Course: Electrophysiology of Heart

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Lecture 5: Action potential of cardiac muscle -1

Hello everyone. So, today we will start our next topic that is action potential of cardiac muscle. Now the concepts which we will be covering in this the few electrophysiological terms action potential of both nodal tissue as well as the myocardial tissues. What are the phases of different action potentials of this tissues and ionic bases and also we will cover few of the clinical and the applied aspects. Now already since resting membrane potential has been discussed. So, just brief recap the basic electrophysiological terms polarization, depolarization, hyperpolarization and repolarization.

Now, polarized means when the state in which the membrane is totally polarized that means at rest there is no net flow of the charges the voltage across the membrane you would not be getting any deflections. The depolarization means the membrane potential becomes less negative and less negative that means it is moving towards the 0 than the resting membrane potential. Hyperpolarization means the membrane potential is more than the resting membrane potential that means RMP. And repolarization means again restoration of the normal polarization state of the membrane that means from the depolarized state to the resting state of the cell membrane.

Now when we talk about the action potential of heart mainly we talk about the cardiac muscle electrical activity. So, the ability to respond to a stimulus is known as excitability. The other term of this excitability is bathmotropism this is one of the feature of a cardiac cell. Now cardiac cell has got various types of action potentials generally we classify into two types of two broader types of action potentials one is fast and the other one is slow. These two type of action potentials are specifically seen in the specific muscle fibers of cardiac muscle.

For example, the fast action potential is usually seen in the myocardium that is atria and the ventricles and the purkinje fibers. The slow action potential is mainly seen in the nodal tissue or the pacemaker tissues like SN node and AV node. To be very specific when we talk about fast action potential the myocardium the in case of myocardium the

action the resting membrane potential will be generally minus 90 milli volt. And in case of purkinje fibers it is usually it ranges between minus 80 milli volt. So, myocardial fibers whether it is atria or ventricles or purkinje fibers usually the resting membrane potential is minus 90 milli volt.

In case of nodal tissue if we talk about nodal tissue which consist of SA node and AV node in case of SA node the resting membrane potential is minus 50 milli volt. And in case of AV node the resting membrane potential is minus 60 milli volt. Now, this also has got a range for example, in nodal tissue usually the resting membrane potential if it is asked in a range it is minus 65 milli volt to minus 40 milli volt this is the range. But if a specific answer is asked for what is the resting membrane potential of sinoatrial node SA node then it is minus 50 milli volt and AV node it is minus 60 milli volt. For myocardial tissue you have to remember it is usually minus 90 milli volt.

Now, we will see what are the fast action potential what is the basis of fast action potential and slow action potential. Now, usually fast action potential consist of 5 phases this is the minus 80 milli volt means the resting membrane potential the membrane potential at rest. So, this is the phase 4 usually the resting membrane potential from here there is a spike or there is an overshoot or there is an steep increase in the depolarization. You can see it is rising to plus 20 usually it rises to plus 35 milli volt because of the influx of the cations. So, this is known as the depolarization phase or phase 0.

So, we have phase 0 that is depolarization in case of fast action potential this depolarization is very steep. Then we have phase 1, phase 1 is the early repolarization or transient repolarization as you can see there is a slight decline or decrease in the potential from positive towards the negative side. So, there is an early or we call it as transient repolarization this is phase 1. Then we have the next phase that is phase 2 this is known as the plateau phase where you can see there is a stagnant maintenance of the resting membrane potential for certain time interval. So, this is phase 2 this is known as the plateau phase.

Then we have phase 3 where there is a rapid decline in the resting membrane potential or there is a resting membrane potential I mean towards the resting membrane potential the voltage gets declined. So, the membrane potential you can say this towards the resting membrane potential that means it is further getting negative from positive to negative that is repolarization or rapid repolarization. Usually we do not call it as complete repolarization we call it as rapid repolarization this is phase 3. And finally, we have the phase 4 which I had already mentioned this is phase 4 is usually RMP resting membrane potential. So, we have 5 phases 0 phase is the depolarization which is steep early repolarization or the transient repolarization.

