愛媛医学 第 29 巻 4 号(平成 22 年 12 月 1 日発刊)

トピックス

オステオポンチン蛋白多型と自己免疫疾患感受性、そのメカニズムを探る

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愛媛医学 29(4):189-192, 2010

心配停止後症候群ー自己心拍再開後の集学的治療への新しい潮流ー

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愛媛医学 29(4):193-199,2010

原著

転移性腎癌に対するスニチニブの使用経験

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愛媛医学 29(4):200-203,2010

Summary

Cytokines have traditionally been the frontline drugs. Recent advances in understanding the molecular biology of renal cell carcinoma (RCC) have led to the development of several targeted agents that show impressive antitumor efficacy. The integration of these drugs into clinical practice has revolutionized the therapeutic management of RCC. Sunitinib is an oral multi-kinase inhibitor that blocks the vascular endothelial growth factor receptor, platelet-derived growth factor receptors alpha and beta, c-kit, and other receptors. Retrospective reviews of metastatic RCC patients with sunitinib therapy in our hospital were performed. At the start, sunitinib was orally administered in 50 mg doses for 11 patients and 25 mg doses for 4 patients, in repeated 6-week cycles (4 weeks on treatment, 2 weeks off). However, the treatment was interrupted during the 4-week treatment due to incidences of severe adverse events. The most common treatment-related grade 3 / 4 adverse events were a decreased platelet count and febrile infection. No patients showed an objective response clinically. Therefore, the starting dose or treatment schedule is now modulated by the patient's age, gender, or build to gain better compliance, although further studies are required to confirm its clinical effectiveness.

Key Words: metastatic renal cancers, sunitinib, adverse events

A study on the cardiac autonomic nerve domination in tachycardia state

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愛媛医学 29(4):204-211, 2010

要旨

頻脈発作中の心臓自律神経活性を知ることは、薬物治療による発作の制御に重要な手掛かりを与えてくれる。しかしながら臨床上これを評価することは容易ではない。線形スペクトル解析は複雑な計算が必要であり、CVRRは

副交感神経のみの情報しか得られず、不整脈に対しては評価が出来ない。幾何学的非線形モデルの一つであるLorenz plotは視覚的に発作の状態を捉えることが出来る上に、比較的簡単な計算により交感・副交感の自律神経活性を個々に評価することが出来る有用な方法である。筆者はこれを用いて正常洞調律(NSR)、洞性頻脈(ST)、発作性上室性頻脈(PSVT)、頻脈性心房細動(AF)の分析を行い、それぞれの自律神経支配を明らかにした。さらに心房細動における心室波形(R波)の出現頻度と心臓自律神経活性(CANA)との相関を求め、R波出現頻度(OFR)を目的変数とし自律神経活性を説明変数とする重回帰分析によってR波出現頻度の予測式を求めることが出来たので以下に報告する。

Key Words: CANA(cardiac autonomic nerve activity), Tachycardia, OFR(Onset frequency of R wave)

Ⅱ型肺胞上皮細胞の酸化ストレス障害に対する麻酔薬プロポフォールの保護作用

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愛媛医学 29(4):212-220,2010

Summary

Supplemental oxygen is commonly used for critically ill patients. However, prolonged exposure to hyperoxia may cause lung injury. Excess epithelial cell death via reactive oxygen species (ROS) promotes pulmonary fibrosis, because proliferation and differentiation of alveolar epithelial type II (AT II) cells play important roles in lung homeostasis and remodeling after injury. From the point of view of hyperoxiainduced lung injury during anesthesia, we examined that propofo (I 2, 6-diisopropylphenol), the widely used intravenous anesthetic, would prevent oxidative cell damage on primary cultured AT II cells.

Methods: Oxidative damage in AT II cells was introduced by hydrogen peroxide (H2O2). Cell viability of AT II cells treated with propofol $(0.01\sim1,000~\mu\text{M})$ and followed by H2O(2 1.0 mM), was evaluated by the cell proliferation assay. Immunostainings of AT II cells treated with propofol $(10~\mu\text{M})$ and H2O2(0.5 mM) were performed to detect oxidative DNA damage and morphological changes.

Results : Propofol at concentrations of 30 and 100 μ M attenuated oxidative damage in the cell viability assay. Immunostaining showed that propofol (10 μ M) improved the oxidative DNA damage of ATI cells.

Conclusions : Our results suggest that propofol (10-100 µM) can exhibit a potential effect as an antioxidant for hyperoxia-induced lung injury during anesthesia.

Key Words: propofol, alveolar epithelial type II cells (AT II cells), hyperoxia-induced lung injury

ラット小脳の生後発生におけるプロサポシンの細胞内局在とmRNAの発現

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Summary

Prosaposin is the precursor protein of four glycoproteins called saposin A, B, C and D, which activate sphingolipid hydrolases in lysosomes. In addition to its role as a precursor of saposins in lysosomes, unprocessed prosaposin functions as a neurotrophic factor in the central and peripheral nervous systems by acting to prevent neuronal apoptosis, to elongate neurites, and to facilitate myelination. In the present study, we examined the chronological changes of prosaposin immunoreactivity and mRNA expression in the rat cerebellum by triple fluorescent immunostaining and in situ hybridization at day 7, 28 and 56. Although the prosaposin immunoreactivity in the

Purkinje cells was strongest on day 56, the expression of Pro+9 mRNA, the long-9 base secretion type of prosaposin, increased at 28 days and decreased at day 56 to the same level as the seventh day. Prosaposin immunoreactivity is very strong in the neuronal cell body, but the binding sites of prosaposin are stronger in the dendrite or neuropile. These results indicate that prosaposin plays an important role not only in the development but also in the maintenance of the adult neuronal network.

Key Words: prosaposin, development, Purkinje cell

総説

抗ラット好中球モノクロナール抗体Urge-8の急性炎症ならびに虚血再灌流障害に対する保護効果

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愛媛医学 29(4):228-234,2010

Summary

Neutrophil activation initiates ischemia-reperfusion (I/R) injuries. This study is performed in order to evaluate the in vitro functions of our anti-neutrophil monoclonal antibody, "Urge-8", and its therapeutic efficacy against several acute inflammatory models in rats (such as acute lung injury model, and acute necrotizing pancreatitis model) as well as several I/R injury models in rat (such as hepatic I/R injury model, myocardial I/R injury model, and gut I/R injury model). The group treated intravenously with Urge-8 showed a lower grade of several pathological injuries (such as lung, liver, heart, and as well as intestinal mucosa), suggesting that the Urge-8 is effective against acute inflammatory, models and several I/R injury models because it suppresses neutrophil functions. Our anti-neutrophil monoclonal antibody, "Urge-8", helps acute inflammatory models and prevents I/R Injuries by suppressing neutrophil functions.

Key Words: anti-neutrophil antibody therapy, ischemia / reperfusion injury, Urge - 8

研究会抄録

第 44 回愛媛臨床血液懇話会

愛媛医学 29(4):235-236,2010

第 121 回愛媛整形外科集談会

愛媛医学 29(4):237-240,2010

第 11 回愛媛 NST(栄養サポートチーム)研究会

愛媛医学 29(4):241-242,2010