狗肺靜脈袖套管之電生理特性研究

Electrophysiological characterization of myocardial sleeves in canine pulmonary vein

中文摘要

研究指出肺靜脈袖套管中的心肌組織可能是異位性放電點的來源，並認爲肺靜脈袖套管可能會引發異位性心房纖維震顫。然而，肺靜脈袖套管是否含有節律性細胞仍不確定，心房心律不整到底由何處所引發的，還有很大的爭議，目前在動物的肺靜脈袖套管之心肌細胞的電生理研究上，並無一致的結果。肺靜脈袖套管是否會有自發性的動作電位產生，而成爲異位性放電點，進而造成陣發性心房纖維震顫，仍需要再進一步探討。

在本次的研究中，利用傳統玻璃微電極紀錄法，記錄 150 隻狗的肺靜脈袖套管心肌細胞的動作電位。了解狗的肺靜脈袖套管細胞在不同的生理、病態狀況及抗心律不整藥物下的電生理變化。

在 150 隻正常健康的狗中，觀察到肺靜脈袖套管的動作電位都是快速反應的，並沒有自發性節律的活動，也沒有早期性或是延遲性後去極化現象產生。

Quinidine 及 d-sotalol 會使膜電位去極化並延長動作電位 90% 間期（APD90）。Nisoldipine 及 ACh 會縮短動作電位間期。4-AP 及 isoproterenol 也會縮短 APD90，但是卻會增加動作電位第 2 期。這些藥物的作用在狗的左心房及肺靜脈袖套管中都相同。Adenosine 使狗的肺靜脈袖套管及左心房細胞動作電位的縮短不明顯，但是卻可以明顯的縮短天竺鼠心房細胞的動作電位。

在 1 mM isoporterenol中，變換刺激的頻率從 0.5 到 1 Hz，或是停止 10 mM ACh 的給予，或是加入 8 mM 的鉀離子，可以引發彈回現象，產生一短暫性的誘發性動作電位。

在停止灌流或是模擬缺氧的情況下，靜止膜電位及最大去極化速度會減少，動作電位間期及振幅也會縮短，但是無法產生誘發性節律。低溫（20-22℃）則會造成動作電位間期的延長及再極化的現象產生。

狗的肺靜脈袖套管在 0.1 mM 的鋇離子濃度下，只會造成舒張期去極化，但是並不會引發自發性節律，而舒張期去極化的現象可以被 cesium 所抑制。在 1 mM 的鋇離子中，會使 22 隻狗的肺靜脈袖套管引發舒張期去極化及自發性節律的產生，但是在 11 隻狗中，只有引發 3 隻狗的左心房細胞產生自發性節律。在 1 mM 鋇離子中，nickel 只能輕微的抑制舒張期去極化的現象，但是 cadmium 及 verapamil 卻可以完全抑制自發性節律的現象。在含有鋇離子及 isoproterenol 中，停止給予 ACh，同樣也可以引發彈回現象的產生。在鋇離子引發的自發性節律中，ryanodine（2 mM）在初期加入時，會使自發性活動產生短暫性的增加，之後則會造成很明顯的抑制。

在正常生理狀況下，狗的肺靜脈袖套管心肌細胞並不會有不正常的節律活動出

現，抗心律不整藥物在肺靜脈袖套管與左心房的作用相同。而在病態的情況下，則可以引發自發性及誘發性節律，這些引發的節律活動則是與細胞內鈣離子過多有關。而在鋇離子之下，狗的肺靜脈袖套管比左心房的心肌細胞較容易引發自發性節律。

英文摘要

Studies have implicated the myocardial tissue of pulmonary vein sleeves as a possible origin of ectopic impulses and serving as a source of ectopic foci in initiating atrial fibrillation in human. However, the existence of pacemaker cells within pulmonary vein sleeves was questioned, because the results of studies were controversial. The animal model for such focal atrial fibrillation was still lacking and cellular mechanism remained to be studied.

In the present study, the conventional glass microelectrode recording technique was used to record intracellular action potentials in canine pulmonary vein sleeves. The cellular electrophysiology under normal and pathological conditions, and drug effects were investigated in the pulmonary vein sleeves from 150 dogs.

In 150 normal healthy dogs, all pulmonary vein sleeves displayed fast-response action potentials. No spontaneous pacemaker activities, neither early nor delayed afterdepolarizations were observed.

Quinidine and d-sotalol depolarized the membrane potential and prolonged the action potential duration, especially in action potential duration at 90% repolarization(APD90). Nisoldipine and ACh shortened the action potential duration. 4-AP and isoproterenol shortened APD90, but increased the plateau duration. The pharmacological responses in the pulmonary vein sleeves were similar as in the left atrial cells. Adenosine shortened the APD90 slightly in canine sleeves and atrial cells, but shortened the APD90 significantly in guinea pig atrium.

In the presence of 1 mM isoporterenol, switching the stimuli frequency from 0.5 Hz to 1 Hz, or washing out of 10 mM ACh, or added 8 mM potassium, induced a rebound phenomenon, triggering a short period of spontaneous activity.

Under conditions, such as stopping flow, or conditions mimicking hypoxia, the resting membrane potential depolarized, upstroke velocity of the action potential decreased, and the APD shortened. Low temperature （20-22℃） repolarized the membrane potential and prolonged the APD.

0.1 mM barium could not induce spontaneous activity, it only depolarized the diastolic action potential, and cesium suppressed the diastolic slope. Diastolic depolarization and spontaneous activity could be induced by 1 mM barium in all the 22 pulmonary vein sleeves, but only in 3 of 11 left atria. In the presence of 1 mM barium, the diastolic slope was only slightly affected by nickel, but was significantly

suppressed by cadmium and verapamil. In the presence of barium and isoproterenol, wash-out of ACh induced a rebound activity. Ryanodine (2 mM) caused a transient increase, followed by a marked decrease of barium-induced automatic activity. The results indicated a lack of arrhythmogenic activity under normal physiological conditions in the canine pulmonary vein sleeves. The pharmacological responses were similar between the left atrium and pulmonary vein sleeves. Abnormal automaticity and triggered activity only occurred under pathological conditions. The automaticity involved intracellular calcium overload. Barium-induced automaticity was more easily induced in pulmonary vein sleeves than in the left atrium.