center „Vivamedi" Tbilisi Georgia.

THE NEED FOR INVESTIGATION AND PREVENTION THE LONG-TERM RESULTS OF HARMFUL EXPOSURE TO LEAD

Giorgi Pataraia, Nana Tchanturidze, Grigol Tchatchia, Tatiana Mermanishvili

Abstract

Introduction. As a result of technogenic human activity, a substantial amount of lead and its compounds are dissipated in the environment, the total mass of which exceeds six hundred thousand tons. The body absorbs lead ions through breathing, in the form of airborne aerosols, and when using contaminated drinking water and food, etc. Lead is collected in depot organs (bone marrow, bone tissue, parenchymal organs), stored there for a long time, sometimes throughout life, and becomes a constant source of toxicity.

The pathogenesis of lead intoxication, clinic and treatment have been comprehensively studied by the international medical community. In the scientific literature, the main emphasis is on the description of the changes caused by toxic doses of lead and the development of treatment methods. Less attention has been given to studies of long-term exposure to lead at low, non-toxic doses. The establishment of long-term results of lead exposure is almost completely ignored; pathological changes 20-30 years after lead exposure.

Goal. Based on the aforementioned issues and taking into account the characteristics of lead (accumulation and permanent presence in the body of the bulk of lead, the long time required to reach the critical mass, lead activation and exacerbation of chronic on going toxicity under conditions of acidosis), a new picture of lead intoxication emerges. Therefore, it became necessary to study, describe and generalize the changes that occur in the body as a result of long-term exposure low doses of lead.

Material and Methods. In experiments reflecting the results of remote exposure to lead, the material taken from rats was studied morphologically. A Leika DM 2500 universal light microscope was used for histological examination, and a Jeol 100 SX electron microscope was used for ultrastructural examination.

Results. The original experimental model developed by us makes it possible to investigate what changes can take place and form basis of what pathological processes present in the body after a long time of staying (work/living) in areas at risk of contamination with non-toxic doses of lead.

Conclusion. A more complete and high-tech study of experimental material (brain, heart muscle, aorta, lung, spleen, liver, kidney, adrenal gland, intestines) under a light (histology, histochemistry, immunomorphology) and electron (ultrastructural, sieve chemistry) microscope, interpretation and generalization of the results obtained will shed light on the pathogenesis of many "known" diseases and will necessitate adjustments of their treatment strategy. We consider it likely that, the new concept – of aggressive prevention[4], which implies the implementation of more effective preventive measures than has been accepted so far, will be justified, since there is a reasonable assumption that "Lead poisoning: a disease for the next millennium".

Healthcare Workers Attitude toward Intimate Partner Violence Against Women

Nana Atchaidze, Nato Pitkshelauri

Abstract

Background: **Intimate partner violence is a widespread problem in the world. According to WHO analysis, which was conducted from 2000 until 2018 in 161 countries 30% of women experience violence from their partner.**

Aim: **We aimed to identify healthcare workers attitude toward intimate partner violence against women.**

Methods: **We have used quantitative research methods. For the interview we used self-administered questionnaires.**

Result: **As a result, We interviewed 140 respondents from different hospitals and wards in Georgia. From them 67% of the respondents thought that the strongest risk to become victim of IPV is "abusive partner", 60.90% of them thought that the strongest risk to become victim of IPV is that" Partner abuses alcohol or drugs" and 37% of respondents thought, that the strongest risk to become victim of IPV is "Gender-female". We have asked to the respondents, what was the warning sign of IPV, and 80.4 % of them thought that it is "Depression", 65.2 % thought that it is "Anxiety" and "Frequent injuries" and only 26.1 % thought that it is " Chronic, unexplained pain. And 54% of respondents have not ever identified intimate partner violence victims.**

Conclusion: **Awareness toward intimate partner violence against women is increase among helathcare workers, but identification still appeared as main fator. Healthcare workers need to improve their acknowledgement regarding identification of victims and addressing the problem.**

Georgian-Norwegian Master Program in Public Health at Tbilisi State University: Students'

Nato Pitkshelauri, George Lobzhanidze, Nino Chikhladze

Abstract

DIKU/SIU founded CPEA-2015/10057 Project *Georgian-Norwegian Master program in Public Health (GeNoC-PH)* was launched in 2016 in Georgia. Project coordinator from Norway was Arctic University of Norway and in Georgia - Ivane Javakhishvili Tbilisi State University. The project aimed: to create Master program in Public Health; to educate students on master and doctoral level to utilize the large amount of data generated from newly developed National Health Register in Georgia, to enhance knowledge transfer between Norway and Georgia in terms of register-based epidemiology and public health and to increase Public Health competence in Georgia. In 2018 the innovative Georgian-Norwegian Collaborative Master Program was designed in the framework of GeNoC-PH Project at the Faculty of Medicine, Ivane Javakhishvili Tbilisi State University (TSU). During the project following activities were carry out: long- and short-term mobility of the students, staff mobility, development of Joint courses, joint teaching and guest lecturing.

The information about the project achievement was disseminate trough different channels, social media, paper ,,Implementation of competence-based Georgian-Norwegian Master program in Public Health'' was presented on EUPHA Conferences in 2017 and the paper ,,Continuous quality improvement through benchmarking and harmonization of second cycle education in public health'' in 2021. Abstracts were published in European Journal of Public Health.

TSU Quality Assurance Service plans and conducts BA, MA and PhD students' surveys in a systematic way. The several types of surveys have been introduced for master students, among them: every-semester student surveys, student satisfaction survey, and survey of students' focus groups.

Master Program students were asked to evaluate each course, professors, and whole educational master Program. For 2018-2020 years average evaluation was 4,5 out of 5. Students underline as a strength of the program: "mobility opportunities", "attractive extra curricula activities", ''professionalism of teaching staff'' ,,interesting courses content and lectures". On a question- "Would you recommend our program to your friend/colleague?" all student's answer was "Strongly recommended".

Based to the survey results, the Georgian-Norwegian Master program in Public Health the Tbilisi State University is very attractive for the students. As a long term impact, new master program will contribute to increase Public Health competence in Georgia, which is line of International project.

EPIDEMIOLOGICAL TRENDS IN PEDIATRIC BURN INJURIES IN GEORGIA

Mariam Andriadze, Nino Chikhladze, Maia Kereselidze

Abstract

INTRODUCTION: Pediatric burn injuries remain significant public health problem in Georgia, as well as worldwide. World Health Organization names fire-related burns as 3rd most common reason of child injury deaths. According to database of National Center for Disease Control and Public Health, burn injuries hold second place among leading causes of pediatric traumatic injuries in Georgia. Children aged 0-14 years constitute almost 50% of annual number of hospitalized patients with burn injuries in the country.

AIMS: The aim of the study was to reveal morbidity and mortality of burned cases, study epidemiological characteristics and trends in Georgia among pediatric population, during 4 years (from 2018-2021).

METHODS: all cases of burn injured patients aged 0-14 years hospitalized from 2018 to 2021 were retrospectively studied. Data was retrieved from Georgian hospital registry (Form 066) and mortality database of National Center for Disease Control and Public Health, Georgia. Variables included patient's age, gender, living status, region of living, type of burn, causes of injury, length of hospital stay, surgical intervention needed, outcomes.

RESULTS: Total number of 2862 pediatric cases were hospitalized due to burn injuries from 2018 to 2021 in Georgia. Almost 60% of male patients and 40% of females were injured each year. Children aged 0-1 accounted for 51% of total studied cases. About 92% of cases were recovered, 8% needed referral to other hospitals, 0.4% discharged against medical advice and 0.17% of cases resulted in death. From 90% to 98% of patients suffered from thermal burns. About 80% of burned cases were caused by contact with hot fluids.