Then the plateau phase then the rapid repolarization that is the third phase and the fourth phase is the resting membrane potential. So, this phases depends on the various conductance of the ions and the permeability of the ions. So, we will see what is the ionic basis of each phases. The when we plot this into x axis and y axis we have the time which is plotted again the membrane potential in milli volt. And we can see that this is the ventricular muscle action potential generally we see this is the resting membrane potential this is phase 0 this is phase 1 this is phase 2 this is phase 3 again this is phase 4.

So, we will see the first phase I mean the 0 phase why it is occurring. So, the rapid depolarization or the spike of the depolarization wave is mainly because of the influx of the sodium ions. The fast channel sodium ions open the characteristics of the sodium channels is these are definitely the voltage gated sodium channels. These sodium channels are voltage gated sodium channels which are opening very fast and these are fast in nature. How fast in nature? It takes 0.

1 millisecond to open this channels which means within this 0.1 milliseconds this many number of sodium channels will open to make this potential gets rise from minus 90 milli volt to plus 35 milli volt. So, this is fast sodium channels and the most important thing is the more fast it opens the more fast or rapidly it gets inactivated also. That means the channels will usually remain open for 1 to 2 milliseconds. The channels will remain open for 1 to 2 milliseconds after that this channels will get inactivated.

That is why I told you that the more rapid this sodium channels get open the more rapidly it gets closed also. And that is the only reason why this the potential the membrane voltage does not get rise till the equilibrium potential of sodium. Obviously the equilibrium potential of sodium is 60 plus 63 milli volt, but it does not get reach till plus 63 milli volt. Plus 63 milli volt means if the if this channels are remain open for a longer duration if there is no limit. So, what do you think how many sodium ions will enter or the sodium ions will enter for how much time.

Obviously the sodium ions will enter till there is an equilibrium between the extracellular fluid and the intracellular fluid. So, at this when the equilibrium will reached at this point if we measure the equilibrium potential or the potential difference across the membrane. So, we will get the equilibrium potential of sodium by calculating with the help of Nernst equation that is 63 milli volt. That is the plus 63 milli volt is the equilibrium potential or the Nernst potential of sodium. But usually the membrane voltage does not reach till plus 63 milli volt.

The only reason is because the sodium channels remain open for a very, very little

number of time that is 1 to 2 milliseconds. After that the sodium channels gets inactivated. So, it could only rise till plus 35 milli volt and this is the only reason once the sodium channels get inactivated it cannot be reopened. And you cannot get any new action potential generated at this stage. So, even if you give a stimulus you would not be getting any new action potential generated.

So, this is the basis of formation of absolute refractory period. Refractory means the cell is not acting to any stimulus. So, this refractory period is occurring absolute refractory period is occurring because of the inactivation of the sodium gates or the sodium channels. So, this is the first this is the 0 phase of the sodium channels. What you have to remember is the sodium channels are very fast their voltage get it sodium channels they only remain open for 1 to 2 milliseconds and then they get inactivated.

The next phase we will move on to the phase 1. After 0 phase the next phase is the phase 1 where there is a early repolarization. Now, this early repolarization is mainly because of the potassium efflux. Now, already the first point is potassium channels opening the opening of the potassium channels. Now, the very important question sometimes it is asked which potassium channels get opens the most important potassium channel is transient outward potassium channels.

Because this stays for a very limited time that is why the name is transient or early repolarization. So, potassium channels is opening means the potassium ions will move from inside to outside. So, there is efflux of the potassium ions. So, why the potential is decreasing there is efflux of the potassium ions as well as there is inactivation of sodium channels. There is inactivation of sodium channels or sodium gates as well as there is efflux of the potassium ions.

This is the two important reasons for this transient or early repolarization. Now, suppose there is only inactivation of sodium channels and there is no potassium efflux at that time this potential will not get decreased. So, it will remain stagnant. So, there has to be efflux of potassium ions the transient outward potassium channels opening there has to be efflux of potassium ions to get this phase 1. Now, coming to the next phase that is phase after phase 0 this is phase 0 this is phase 1 now the phase 2.

