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Wei-Chih Liao is clinical assistant professor and attending physician of Department of Internal Medicine of the National Taiwan University Hospital in Taipei, Taiwan. He received his MD degree from College of Medicine, National Taiwan University, and is a PhD candidate of College of Public Health, National Taiwan University.

Dr. Liao’s main research interests focus on interventional endoscopy and clinical and epidemiologic research for pancreato-biliary diseases. He has published a series of studies investigating the optimal endoscopic treatment for bile duct stones and technical advances to reduce its complication and failure rate. In the field of pancreatic cancer, he has also published studies on potential diagnostic and prognostic biomarkers and on methods for prognosis prediction and treatment selection.

Dr. Liao also actively engages in activities of related societies and journals. He is the reviewer of several international journals, including Annals of Internal Medicine, Gastrointestinal Endoscopy (Outstanding Reviewer 2012-2013), PLOS ONE, and so on. In addition to participation in local societies, he is also an active member of the American Society for Gastrointestinal Endoscopy (ASGE), and has been selected by ASGE as an Ambassador for the ASGE Ambassador Program.
Adjuvant treatments for resected pancreatic adenocarcinoma: a systematic review and network meta-analysis

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Lancet Oncol (Published online Sep. 12, 2013. http://dx.doi.org/10.1016/S1470-2045(13)70388-7)

Great controversies exist regarding the optimal therapy after resection of pancreatic adenocarcinoma (PAC). Previous trials evaluating adjuvant 5-FU and gemcitabine yielded contradictory results, and whether chemoradiation should be given is highly debated. Because of differences in outcome measures and patient mix, synthesis of evidence on this issue is challenging and only narrative reviews are available, thus the controversies remain. To identify the optimal adjuvant therapy, we overcame the above difficulties and conducted a random-effects network meta-analysis to compare the major adjuvant therapies (fluorouracil, gemcitabine, chemoradiation, chemoradiation plus fluorouracil, and chemoradiation plus gemcitabine) in terms of overall survival and toxicities. Compared with observation, the hazard ratios (HRs) (95% credible intervals) for death was 0.62 (0.42–0.88) with fluorouracil, 0.68 (0.44–1.07) with gemcitabine, 0.91 (0.55–1.46) with chemoradiation, 0.54 (0.15–1.80) with chemoradiation plus fluorouracil, and 0.44 (0.10–1.81) with chemoradiation plus gemcitabine. We further noted that the percentage of patients with positive lymph nodes was inversely associated with the survival benefit of adjuvant therapies. After adjustment for this factor, 5-FU [HR 0.65 (0.49–0.84)] and gemcitabine [HR 0.59 (0.41–0.83)] improved survival compared with observation, whereas chemoradiation resulted in worse survival than 5-FU [HR 1.69 (1.12–2.54)] or gemcitabine [HR 1.86 (1.04–3.23)]. In terms of toxicity, chemoradiation plus gemcitabine was ranked the most toxic, with significantly higher hematologic toxicity than second-ranked chemoradiation plus 5-fluorouracil [odds ratio 13.33 (1.01–169.36)].

This meta-analysis reveals that chemotherapy with fluorouracil or gemcitabine is the optimal adjuvant therapy for PAC and reduces mortality after surgery by approximately one-third. By contrast, adjuvant chemoradiation plus chemotherapy is less effective in prolonging survival and more toxic than chemotherapy.

Extended Readings

2. Lancet Oncol (http://dx.doi.org/10.1016/S1470-2045(13)70403-0). Bayesian analysis unravels pancreas-cancer adjuvant therapy.
Study Highlights

What Is Current Knowledge

- Major adjuvant therapies for pancreatic adenocarcinoma include fluorouracil, gemcitabine, chemoradiation, chemoradiation plus fluorouracil, and chemoradiation plus gemcitabine. The optimum treatment remains controversial.
- Adjuvant fluorouracil significantly improved survival after surgery in ESPAC 1 trial, but trials evaluating gemcitabine, which is superior to fluorouracil in inoperable pancreatic adenocarcinoma, observed only non-significant benefit.
- Adjuvant chemoradiation is the standard of care in the USA, but it is considered harmful and infrequently used in Europe and UK.