CONCLUSION: Most frequent types of burns were thermal burns, caused by contact with hot fluids. The most vulnerable age group was children aged 0-1 years. Before Covid-19 pandemic, most affected region was Tbilisi, whereas during covid-19 years, the most damaged region was Kakheti.

Downward trend was detected in number of hospitalization during study period, reducing cases from 1000 to 400. Presumably, Covid-19 pandemic has contributed in the reduction of hospitalizations significantly. More researches are needed for further analysis of epidemiological characteristics for burn injuries and in order to plan effective preventive measures.

Accreditation of Doctoral Programs in Public Health in Georgia

Nino Chikhladze, Nato Pitkshelauri, Natia Skhvitaridze

Abstract

Georgia joined the Bologna process in 2005 and since that time 3 cycle of education (BA, MA, PhD) was introduced in the country. Exception are programs in the fields of medicine, veterinary and teacher education, they are defined by the national legislation as one-cycle integrated programs equivalent to the Master's level. In 2005 external and internal mechanisms of Quality assurance was implemented in the higher educational system. External quality assurance is administered by the National Center for Educational Quality Enhancement (NCEQE), internal mechanisms are used in the higher educational institutions (HEIs).

Institutional evaluation is a mandatory for all HEIs which provide the right to deliver educational programs. According to the legislation in Georgia there are three types of HEIs (University, Teaching University and College). Just HEIs with status of ,University' is authorized to deliver doctoral programs.

Accreditation (programs' evaluation) is obligatory for regulated professions (medicine, veterinary, law, teacher preparation and maritime education) and for doctoral programs as well. Only after accreditation doctoral programs in any fields, including Public Health, can be implemented. During the accreditation process the panel of external experts evaluates the compliance of educational programmes with accreditation standards, each standard is broken down into the sub standards. This set of accreditation standards apply to all education programs, including doctoral programs in Public Health.

Erasmus + project "Doctoral Programmes in Public Health and Social Science" (DPPHSS) was launched in November 2018. Project aimed modernization of Public health Doctoral Programme in Georgia and Armenia. The project involves four universities from two beneficiary countries, among them are two universities from Georgia: Ivane Javakhishvili Tbilisi State University and University of Georgia. In the framework of ongoing Erasmus project doctoral programs in Public Health was updated and re-accredited based on national accreditation standards by NCEQE in both Georgian Universities.

At TSU the doctoral programme "Public Health and Epidemiology" was developed, updated and amended based on Resolution №100 of the TSU Academic Council. Updated program and syllabi was reviewed on several meetings of Public Health Curriculum Committee consisting of 8 members involved in the Erasmus + DPPHSS project. Doctoral programme "Public Health and Epidemiology" was approved by the TSU Faculty of Medicine Board Meeting #13 in November and by TSU Academic Council Meeting (#142/2019) in December 2019. On 29-30 April 2020 at TSU there was a Site-Visit of expert panel and on 17 July 2020 Doctoral program get Accreditation with full compliance to the national standards.

Successful completion of the accreditation process of the Public Health Doctoral Programme in Public Health in Georgia in in line with goals set by the Erasmus + DPPHSS international project.

Determination of Admission Criteria for Global Public Health Master Program at the University of Georgia

Tamar Lobjanidze, Natia Skhvitaridze, Mariam Lobjanidze, B Ramirez, Giorgi Shakarishvili

Abstract

Background:

Recent events in the world, wars, pandemics, have once again raised the issue of the need for competent human resources in global public health. In fact, in the developing countries, there are no global public health or global health master's degree programs existed. In this matter, the Republic of Georgia is no exception, although there are master's degree programs in public health where global health is mostly offered as an elective or core course of the curriculum.

The Master's program in Public Health and Healthcare Policy has been operating at the University of Georgia (UG) since 2006. Here, global health is also provided as a core course of the curriculum and is created in frame of collaboration with Arctic University of Norway (UiT). According to academic personnel and student interviews, course is favored and characterized by growing interest. UG is also involved in the ERASMUS + project: Building Academic Capacity in Global Health in Eastern Europe - Central Asia Region (BACE).

The School of Health Sciences (UG), initiated to create new Global Public Health Master Program, which will be response towards local, regional and international challenges and demand.

Objective

Main objective of developing GPH program was to address and meet national and international global health education needs and challenges. The aim of the study was to identify evidence-based prerequisites for the MPH in GPH (UG). We conducting document review based on the GPH competency model (GPHCM) and evaluated: 1) GPH & MPH programs of the top 20 world university ranking (THE/2022); 2) CUGH associated programs; 3) Georgian MPH programs; 4) Georgian education documents (such as Georgian National Qualifications Framework (GNQF)); 5) Main directions of career development in global health. In addition, interviews with national experts were conducted (in education, employment, program leaders) using the Delphi method.

Results

Study found that depending on the scope and content of the program, prerequisites for obtaining MPH in GPH varies. In addition to English competence and a high GPA, working or research experience or interviews or additional exams or other are required. In Georgia, there is no adopted GPHCM, but GNQF allows the establishment of MPH in GPH. UG new Master program (120 ECTS) will include 99 ECTS core (including research practicum & thesis) and 21 ECTS elective courses based on 6 domains of GPHCM. The program will mostly focus on population health management at a global level.

Conclusions

Study findings suggest any undergraduates with appropriate conditions could be eligible for admission to the UG (MPH in GPH). UG Admission prerequisites for Health Science undergraduates determined as follows: National entrance exam, English proficiency B2, health related working experience and motivation letter. Additionally, Admission prerequisites for Health Science undergraduates are basic knowledge of epidemiology and medical terminology (if credits available or test).

Childhood Adverse Experience among Students

Maia Bitskinashvili

Abstract

In a study we conducted that looked at childhood psychological traumas in students, we have a clear picture of how prevalent childhood trauma is in our community. According to the studies conducted of the students' population show that the cumulative effect of adverse childhood experiences (ACEs) is a predictor of poor health, psychological disorders and problem with learning and education.

Quantitative methods of Research were used and the questionnaire was created based on existing international experience, including WHO-The ACE International Questionnaire (ACE-IQ). Questions covered family dysfunction; physical, sexual and emotional abuse and neglect by parents or caregivers; peer violence; witnessing community violence, and exposure to collective violence.

1239 students participated in the survey and criteria of inclusion in the survey was students aged 18 and more. SPSS program was used for statistical analysis. According to the results of our research almost half of the surveyed students were victim of physical, emotional or sexual violence and almost half of them didn't share the fact of violence with anyone.

Road Traffic Injury Epidemiology on the Example of One Hospital in Tbilisi

Giorgi Tskaroveli, Maka Jorbenadze, Ketevan Axlobadze, Nino Chkhaberidze, Nato Pitskhelauri

Abstract

Background: Road Traffic Injury is a major issue of global health. It is responsible for approximately 1.3 million deaths and from 20 to 50 million injuries each year. The road traffic injury represents the quarter of injury related death, mostly (50%) in young adults between the 15 – 44 age group. Around 85% of Road Traffic Injuries occurred in low- and middle- income countries and give a heavy burden on national and regional economies. But good news is that road traffic injuries are preventable - in high income countries appropriate interventions have contribution in reduction of road traffic injury morbidity and mortality.

Objectives: The aim of this research was to describe the epidemiological characteristics of Road Traffic Injuries on the example of one of the largest hospitals in Georgia.

Method: The study design consisted of a retrospective observational study of Road Traffic Injury patients at University Hospital in Tbilisi over six months (January 1st 2018 to June 30st 2018). Visits were identified from existing electronic medical records. Data collected included patient demographics and injury characteristics.

Results: A total of 216 road traffic injured patients aged 0 to 77 years were evaluated during the study period and about 64% (n=132) of them were male. Most of the injured patients were young adults (25-44 years, 36%) and school-age children (6-17 years, 27%). Most of the patients (59%, n=122) suffered from moderate injuries and needed only outpatient treatment. The most injured body regions were head (41%) and low extremities (16%).