Phase 2 as I told you is the plateau phase. Phase 2 is the plateau phase. Plateau means there is something which is occurring in this phase where there is no net increase or decrease in the membrane potential occurring. So, why is it happening? So, there is simultaneous opening of the calcium channels.

The first one is calcium entry. Now, this calcium entry is occurring with the help of

voltage gated obviously, L type of calcium channels the voltage gated L type of calcium channels. So, this calcium channels gets influxed along with that the potassium channels are also present that means, the potassium efflux is also occurring. Now, potassium efflux as well as the voltage gated calcium channels there is a balance between the outward flow of the ions and inward flow of the ions which is causing or which is resulting in this plateau phase. So, this two reasons that is calcium permeability or calcium entry and the potassium efflux. So, this counter balance is maintained that is giving rise to the plateau phase of the or phase 2 of the ventricular or myocardial potential.

Now, coming to the phase 3. So, this phase 3 is mainly because of the rapid repolarization. Now rapid, why rapid repolarization is occurring? Now, rapid repolarization is occurring because at this stage at the onset of rapid repolarization we can write this onset of rapid repolarization the calcium permeability decreases. It is not that the calcium channels are totally closed, but the calcium permeability decreases compared to the potassium efflux. So, that is why the more potassium ions are getting out than the entry of the calcium ions, that is why this membrane voltage is decreasing or it is going towards the resting membrane potential. So, the calcium channels permeability or the calcium ions permeability is getting decreased.

The second thing is there is further opening of the potassium channels that means more potassium efflux is occurring. So, more potassium channels already I have told you there is in the phase 1 when there is early repolarization there was transient outward potassium channels. Here there is potassium rectifier potassium channels. So, this is K r also we have another channels that is potassium inward rectifier. So, these two type of channels are very important.

So, this is for further knowledge. So, these potassium channels also open. So, at the end of this stage the calcium channels at this stage the calcium channels will get closed there will be closure of the calcium channels and there will be total opening of the potassium channels. Potassium channels mainly the inward rectifier potassium channels which also remain open during the resting membrane potential or the phase 4. So, this is what we were talking about the phase 4 that is resting membrane potential which causes the restoration of the sodium and the potassium and the calcium ions whichever has occurred. Now, so this phase rapid repolarization is mainly because of the potassium efflux with the help of potassium inward rectifier channels and the stoppage of the calcium entry.

The final phase is the phase 4 that is resting membrane potential where it has to be maintained. Now, resting membrane potential means or the phase 4 means whatever

imbalance has occurred in this membrane in this action potential event. That means entry of sodium entry of calcium efflux of potassium this has to be restored. So, how this has to be restored? This is mainly done by two main pumps. The first pump is the sodium potassium ATPS pump.

This is the primary transport pump in our body. Now, this sodium potassium ATPS pump as you can see in the cell this is a cardiac cell it is throwing out 3 sodium outside and it will cause the 2 potassium ions inside. So, this sodium potassium ATPS pump along with another pump that is sodium calcium exchanger. Sodium calcium exchanger. Now this sodium calcium exchanger as the name suggests exchanger this is the antiport in our body.

This is antiport or we can also call as secondary transport pump. The primary transport pump is sodium potassium ATPS pump and sodium calcium exchanger is the antiport of the secondary active transport pump. Now, what happens whichever calciums or sodium has gone inside the cell I need to throw this sodium and calcium out of the cell and bring back the lost potassium. So, this is done mainly by this two pump. You can see the sodium is going outside and the potassium is taken inside.

Now, to make the calcium also outside the sodium potassium ATPS pump has to act. The sodium will enter inside the cell from outside and this sodium will again with the help of potassium ATPS pump will go outside. And in this way also the sodium calcium exchanger will act by throwing out the calcium outside. So, the secondary active transport or the sodium calcium exchanger is dependent on the sodium potassium ATPS pump or the primary transport. So, sodium calcium exchanger depends this is very important term depends on the primary active transport that is the sodium potassium ATPS pump.