What Is New Here

- Chemotherapy with fluorouracil or gemcitabine is the optimum adjuvant treatment and reduces mortality after resection by about a third.
- Chemoradiation alone has little benefit.
- Adding chemoradiation to chemotherapy provides little further survival benefit, but increases toxic effects.
- Lymph node positivity negatively affects the survival benefit of adjuvant treatments.

Extended Readings

2. Lancet Oncol (http://dx.doi.org/10.1016/S1470-2045(13)70403-0). Bayesian analysis unravels pancreas-cancer adjuvant therapy.
Dr. Lih-Chu Chiou is a professor at Department of Pharmacology, College of Medicine, National Taiwan University (NTU). After graduated from School of Pharmacy at NTU, she was enrolled in the Graduate Institute of Pharmacology at NTU and advised by Prof. Chuan-Chiung Chang. She was trained as an electrophysiologist specialized in neuroscience. After receiving her PhD degree and being promoted to associate professor, she was awarded by National Science Council (NSC) for an overseas study for 1 year at University of Texas Medical Branch, Galveston, USA, where she learned the brain slice patch clamp recording technique. In October 1995, she came back to NTU and established her laboratory specialized in brain slice electrophysiology.

Dr. Chiou has been granted by National Health Research Institutes (NHRI) continuously for 10 years since 2000, accompanied with the third time NHRI award currently, as well as by NSC yearly. Her research mainly focused on two neuropeptides systems, nociceptin/orphanin FQ (N/OFQ) and orexins. Her lab has participated in the development of novel ligands of N/OFQ receptors, a novel opioid receptor family, by characterizing their pharmacological properties in brain slices containing the periaqueductal gray (PAG), a midbrain area for initiating descending pain inhibition. They also elucidated the clinical implications of these two novel neuropeptide systems in neurological and psychiatrically disorders, including neuropathic pain, migraine, addiction, Tourette syndrome, schizophrenia, ADHD, depression and asthma, through establishing animal models and measuring patients’ plasma neuropeptide levels via close collaborations with clinicians.

Their lab's achievements in the field have rendered Dr. Chiou receiving awards and speech invitations at several international conferences, such as 3rd EPHAR (Lyon, France), XIV IUPHAR (San Francisco, USA), 80th JPS (Nagoya, Japan) and 2013 Gordon Conference, as well as invitations for writing review articles for prestigious journals, such as Eur J Neurosci, and reviewing international grants (National Medical Research Council Singapore, and Asthma UK). Dr. Chiou also serves as an ad hoc journal reviewer for several high impact international journals, such as Biochem Pharmacol, Brit J Pharmacol, Intens Care Med, Int J Neuropsychopharmacol, J Neurosci, J Nucl Med, J Pharmacol Exp Ther, Med Res Rev, Mol Pharmacol and Neuropharmacology. Dr. Chiou is an active member of the Society for Neuroscience and the International Narcotics Research Conference (INRC). She is an executive committee member of INRC, one of the three representatives for the Rest of World, except North America and Europe.
Hypofunction of glutamatergic neurotransmission in the periaqueductal gray contributes to nerve injury-induced neuropathic pain