Conclusions: More research is needed to identify Road Traffic Injury related risk-factors useful for planning effective preventive strategies.

Keywords: Road Traffic Injury, Epidemiology, Georgia.

Unintentional Poisoning Hospitalizations Among Children Under 5 Years in Georgia

Ia Baghashvili, Nino Chkhaberidze, Ketevan Axobadze, nino Chikhladze

Abstract

Abstract

Background: Poisoning is the fourth leading cause of unintentional injury among children. The 13% of all cases of poisoning occurred among children and young people under the age of 20 years. But the majority of poisoning cases occur under 5 years of age, particularly those in low-income and middle-income countries. . Common poisoning agents in high-income countries include pharmaceuticals, household products (e.g. bleach, cleaning agents), pesticides, poisonous plants and bites from insects and animals.

Objectives: The aim of this study was to describe the epidemiological characteristics of children unintentional poisoning in all hospitals of Georgia.

Methods: The database of the National Center for Disease Control and Public Health of Georgia for 2015-2020 was obtained to identify unintentional poisoning cases treated in hospitals.

Results: Poisoning accounted for 16% of all hospitalization between 2015-2020 with the peak on 2017. Totally poisoning represents 2551 cases. Males accounted 55% (n=1242) of all poisoning related hospitalization. In 55% of all cases poisoning was caused with non medicinal substances mostly with pesticides (41,5%), corrosive substances (32.7%), organic solvents (17,8%). In 45% of cases poisoning was caused by medical substances: agents primarily affecting the cardiovascular system (29.9%) psychotropic drugs (16%) antiepileptic, sedative-hypnotic and antiparkinsonism drugs (11.5%)

Conclusions: In Georgia the environment around the toddlers is not save and requires more attention. Future studies focused on risk groups are important to prevent unintentional poisoning injury in children.

Keywords: Poisoning, Children, Epidemiology, Georgia

Principles and Foibles of Precision Medicine

Otto Rienhoff

Abstract

- **Introduction**

  The term "precision medicine" is used often as a positive phrase to summarize vaguely the future of a medicine, which is supported massively by digital inventions, artificial intelligence, and IT-infrastructures. The vague term allows many persons in policy and management to sell their ideas in a positive colorful form to believers. However, because of its vagueness the term is also hiding substantial problems of the clinical fields in the future, which are not easy to solve.

- **Goal**

  To focus on open questions and specifically address the challenges of the new data rich medicine and how to enable in the future a personal, empathic, and trustful exchange between doctors and patients in a constantly changing knowledge environment. It shall become clear that "precision medicine" needs infrastructural and knowledge management inventions in the traditional health care systems and new IT-solutions to support collaboration between doctors and patients.

  Material and Methods

  The paper is based on personal experience regarding the clinical management and studies of rare diseases. In addition, it reflects publications analyzing the problems and the state of CDSS systems during 60 years after their first utilization. Further, it reflects publications of studies of the German National Council in Research Data Infrastructures (RFII).

- **Results**

  Medical Schools tend to include usage of IT-technology and digital tools into their curriculum. Very slowly, this process is moving ahead. The issue is not very much addressed in the professional update training of physicians during their working life. The change into data based handling of knowledge in treatment processes and individual linking of patient data and therapeutic options is still in its early stage of development. The inclusion of KI-and CDSS tools into the clinical decision process and an adequate documentation of this is in its infancy. It needs to be understood and trained. A trustful personal exchange between doctors and patients about rare diseases and rare combinations of factors in a precision medicine diagnostic process also to include a documentation of diagnostic steps and therapeutic actions in a way that is understood by both of them. This is one of the key challenges in clinical reality on the long way to the promised precision medicine world. One option to support the documentation of facts and exchange between patients and doctors is the model of a digital twin linking data worlds of doctors and patients and supporting legally transparent decision flows. The digital twin concept is not easy to build up, but may be a key element in a new generation on IT systems in clinical medicine keeping the more and more complex and dynamic knowledge and data worlds understandable for all parties.

- **Conclusion**

  The complexity of long-term data management for clinical purposes needs new structuring solutions because the currently available software systems optimize interfacing between different data worlds but do not focus of a productive physician – patient dialogue and its long-term documentation. Therefore, it is a good option to conceptualize the idea of a digital twin as data model for this purpose by a powerful design phase that is followed by efficiency and usability validation studies. Currently the ideas about a digital twin are often cited but systematic architectural research is missing. Corresponding to this research the medical faculties in the world have to modernize their curricula for empowering the next generations of doctors to work with

such support tools for their dialogue with their patients – building up a new trust concept for empathic physician action which can be on the latest level of data based medical research and treatment knowledge.

Quality Management in Data Driven Medical Research

Otto Rienhoff

Abstract

- **Introduction**

  Medical Research faces measurements growing in numbers, in resolution, and in complexity under nationally different legal and ethical regulations. The internet is pushing this development. Well-known and new publication platforms become more and more divers. Publishing companies have been bought by money investors and changed their value systems. All this leads to unmanageable data oceans with billions of not easy to validate published "results".

- **Background**

  The development over the last two decades is reflected in some publications. The National Library of Medicine in Washington is analyzing this historical change in collaboration with other national libraries, e.g. NLM, Washington and ZBmed, Cologne. International organizations are trying to find solutions for these problems, e.g. addressing "open science", "FAIR data" or other concepts. An important irritating aspect is, that the costs for reading publications may be very different – motivating persons with little resources to utilize primarily "free" publications. All these changes make it very difficult to understand, how literature and knowledge management will be in the future, how modern libraries have to work, how young scientists and health professionals have to be trained regarding updating their skills etc. etc.

- **Goal**

  To derive some general recommendations for national strategies for the digital transformation of medical research and health care based on lessons learnt in different countries.

- **Material and Methods**

  Strategy papers from Germany, the EU, and other countries are evaluated by the German Council for Information Infrastructures (RFII). These results are reflected based on personal activities in relation with NLM and ZBmed. In addition it is reflected how long the learning process took in Germany and how difficult it is in Germany to update the existing scientific and clinical systems to deal with such changes.

- **Results**

  The key success factor of science management has become the way how data is handled, its origin documented, and its use checkable by third parties. The uncontrollable amount of low-level publications has to be massively changed to get to transparent and handable new forms of scientific exchange. Validation of results became more important than ever.

  The Göttingen University and its integrated Medical School and teaching hospital (UMG) have been addressing these issues over many years already – with very different success. The paper reports on many findings out of this process to describe how complex the change from the traditional clinical research and clinical care to the highly dynamic knowledge management of the future will be. As one consequence, the University, the UMG, and a Polytec have established the Göttingen Medical Campus to address these new developments together. Since 2000 about new

Professorships were started dealing with these issues in various faculties and working together in the Campus Institute of Data Science (CIDAS).

Another learning process has been the building up of national collaboration platforms in science since 1999 – starting with the Telematics Platform for Medical Research Networks (TMF) – and mostly funded by the national ministry of Research (BMBF) in Berlin. The latest new structure in this context are the national Medical Informatics Initiative (MII) and the National Research Data Infrastructure (NFDI).

The presentation tries to address important experience from these processes in the last two decade. These "learnt results" are clearly convincing how much impact the new data rich science world will have on research organizations, funding programs, and training procedures for scientists. It cannot formulate conclusions but prove that we are in a historical change process taking several decades.

- **Conclusion**

Institutions and countries who want to play an important role in the scientific world have to strategically work to move away from two outdated realities:

(1) From non validatable publications in great numbers to serious modern forms of publications based on published and checkable data and data provenance information.

(2) From small and often instable analog (specimen) and digital data collections in isolated small research labs to professionally handled data management sites of financially stabile organizations on the levels of medical schools or universities.