So, sodium calcium exchanger will only be able to throw out the excess calcium when the sodium potassium ATPS pump is also acting. So, if I block this I mean this two pumps work in conjunction. So, if in any way if I block this sodium potassium ATPS pump suppose this pump is blocked. So, this pump will also not act because both are interdependent even if the sodium the primary active transport is not dependent, but the secondary active transport is dependent that is why the name is secondary. So, it is dependent on the primary active transport.

So, if the sodium calcium exchanger has to work the sodium the primary active transport pump that is sodium potassium ATPS pump has to work also. So, there is a drug which we use that is degoxing or the cardioglycosides or digitalis this usually block this sodium potassium ATPS pump. Now, when this drug will block the sodium

potassium ATPS pump obviously, this pump will not be working. Now, when the primary active pump is not working the secondary active pump will also not work that means, this cardiac cell will not be able to throw out the excess calcium. So, here the calcium will increase in the cell, when the calcium will get increase in the cell this cells will go into increased myocardial contractility the heart will pump more.

So, that is the basis or the corner store of the treatment for heart failure that means, in spite of blocking of the sodium potassium ATPS pump still this drug is able to increase the myocardial contractility. Because calcium is the ion which is very much essential for the contraction of the muscle. So, that is why in this way digitalis or degoxing which blocks the sodium potassium ATPS pump will increase the will increase the myocardial contractility. So, this is the basis of degoxing or the cardiac glycosides which increase the contractility of the heart. Now, we come to the pacemaker potential or the pre potential we have seen the curve of fast action potential.

The fast action potential curve is suppose this is resting membrane potential which is minus 90 milli volt. So, it is very steep and then it is decreasing. So, it has got usually 5 phases what are the phases 0 phase, 1 phase, 2 phase, 3 phase and 4 phase, fourth phase is the resting membrane potential. So, this is the curve of fast action potential or the action potential which is generated from a ventricular muscle myocardium. Now, we will see what is the action potential curve in case of nodal tissues.

So, nodal tissues has got this is as I told you a very unstable membrane potential, this ranges between minus 60 to minus 40 milli volt. If specific answer is asked SA node is minus 50 and AB node is minus 60 milli volt. So, due to this continuous change in membrane permeability what happens you can see this is the resting membrane potential. This resting membrane potential this is minus 60, this is not a constant line, this is not a straight line, this is a line which is constantly unstable you can see fluctuating.

That means, it is fluctuating between minus 60 to minus 40. So, that is what I told you pacemaker tissue or the nodal tissues is having unstable resting membrane potential, because there is a spontaneous change in the resting membrane potential of nodal tissue that is why it is called as pacemaker potential, pre or pre potential. So, you can see this is the resting membrane potential, this is equivalent to the phase 4. Then there is a gradual increase in the depolarization suppose it will rise to not plus 35 it will rise to say a bit lesser that is plus 10 milli volt. So, this depolarization phase is again 0 phase, then there will be rapid repolarization to the resting membrane potential with a slight hyper polarization. So, this phase is corresponding to your third phase or the repolarization phase of your fast action potential.

So, you can see there are only three phases in case of pacemaker potential or pre potential 0, 3 and 4. We do not have phase 1 and phase 2, this we do not have this two phases we do not have in nodal tissue, because to be very specific phase 1 is not there, because the channel proteins which is required for phase 1 that is not present in the nodal tissues which are present in the other myocardial tissues or the ventricular or the atrial muscle fibers. So, that is why the pacemaker potentials or the pre potentials are only having three phases that is 0 phase, the depolarization phase which is a gradual depolarization. Then we have a rapid repolarization phase which is again a bit gradual not steep and also we have the resting membrane potential that is the fourth phase. And in this way there is a continuous change in the membrane permeability, the ionic basis of the pre potential and the pacemaker potential will discuss in the other class.

So, till now what we have learned we have the five phases of fast action potentials and we have the slow action potential which is of three phases. The ionic basis of this two action potentials are entirely different, the fast action potential ionic basis is different that is mainly because of the sodium ion influx, the rapid depolarization is mainly because of the sodium ions. Compared to the slow action potential which we will see the ionic basis in the further class, till now we have to remember the sodium influx constitutes the main depolarization in the fast action potential. So, this is the main attribute of the fast action potential. So, with this I would like to conclude today's topic. Thank you.