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Neuropathic pain, a chronic pain due to neuronal lesion, remains unaltered even after the injury-induced spinal afferent discharges have declined, suggesting an involvement of supraspinal dysfunction. The midbrain ventrolateral periaqueductal gray (vlPAG) is a crucial supraspinal region for initiating descending pain inhibition while its role in neuropathic pain remains unclear. Therefore, we examined neuroplastic changes in the vlPAG of midbrain slices isolated from neuropathic rats induced by L5/L6 spinal nerve ligation (SNL) via electrophysiological, and neurochemical approaches. Significant mechanical hypersensitivity was induced in rats 2 days after SNL and lasted for more than 14 days. As compared with the sham-operated group, vlPAG slices from neuropathic rats 3 (NP3) and 10 (NP10) days after SNL displayed smaller excitatory post-synaptic currents (EPSCs) with prolonged latency, less frequent and smaller miniature EPSCs, higher paired-pulse ratio of EPSCs, smaller AMPA receptor (AMPAR)-mediated EPSCs (EPSCAMPAs), smaller AMPA currents, greater NMDA receptor (NMDAR)-mediated EPSCs (EPSCNMDAs), greater NMDA currents, lower EPSCAMPAs/EPSCNMDAs ratios and up-regulation of NR1 and NR2B, but not NR2A, GluR1 or GluR2, subunits of glutamate receptors. There were no significant differences between NP3 and NP10 groups. These results suggest that SNL leads to hypo-glutamatergic neurotransmission in the vlPAG, resulting from both pre-synaptic and post-synaptic mechanisms. Up-regulation of NMDARs might contribute to hypofunction of AMPARs via subcellular redistribution. Long-term hypo-glutamatergic function in the vlPAG may lead to persistent reduction of descending pain inhibition, resulting in chronic neuropathic pain.
Study Highlights

What Is Current Knowledge

- Neuropathic pain, with the prevalence of 6-8%, is one of the leading causes of intractable chronic pain. To explore the neuropathic mechanisms of neuropathic pain is helpful for the development of an effective therapy strategy which is an unmet clinical need.
- Both peripheral and central sensitizations have been proposed to be the mechanisms of neuropathic pain. Peripheral ectopic discharges occurred soon after nerve lesion but subsided gradually over time. Therefore, additional central mechanisms should play a role for maintaining the long-lasting neuropathic pain.
- Increased descending pain facilitation arising from the supraspinal nuclei, including rostral ventral medulla (RVM) and anterior cingular cortex, has been reported in neuropathic animals. In contrast, decreasing descending pain inhibition could be also the cause of neuropathic pain though not yet reported.
- The periaqueductal gray (PAG) is a crucial midbrain region for initiating descending pain inhibition. It integrates inputs from a variety of higher centers, such as the hypothalamus and amygdala, and sends excitatory outputs to the RVM that sends inhibitory outputs to the spinal dorsal horn, forming the PAG-RVM-spinal descending pain inhibitory pathway.

What Is New Here

- Here, we for the first time revealed hypofunction of glutamatergic transmission in the PAG, which may lead to decreased descending pain inhibition and contribute to the development and maintenance of neuropathic pain, in rats receiving spinal nerve ligation.
- Hypo-glutamatergic activity in the neuropathic group is mediated by both presynaptic and postsynaptic mechanisms, including decreased glutamate release, smaller AMPAR-mediate response, larger NMDAR-mediated response and lower excitability of PAG neurons.
- The neuropathic group exhibited upregulation of NR1 and NR2B subunits of NMDARs but no change in GluR1 and GluR2 subunits of AMPARs.
- Unilateral peripheral injury induced bilateral changes in the PAG.

Extended Readings

4. Science Signaling 2013; 6:ra34. An increase in synaptic NMDA receptors in the insular cortex contributes to neuropathic pain.
Awards

恭喜 本院醫學工程學研究所林峰輝教授榮獲財團法人徐有庠先生紀念基金會第11屆有庠科技講座生技醫藥類獎

恭喜 本院解剖學暨細胞生物學科謝松蒼教授榮獲財團法人徐有庠先生紀念基金會第11屆有庠傑出教授獎醫療技術類

恭喜 本院社會醫學科陳彥元助理教授、耳鼻喉科楊宗霖副教授、內科劉志銘醫師榮獲102年度吳大猷先生紀念獎