(3) From interested computer fans to professionally trained data curators and to physicians enabled to update constantly their clinical work methods based on support systems for them and for their patients. The support systems reflecting and allowing a special individualized clinical decision at the state of art of clinical research.

Neuromuscular comorbidity of COVID-19

E Nebadze, R Shakarishvili, N Kvirkvelia

Abstract

Backgraund. The outbreak of the novel and highly infectious COVID-19 has resulted in hundreds of millions of infections and millions of deaths globally. Infected individuals experience upper and lower respiratory complications that range in severity and may lead to wide-spread inflammation and generalized hypoxia or hypoxemia that impacts multiple organ systems, including the central and peripheral nervous systems. According to the data available today, the neurological symptoms associated with COVID-19 infection are described in detail. Based on these studies, it can be assumed that SARS-Cov-2 may be neurotropic and / or contribute to or create conditions conducive to direct or indirect damage to the nervous system. Aim: The aim of the study was to identify complications of COVID-19 infection in patients with neuromuscular diseases (myasthenia gravis, chronic polyneuropathy, myopathy).
Material and Methods: The study included 20 patients infected with COVID-19 with generalized myasthenia gravis, 8 with chronic polyneuropathy and 5 with progressive dystrophy. Among patients with myasthenia gravis, there were 15 women and 17 men aged 50 to 69 years. Among 8 patients with chronic polyneuropathy, there were 3 women and 5 men aged 25 to 74 years, and among patients with progressive dystrophy - 3 women and 2 men aged 36 to 62 years. Patients were examined approximately at intervals of 3 weeks to 2 months after infection with COVID-19. Patients underwent CT scan of the chest, ENMG, titers of antibodies to AChE, MuSk, Titin, LIA-ANA profile were determined, blood tests were performed, CPK and C-reactive proteins were determined in the blood. Results. In 15 patients out of 20 with myasthenia gravis, an exacerbation of the condition was noted, mainly with respiratory symptoms, of which Lambert-Eaton syndrome was diagnosed in one patient after infection with COVID-19 and in 3 had motor-sensory polyneuropathy with a predominant lesion of sensory fibers; the condition of 5 patients did not change, the infection was asymptomatic. In 8 patients with chronic polyneuropathy in remission after infection with COVID-19, an exacerbation of the condition was noted, namely, a deepening of the degree of axon damage, expressed in the lower extremities and sensory fibers, in one patient EMG study revealed changes characteristic of polymyositis. Of the 5 patients with progressive dystrophy, 2 had motor-sensory polyneuropathy against the background of myalgia, in 2 patients an increase in muscle damage was detected electrophysiologically, in one case EMG revealed changes characteristic of polymyositis. Conclusion. Based on the results obtained, it can be assumed that not only comorbid pathology occurs as a result of infection with COVID-19, but the COVID-19 virus can also be considered as a modifying factor in the course of the disease.

How to Protect DNA Genomes: Lessons from Hyperthermophilic Viruses

David Prangishvili

Abstract

Genetic research involving genomic DNA samples can easily be altered or corrupted by genomic DNA degradation. Once genomic DNA unfolds or breaks apart, the conclusions provided by any examination or assay may not be valid. Thus, proper storage is required to ensure high experimental standards. Prominent examples of efficient conservation of dsDNA molecule and keeping it stable for prolonged time intervals are provided by viruses which thrive in adverse conditions. We have studied arrangement of DNA genomes in diverse viruses isolated in our laboratory from extreme geothermal environments where temperatures exceed 80°C and are usually destructive for DNA [1,2]. In my talk I will summarizes the results of structural reconstruction of these viruses at near atomic resolution by cryo-electron tomography which provide insights into the details of DNA packaging and shade light on molecular mechanisms behind the high stability of viral DNA [3-8].

References

1. Prangishvili D. 2013. The wonderful world of archaeal viruses. *Ann. Rev. Microbiol.* 67: 565-585.

2. Prangishvili D, DH Bamford, P Forterre, J Iranzo, EV Koonin, M Krupovic. 2017. The enigmatic archaeal virosphere*. Nature Rev. Microbiol*. 15: 724–739.

3. DiMaio F, X Yu, E Rensen, M Krupovic, D Prangishvili#, EH Egelman#. 2015. A virus that infects a hyperthermophile encapsidates A-form DNA. *Science* 348: 914-917.

4. Ptchelkine D, S Gillum, T Mochizuki, S Lucas, Y Liu, M Krupovic, SEV Phillips, D Prangishvili#, JT Huiskonen#. 2017. Unique architecture of thermophilic archaeal virus APBV1. *Nature Commun*. 8: 1436.

5. Kasson P, F DiMaio, X Yu, S Lucas-Staat, M Krupovic, S Schouten, D Prangishvili#, EH Egelman#. 2017. An envelope of a filamentous virus carries lipids in a horseshoe conformation. *Elife*, 6: e26268.

6. Liu Y, T Osinski, F Wang, M Krupovic, S Schouten, P Kasson, D Prangishvili*, EH Egelman*. 2018. Structural conservation in a membrane-enveloped filamentous virus infecting a hyperthermophilic acidophile. *Nature Commun*. 9:3360.

7. Wang F, Y Liu, S Zhangli, T Osinski, GAP de Oliveira, JF Conway, S Schouten, M Krupovic, D Prangishvili #, EH Egelman #. 2019. A novel packing for A-form DNA in an icosahedral virus. *Proc. Natl. Acad. Sci. USA* 116(45):22591-22597.

8. Baquero DP, AD Gazi, M Sachse, J Liu, C Schmitt, M Nilges, S Schouten, D Prangishvili#, M Krupovic#. 2021 A filamentous archaeal virus is enveloped inside the cell and released through pyramidal portals. *Proc. Natl. Acad. Sci. USA* 118(32):e2105540118.

Myo-Inositol Limits Kainic Acid-Induced Epileptogenesis in Rats

G Gamkrelidze, M Kandashvili, M Tsverava, T Lortkipanidze, E Lepsveridze, V Lagani, M Kokaia, R Solomonia

Abstract

Background. Epilepsy is a severe neurological disease characterized by spontaneous recurrent seizures (SRS) and affects 1% of human population. A complex pathophysiological process referred to as epileptogenesis transforms a normal brain into an epileptic one. Prevention of epileptogenesis is a subject of intensive research and of great biomedical importance. Currently, there are no clinically approved drugs that can act as preventive medication.

Aims. Our previous studies have revealed highly promising antiepileptogenic properties of a compound–myo-inositol (MI) and the present research is aimed to broaden previous results and demonstrate the long-term disease-modifying effect of this drug, as well as the amelioration of cognitive comorbidities.

Materials and Methods. Status epilepticus (SE) was induced by kainic acid (KA) injections. MI and saline treatment was continued for 4 weeks. Electrophysiological recordings in the hippocampus, morphological and biochemical analysis and Morris water maze experiments were conducted 8 week after the SE.

Results. MI treatment for 28 days reduces frequency and duration of behavioural SRS not only during the treatment, but also after its termination for the following 4 weeks. For the first time, we show that long-term treatment with MI: (i) decreases the frequency and duration of electrographic SRS in the hippocampus; (ii), ttenuates cell loss in the CA1 and CA3 subfields of hippocampus and (iii) has an ameliorating effect on spatial learning and memory deficit associated KA induced with epileptogenesis

MI treatment alters micro-RNA expression spectrum and decreases the level of the glial fibrillary acidic protein. The expression of sodium-MI transporter, LRRC8A subunit of volume-regulated anion channels, micro-RNA 6216 and its target - protein tyrosine phosphatase receptor type R, are altered in a such way to counteract the epileptogenesis. All these effects are still present even 4 weeks after MI treatment ceased. This suggests that MI may exert multiple actions on various epileptogenesis-associated changes in the brain and, therefore, could be considered as a candidate target for prevention of epileptogenesis.

Conclusion. Obtained data our could open novel possibilities to develop MI treatment as possible future approach for preventive strategy to modify disease initiating process and its progress - epileptogenesis - and lay foundation for further translational development of the MI research.

References

1. **Tsverava et al., *BioMed Research International*, 2019, Article ID 4518160.**
2. **Kandashvili et al., 2022, *Int J Mol Sci*., 23:1198**

Bio-Medical Imaging and Its Application Beyond Clinical Medicine

Ann Margvelashvili

Abstract

Background

Record of interest in the human body starts from ancient times, about 1600 BCE. Already in the 2nd century, Galen was a skilled surgeon performing operations. He discovered that the larynx generates voice and was a pioneer in research on the human spine. Later in the 16th century, Vesalius conducted highly precise dissections, producing detailed plates together with the artists present during the dissection process. In 1895 Röntgen discovered the X-rays, enabling the visualization of the internal structures of the living humans revolutionizing modern medicine. The development of modern visualization techniques opened new horizons not only in medicine but in other fields of science.

Aim

The research aims to show the capabilities and application of biomedical imaging techniques beyond clinical applications, thus, advancing the different fields of science.

Materials and Methods

Five crania and four mandibles of early humans from Dmanisi, Georgia dated to 1.77 million years were analyzed. Data acquisition was performed through computer tomography and synchrotron tomography. Data was transferred to high-performance workstations and analyzed in 3D softwares such as VGStudio-Max, Avizo, and OsirixMD. The 3D models of the fossil hominins were produced on Eden260 using 3D softwares GeoMagic and Objet.

Results

Through modern techniques of biomedical imaging reconstruction and visualization of fossil hominins were performed. Morphological features and pathologies such as hypercementosis, dental caries, traumatic injuries, and infectious diseases were identified. Moreover, the traces of predation on hominins were recognized, thus providing additional information on the lifestyle of early humans.

Conclusion

Biomedical imaging is key in the research and analysis of fossil materials in the fields of paleontology and paleoanthropology. The data acquisition through computer tomography is a non-invasive way to virtually preserve the fossil material, reconstruct it, and produce 3D models. Modern research on the physiological and pathological conditions of the fossil material is only possible through biomedical imaging, thus, reconstructing not only the morphology of the bones but also implying the lifestyle and survival strategies of the fossil findings.

Electromagnetic Properties of the Blood Flow

Merab Beraia

Abstract

There is a lot of uncertainty in the theory of hemodynamics: The amount of work need to displace the blood in the systemic circulation, exceeds the work done by the left ventricle.

Blood flow acceleration increases from the left ventricular outflow tract to the sinotubular junction and the ascending aorta, while it must be decreasing due to the turbulences. With this, blood recovers increased flow resistance between the heartbeats with the Womersley number alterations in the rhythm of the accompanying ECG. Viscoelastic transformation is heavily expressed in coagulation. There must be a relationship between the ECG and blood transient flow resistance.

Was studied the influence of the electromagnetic field on blood flow and coagulation. Venous blood was affected by the oscillated electromagnetic field (500-5000Hz.), with the square wave input signal in 25 healthy individuals.

Was revealed to decreased flow resistance and hypocoagulation in normal blood samples, and thrombolysis after the blood stasis.

Ac electric field from the myocardial depolarization initiates electroacoustic phenomena. An emerging repulsing electromagnetic force acts on the RBC and in addition to the pulse pressure from the heart, promotes blood motion and viscoelastic changes.

The alterations of the blood inertial and elasticity, in addition to hemodynamics, are facilitated by the magnetic features of the hemoglobin.

Although electromagnetic influence is carried out on the arterial and venous blood, structural changes with the increasing entropy are specified only for the pulsatile blood. It must be associated with the frequency dispersion of the substance at the boundary reflection and activation of the coagulative system at the low shear velocity in the vena.

The external electromagnetic signal can manage the blood coagulation process, including thrombolysis.

Local Drug Delivery System for the Treatment of Tongue Squamous Cell Carcinoma

Mariam Kakabadze, Tamar Rukhadze, Manana Kakabadze

Abstract

***Background*. The global incidence of oral cancer is >300,000 cases, annually resulting in 145,400 cancer-associated deaths. The most widespread malignant tumor of the mouth is squamous cell carcinoma. It occurs in 80-90 % of all oral cancer cases. The treatment of oral squamous cell carcinoma includes surgery, chemotherapy, radiation therapy, and immunotherapy. Surgical resection is a key treatment method for tumors of the oral cavity and oropharynx. However, after tumor resection, the presence of residual tumor cells is frequent, which usually leads to tumor recurrence. *Aim.* The aim of this study was to develop a targeted drug delivery system with two functions, which can suppress tumor growth and accelerate wound healing. *Material and Methods*. The system consists of a two-layer multicomponent fibrin-based gel (MCPFTG). The internal layer of MCPFTG, which comes in direct contact with the wound surface, contains cisplatin that is placed on a CultiSpher-S collagen microcarrier. The external layer of MCPFTG consists of a CultiSpher-S microcarrier with lyophilized bone marrow stem cells (BMSCs). The efficacy of MCPFTG was evaluated in a rat model of squamous cell carcinoma of the tongue created with 4-nitroquinoline 1-oxide. *Results*. The results of the study showed that, within 20-25 days, a non-healing wound of the tongue was formed in animals that underwent only 85% resection of squamous cell carcinoma, while rapid progression of the residual tumor was concomitantly observed. Immunohistochemical methods revealed high expression of cyclin D1 and low expression of E-cadherin in these animals. Additionally, high expression of p63 and Ki-67 was noted. In 80% of animals with squamous cell carcinoma of the tongue that were treated with MCPFTG after 85% tumor resection, a noticeable suppression of tumor growth was evident throughout 150 days, and tumor recurrence was not detected. Immunohistochemistry revealed low or moderate expression of cyclin D1, and high expression of E-cadherin throughout the whole observation period. Conclusion. The local drug delivery systems are promising method of treatment of squamous cell carcinoma. Our system reduces the toxicity of cisplatin and improves its antitumor activity. Thus, the present study suggests novel opportunities for the development of a drug delivery system for the treatment of squamous cell carcinoma.**

Patient Centred Care – An Integrated Part of Oncology Care?

Kaasa Stein

Abstract

Background

Integration of oncology and palliative care (PC) combines two paradigms: the tumour-directed approach, which is the main focus of oncology, and the host-directed approach, which is the focus of PC. Contemporary PC aims to prevent, treat and reduce symptoms and suffering and to preserve and improve quality of life.

A Lancet Oncology Commission was written on how PC and oncology can be integrated by combining these two approaches focusing content, models, organization of cancer care, public health, politics, education and research.

Methods

An international panel was established, consisting of experts in oncology, PC, public health and psycho-oncology. Literature searches were conducted, author meetings were held, and an interactive writing process was conducted.

Results

Integration is a complex process that involves various components of the health care system. The published RCTs on integration demonstrate health gains, but how and when to integrate is uncertain. Still, early delivery of specialist palliative care promotes patient-centeredness including shared-decision making, family involvement and regular use of patient-reported outcome measures. Barriers to integration include the perception of PC as end-of-life care, deficient planning at local, national and international levels, and insufficient infrastructure and funding. Furthermore, death and dying are stigmatized. The present competence in combined oncology and PC varies substantially and must be defined at all levels. The commission proposes to use standardized care pathways (SCPs) and multidisciplinary teams (MDTs) to promote integration. Integration raises new research questions: how much, when and how should PC be delivered and what is the minimum model for good care?

Conclusions

Integration involves the transition from a dualistic perspective - the tumor and the host- to a combined perspective. Integration must be recommended by health care authorities and decision-takers, followed by resource allocation and priority-setting. In all areas, the present volume of PC is too small to support integration on a broad scale. Implementation of integrated models is best secured by MDTs and SCPs. The combined perspective must be reflected in care models, education and research funding.

Risk of Development, Outcome, and New Tumor Markers of a Hepatocellular Carcinoma

Levan Gogichaishvili, Gia Lobzhanidze, Mikheil Jangavadze

Abstract

Background: HCV infection and its complications, especially hepatocellular carcinoma, is a substantial public health burden. In 2015 "Nationwide hepatitis C elimination program" was launched in Georgia. According to the protocol, patients with HCC also receive DAA antiviral treatment. Many studies shows that Gankyrin is one of the main players in hepatocellular carcinogenesis. It expression increased not only in HCC tissues, but also in cirrhotic livers, while Gankyrin absent in normal liver samples

Aim: The aim of this study was to define the effect of the different DAA therapy regiments on the incidence or recurrence of HCC and its prognosis and to investigate the feasibility of plasma circulating Gankyrin mRNA as a HCC biomarker.

Methods and Materials: Overall, 408 patients were recruited between April 2015-March 2016. The selection criteria were as follows: age 50-65 years; Liver fibrosis level F3-F4 or cirrhosis at least 15 years of disease history; HCV positive diagnosed by PCR method; 4. absence of previous complications of cirrhosis. Child-Pugh class A or B; and absence of severe extrahepatic disease. Clinical monitoring and management of adverse events were performed on a regular base. HCV All patients included in the study received anti-HCV treatment with direct-acting antivirals (DAAs) within the national hepatitis C elimination program in accordance with national protocols. During April 2015-March 2016 treatment was provided with sofosbuvir (SOF) in combination with ribavirin (RBV), with or without pegylated interferon (IFN). Since March 2016, ledipasvir/sofosbuvir (LDV/SOF) was prescribed to all patients with or without RBV depending on the HCV genotype, level of fibrosis, and previous treatment experience. Incidence and mortality rates per 100 person-years (PY) of follow-up were calculated as number of events divided by the total person-years of observation multiplied by 100. Bivariate comparisons were tested by Pearson's chis-square or Fisher exact test as appropriate. Factors associated with the occurrence of HCC were evaluated in Cox proportional hazards regression model. All analyses were conducted using SAS v9.4. P values of <0.05.

Plasma samples were isolated from 4 mL of peripheral blood from patient with HCC (n=32), HCC with MTS (n=5), Cirrhosis - (n=7), HCV positive - (n=5), and healthy individuals. Fresh Total DNA/RNA/miRNA was extracted from blood plasma using RecoverAll™ Total Nucleic Acid Isolation Kit. RT-qPCR was performed using TaqPath 1-Step Multiplex Master Mix. Human 18S ribosomal RNA was used as an internal reference gene. The relative expression levels were calculated using $2-\Delta\Delta Cq$ method using SAS-Studio Mann-Whitney U test was used to determine the statistical significance for comparisons between groups.

Results: we find that neither different DAA regimens nor treatment duration affects HCC risk after antiviral treatment. There are no significant changes in mortality rate due to HCC in these groups. Gankyrin RNA expression is significantly increase in plasma of HCC patients, especially in metastatic diseases.

Conclusion: Therefore, it can be concluded, that HCC status is not a contraindication for DAA treatment, especially at the early stages of cancer, when a tumor is curative. Plasma circulating Gankyrin mRNA is high sensitive HCC biomarker for liquid biopsy.

Application of Liquid Biopsy for Hepatocellular Carcinomas using Plasma Circulating p28/Gankyrin RNA and miRNA-s

Mikheil Jangavadze, Leavn Gogichaishvili, Zanda Bedinashvili

Abstract

Background:

Gankyrin/PSMD10 plays an important role in tumorogenes, especially hepatocellular carcin ogenesis.
Protein expression significantly increased in Hepatocelular Carcinoma (HCC). Gankyrin and miRNA-s may be used as a diagnostic and prognostic marker for the HCC and for monitoring of tumor recurrence.

Aim:

To investigate the feasibility of plasma circulating Gankyrin mRNA and miRNA as a HCC biomarker.

Methods and Materials:

Total DNA/RNA was extracted from FFPE of tumor and adjacent liver tissues n=35. Control samples: cirrhotic (n=10) and normal (n=10) liver. Plasma samples were isolated from 4 mL of peripheral blood from patient with HCC (n=32), HCC with MTS (n=5), Cirrhosis - (n=7), HCV positive - (n=5), and healthy individuals. Fresh Total DNA/RNA/miRNA was extracted from blood plasma using RecoverAll™ Total Nucleic Acid Isolation Kit. RT-qPCR was performed using TaqPath 1-Step Multiplex Master Mix. Human 18S ribosomal RNA was used as an internal reference gene. Expression of Gankyrin/PSMD10 mRNA and 122 miRNA, 130 miRNA, 15 miRNA, 152 miRNA, 200A miRNA, 200B miRNA, ,21 miRNA, 26 miRNA, 9 miRNA was evaluated. The relative expression levels were calculated using $2-\Delta\Delta Cq$ method using SAS-Studio Mann-Whitney U test was used to determine the statistical significance for comparisons between groups.

Results

In the blood plasma of the patients with cirrhosis, HCV without cirrhosis and healthy individuals cell free RNA of Gankyrin/PSMD10 was not detected. While significant expression was observed in patients with HCC. As for the tissue samples, the following results were obtained. Garkirin/PSMD1 RNA expression was lower in healthy liver tissue. While a 3.2 folde change was observed in cirrhotic liver sa mpes, compared to a healthy one. In the HCC tissue samples and its surrounding liver tissue si gnificant expression was identified – 120.7 and 68.5 fold change relatively. Also miRNA expression profiles was determine for different tissues.

Conclusion

The obtained data indicate that plasma Garkirin/PSMD10 RNA can be used as a diagnostic as well as prognostic and monitoring tool for HCC recurrence. Garkirin/PSMD10 RNA expression data in tissue indicate that gene upregulation begins in cirrhosis. It was confirmed also by miRNA expression profiles. It reaches a maximum in HCC. In non-cancer tissue surrounding the tumor (also cirrhotic) the expression is significantly higher. There is not clear it is consequence of "malignant" process, or its upregulation is a first step of "malignant" transformation. If later will be confirmed – we will have good prediction marker for patient with cirrhosis for determine of HCC risk.

Our findings indicates the potential role of Garkirin/PSMD10 expression in liver biopsy to predict cancer risk in cirrhotic patients.

Successful Immunotherapy in Advanced Lung Cancer

David Tabagari, Davig Giorgadze, Tamta Makharadze, Mariam Zhvania, Elene Dolmazashvili, Salome Kordzaia

Abstract

Background: Lung cancer is the most prevalent malignant disease in men worldwide, and third most common in female population. In Georgia, its incidence was 600 in 2020. In recent years, worldwide, the trend of decreasing mortality rate and increasing in prevalence has been detected, which can be due to development of new, more effective methods of treatment such as immunotherapy.

Our body is capable of producing immune response against tumor cells. The main soldiers of immune system are cytotoxic T lymphocytes and NK cells. After some time and adjustments, tumor cells become resistant to our immune response, by overexpressing special molecules such as PD-L1. These molecules play essential role in suppressing effector T cell functioning. In recent years, lots of immune checkpoint inhibitors – monoclonal antibodies have been registered for treatment of advanced lung cancer: Cemiplimab (Libtayo) - anti PD-1 antibody and Ipilimumab – anti-CTLA4 antibody which interfere tumor cells in T cell inhibition.

Aim: Demonstration of 2 case studies of successful treatment of advanced Non-small cell lung cancer (NSCLC) with anti-PD1 and anti-CTLA4 immunotherapeutic drugs.

Patients: 64 y.o. male, with morphologically and immunohistochemically verified diagnosis of lung adenocarcinoma, with metastatic lesions in mediastinal lymph nodes and L4 vertebrae. Treatment was conducted by immunotherapeutic drugs: anti PD-1 antibody – Cemiplimab and anti-CTLA4 antibody – Ipilimumab. Another patient - 63 y.o. male, with morphologically and immunohistochemically verified diagnosis of squamous cell carcinoma of the left lung, with metastatic lesions in contralateral hilar lymph nodes. Treatment was conducted by immunotherapeutic drug Cemiplimab.

Results: In 2018, oncological team of Multiprofile Clinic Consilium Medulla received the patient - 64 y.o. male with metastatic lung adenocarcinoma, with PD-L1 – 1%, and treated him with combination of Cemiplimab 350mg i.v. Q3W and Ipilimumab Q6W with success: after 9 cycles of Cemiplimab and 4 cycles of ipilimumab, patient developed complete response to the treatment. Complete response is still remaining after 26 months from the end of treatment and the patient is considered free from the disease for 34 months.

In 2019, another patient – 63 y.o. male with metastatic squamous cell carcinoma of the lung and PD-L1 expression of 60%, received treatment with Cemiplimab 350mg i.v Q3W. After 12 cycles, patient developed complete response to the treatment. The patient is considered free from disease for the last 21 months.

Like all treatments, immunotherapy has its risks and benefits. Risks involve the over-activation of our immune system, which in turn manifests itself in the form of various autoimmune processes - termed as immune related adverse events (IrAEs). Our patients were not an exception: In exchange for a full response to treatment, IrAEs – hypothyroidism, that made them dependent on thyroxine replacement therapy for the rest of their lives, as well as pneumonitis have been developed. The latter became the reason for stopping the treatment in both cases. These challenges identified during the treatment period made us wonder whether it is advisable to infuse immunotherapeutic drugs once every 3 weeks and over-stimulate the immune system and whether there is a chance of getting the same effect on treatment if infusion of immunotherapeutic drugs is conducted once every 6 weeks, which would theoretically decrease the risk of development of IrAEs. This question remains unanswered and needs conduction of multiple trials.

Concluison: Despite treatment-associated challenges, immunotherapy represents a promising future for patients with advanced NSCLC

Modern Radiotherapy of Brain Tumors

N Kalandarishvili

Abstract

There are many kind of tumors, Brain tumors account for 1.4% of all cancers. Median age of brain cancer is 58 years. Incidence is 6.4 per 100 000 men and women per year. The 5-year survival for localized brain and other nervous system cancers is 36.3%. Brain cancers account for 2.6% of all cancer deaths. Sixty per-cent of all primary brain tumors are glial tumors and two-thirds of these are clinically aggressive, high grade tumors.

Indications of radiotherapy are High Grade Gliomas, Residual disease, Recurrent disease and Benign Tumors. If we talk about examples of high grade tumors here are some of them: Anaplastic astrocytoma (grade III), Glioblastoma (grade IV), Papillary tumor of pineal region Moderately differentiated parenchymal pineal tumor (grade III), Pineoblastoma (grade IV).

There are many kinds of benign brain tumors, here are some examples, in particular: Meningioma, Pituitary tumors, Craniopharyngioma, Hemangioblastoma and Hemangiopericytoma, Glomus Jugular Tumor, Pineocytoma, Chordoma, Vestibular Schwannoma, Ganglioglioma, Central neurocytoma.

Types of radiotherapy techniques include Conventional 2D approach, 3 dimensional conformal radiotherapy (3DCRT), Stereotactic Radiosurgery and stereotactic Radiotherapy, Brachytherapy and Proton Beam Therapy.

Two Dimensional planning for Brain Tumors include, firstly contouring target outlines, then place a field, Immobilization, particularly: head rest, thermoplastic mask and base plate.

Disadvantages of conventional planning: Irradiation of large volumes of brain with normal tissue also, Higher toxicity and side effects, Lack of 3D visualization of tumors and 2D planning of 3D tumors.

Taking planning CT slices in Neurooncology: Different from diagnostic imaging, Use appropriate immobilization device, Image the patient in treatment position.

Planning MRI includes following steps: Position ideally in treatment position with orfit & base plate, Transfer images to planning system. Imaging: CT, CT-MR Fusion and PET Scan – limited but emerging role.

Advantages of 3D planning are that it is ideal for all cases, it is also conformal, it has capability of maximum sparing of normal tissue and lower toxicity.

There are some advantages of SRS and SRT over 3DCRT for example: High conformity, To treat small lesions not amenable to 3D CRT, Higher tumor dose, Save larger amount of normal tissue.

Indications for SRS are benign and malignant brain tumors, arteriovenous malformations and well circumscribed targets in a size less than 4 cm in diameter. Indications for SRT are lesions more than 4 cm in size and lesions located near critical structures.

Radiation therapy includes stereotactic radiotherapy that also includes the following: Gamma Knife, LINAC based and Cyberknife. Gamma knife is designed to provide an overall treatment accuracy of 0.3 mm. Gamma knife has three main components, Spherical source housing, 4 types of collimator helmets and Couch with electronic controls.

Proton Beam Therapy is used for Low grade & High grade glioma, Benign brain tumors: Vestibular Schwannomas/Acoustic Neuromas, Meningioma, pituitary adenoma, AVM, Skull base tumors: chordoma/Chondrosarcomas, pediatric brain tumors: Medulloblastoma, Germ cell tumors.

To sum it up, multiple options and techniques are available for treating brain tumors. Need to use the optimum technique, decision to be based on need of patient and available technique.

NSAIDs Attenuate TRP Channels Activated by their Agonists

Ivliane Nozadze, Merab Tsagareli

Abstract

Background. The transient receptor potential (TRP) cation channels have been extensively investigated in the transduction of thermal, mechanical, and chemical stimuli underlying the somatic sensation. These channels are the largest group of sensory detector proteins expressed in nerve terminals and pain receptors and are activated by temperature and chemicals that elicit hot or cold sensations. Chemical stimuli include menthol, cinnamaldehyde (CA), gingerol, capsaicin (CAPS), allyl isothiocyanate (AITC) (a natural compound of mustard oil), camphor, eugenol, and others. The thermal thresholds of many TRP channels are known to be modulated by extracellular mediators and released by tissue damage or inflammation, such as bradykinin, prostaglandins, and growth factors. Antagonists of these channels are likely promising targets for new analgesic drugs at the peripheral and central levels.

Aims. Because some non-steroidal anti-inflammatory drugs (NSAIDs) are structural analogs of prostaglandins, here we examined three widely used NSAIDs (diclofenac, ketorolac, and lornoxicam) on the activation of TRPA1 and TRPV1 channels by their agonists CA, AITC, and CAPS, respectively.

Material and Methods. We measured nociceptive thermal paw withdrawal latencies and mechanical thresholds bilaterally in male rats at various time points following intraplantar injection of CA, AITC, CAPS, producing thermal hyperalgesia and mechanical allodynia, and of NSAIDs and TRP channels antagonists.

Results. We found that intraplantar injection CA, AITC, and CAPS significantly decreased the latency of the thermal withdrawal reflex (thermal hyperalgesia) compared to vehicle or the contralateral hindpaw. The same findings were observed for the paw withdrawal threshold (mechanical allodynia) and hence resulted in the facilitation of these defenses reflexes. In approximately two hours the effects of CA, AITC, and CAPS returned to baseline. Pretreatment with all three NSAIDs in the ipsilateral (injected) hindpaw produced a significant reduction of sensitivity to pain (antinociception). In other experiments, when pretreated with the TRPA1 antagonist (HC-030031) we found a significant attenuation of thermal hyperalgesia and mechanical allodynia evoked by CA and AITC. In the second session, pretreatment with the TRPV1 antagonist (AMG-517) produced a significant reduction of these pain behavior responses.

Conclusion. Our data clearly show that noxious chemical irritants (CA, AITC, CAPS) eliciting thermal hyperalgesia and mechanical allodynia are mediated via the activation of TRPA1 and TRPV1 cation channels. We suggest that our study indicates a novel mechanism involving the anti-inflammatory and analgesic effects of NSAIDs, which may be involved in direct inactivation or desensitization of TRPA1 and TRPV1 channels and could be used therapeutically for pain treatment.

Acknowledgment. The work was supported partially by the grant from Shota Rustaveli National Science Foundation of Georgia (SRNSF) (grant #31-40).

Ultrasound in Diagnosis of Pulmonary Congestion in Patients with Heart Failure.

M Tsverava, D Tsverava

Abstract

Pulmonary congestion and Oedema is useful marker of HF, but its diagnosis is chalenging. The aim of this study was to determine the place of pulmonary ultrasound in patients with DHF.

Objective: To find Sonographic changes of lung in patients with Congestive Heart Failure, and to find Sonographic signs of pulmonary edema and congestion in patients with Congestive Heart Failure.

Material and Method: We studied 280 patients with heart diseases who had different grade CHF (100 – female, 180 – male; mean age 62,6±9,7 year). A control group: 80 normal persons, patients with arterial hypertension or stable angina (32 – female, 48 – male; mean age 63,6±9,8 year), who had no signs of heart failure. No one in HF or control group had any signs of pulmonary diseases and became any treatment before examination. The transthoracic ultrasound examination was performed with 3 – 3,5 MHz sector and 3,5 – 4 MHz convex transducer. The patients were examined in vertical (seated) or horizontal (lying) position, from 10 points of thoracic wall which corresponded to the projection of lower, middle and upper lobes of a right lung and upper and lower lobes of left lung.

Results: The normal ultrasound lung pattern is characte-rized by, parallel lines or there are irregular reflections on screen. In patients with CHF we significantly often found the one of the sorts of reverberation phenomenon - "Comet tail Phenomenon" (CTPh) (97,5% versus 41,25% in control, p<0,005). The comet-tail phenomenon was defined as a hyper-echogenic narrow-based reverberation type of artifact, spreading from the visceral pleura to the distal edge of the screen . In patients with CHF we significantly often found the one of the sorts of reverberation phenomenon - "Comet tail Phenomenon" (CTPh) (97,5% versus 41,25% in control, p<0,005). The comet-tail phenomenon was defined as a hyper-echogenic narrow-based reverberation type of artifact, spreading from the visceral pleura to the distal edge of the screen.

Conclusion: Thoracic US is sensitive and accurate method for evaluation pulmonary congestion/oedema in patients with CHF. The US sign of pulmonary congestion in HF is a "Comet tail phenomenon", which is protracted, prominent, multiple and registered from larger area of thoracic wall (4 points or more).

QT Prolongation after PVCs – New Diagnostic Criteria for Long QT Syndrome or for Lifethreatening Arrhythmia

Khatuna Jalabadze, pavle Machavariani, Anzor Melia, Ia Avaliani, Kakha Etsadashvili

Abstract

Background: Long QT Syndrome (LQTS) is a congenital or acquired disorder of cardiac ion channels resulted in disturbances of myocardial repolarization. The diagnosis is usually based on QT prolongation >460msec in respect of 12-lead ECGs, or in the presence of a confirmed LQTS mutation. QT interval prolongation >480msec is highly diagnostic, but there are several limitations and difficulties to make diagnosis: QT measurement accuracy, QT behavior during different HR, age and gender, or genotype.

Aim: On the basis of two consequent patients, we found that prominent QT prolongation after Premature Ventricular Contraction (PVC) might be one of the powerful criteria to suspect LQTS or life-threatening arrhythmia. The interesting finding of their ECGs was the QT prolongation only after the ventricular ectopic beats. While reported QTc was 430msec, QT interval followed the first sinus beat after PVC ranging from 520 to 600msec. Both of them were admitted in clinic with life-threatening arrhythmias. Later, one of them was diagnosed with congenital and another with acquired LQTS.

Methods: we studied QT interval behavior after PVC in three prespecified subgroups that included (1) electrocardiographically affected LQTS subjects (QTc ≥480 ms) – 7patients, (2) unaffected,otherwise healthy subjects (QTc<460 ms) – 23 patients and compared with third group including 2 of index patients. 24-hour-ECG records were analyzed. QT corrected was calculated by Bazet's Formula.

Results: Mean QT interval after PVCs was 490msec in the first and 500msec in the second group, consequently, differently from the third (index) group, where QT interval after PVCs prolonged up to 600msec.

Conclusion:QT prolongation following premature ventricular beat (PVB) is a known finding but not fully investigated. The knowledge related to this phenomenon is based on the small studies or observations and particular cases. Our study shows that QT prolongation just after PVCs might be one of the strong markers to reveal QT abnormality leading to malignant arrhythmias due to congenital or acquired disorder of cardiac ion-channels.

Patient Centered Care Pathways – More Involvement of the Patients – Better Patient Care?

Kaasa Stein

Abstract

Prof. Kaasa is Head of Department of Oncology at Oslo University Hospital, Professor of Palliative Medicine at the Institute of Clinical Medicine, University of Oslo and Director of the European Palliative Care Research Centre.

Introduction

Cancer is a major public health and economic issue, and the burden it imposes is set to exponentially increase. There were over 19 million cases in 2020, and we can expect 29 million cases by 2040 due to population growth and aging. In 2020, cancer was the second leading cause of death globally, accounting for an estimated 10 million deaths. About half of the cancer patients survived. Lung, prostate, colorectal, stomach and liver cancer are the most common types of cancer in men, while breast, colorectal, lung, cervical and thyroid cancer are the most common among women. Thanks to innovative technologies for early detection and early prevention, as well as new therapies for more effective anticancer treatments, the death toll will most likely not increase proportionally. Instead, with these advances, higher cure rates and more patients living longer with cancer, the importance of supportive, palliative, survivorship and end-of-life care for cancer patients will increase.

The MyPath consortium is funded by EU for five years starting 010922. The consortium consists of fourteen partners, including nine centers, two companies and three professional and patient organizations.

The Challenge: There is a need for a radically new approach to improved supportive, palliative, survivorship and end-of-life care of cancer patients that also benefits families, communities and health systems. Cancer care still has silos, and to this day, there is no technological support available that is suitable for different cultures, settings and environments. The 'holy grail' in cancer care is the delivery of patient-centred care, which is known to work best for every patient, with their increased involvement in care. As stated in a call for action put forth by the European Cancer Control Joint Action , the gold standard of care consists of a combination of patient- and tumour-centred approaches. Several randomised controlled trials (RCTs) have provided evidence that the integration of patient-centred care in standard oncology care results in better patient and caregiver outcomes. Such care results in reduced symptom burden, better symptom management, increased patient and caregiver satisfaction with care, less psychological distress and better quality of life, and it is thought to prolong patients' survival.

The Solution: MyPath combines novel patient-centred care pathways (PCCPs), patient-reported outcome measures (PROMs), patient-reported experience measures (PREMs) and treatment decision support incorporated in a user-friendly digital platform. MyPath will be integrated in routine cancer care, and its implementation in 9 cancer centres in Europe will be formally studied to prove its effectiveness and sustainability.

The electronic PROMs and PREMs of Eir, a platform developed to improve the process of recording patient outcomes, will be improved in MyPath. New features will be made available in the project along with treatment decision support, and MyPath will be configured on the eHealth platform of our SME partner, Imatis.

We will implement MyPath using an implementation science methodology, with the aim of establishing integrated and efficient patient-centred care that is respectful of, and responsive to, individual patient preferences, needs and values.