Course: Electrophysiology of Heart

Professor: Dr. Arijita Banerjee

Department: Dr B.C.Roy Multi-speciality Medical Research Centre

Institute: IIT Kharagpur

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Lecture 16: Autonomic regulation of heart

Hello everyone. So, today we will start our next topic that is Autonomic Regulation. So, so far we had discussed all about the abnormalities we have seen in ECG. Today we will discuss about the autonomic pathway, what are the cardiac and the vascular receptors and how signal transduction occurs in this receptors that is the cardiac and the vascular signal transduction. Now, before moving on to the main topic we will discuss about this ECG, this is the patient which who has presented in an emergency with a severe chest pain for half an hour. So, what we see in this ECG, the first and foremost we should see about the sinus rate.

So, the rate is if you just calculate, so we have 1, 2, 3, 15 and 17, so 1500 by 17 it will be approximately 80 beats per minute, it will range between 80 75 to 80 beats per minute that is the rate. So, and then the rhythm, rhythm is usually what we are saying over here is regular. So, it is a regular rhythm, how we are getting the PQRS complexes. So, P wave is usually normal, we are having a P wave which is the P waves are usually normal, then the QRS complexes also we are getting within the normal range.

Now, if we see for the, we have to see for the T waves, for the T waves we can see T waves and ST changes, in we can see in the lead 1 there is ST segment elevation. So, in lead 1 we have seen ST segment elevations, we have to find out what where we have other ST segment elevations, we do not have in lead 2 and lead 3 AVR, we have in AVL ST segment elevations. T wave inversion is not yet, we can see T wave inversion also in case of AVL as well as very less T wave inversions we can see in lead 1, but in case of AVL we can see T wave inversion. So, lead 1 ST elevations AVL lead 1 and also we can see it in V 2, V 3 V 2, V 3, V 4, V 5, V 6. So, ST segment elevations we are getting from V 2 to V 6, which means the interior leads as well as the lateral leads with the lateral leads is 1 AVL and V 5, V 6 usually the lateral leads depict that.

And interior we have generally V 2, V 3, V 3 and V 4, but here V 2 is also affected, so interior and lateral portions we could see. And we have seen the T wave inversion in

case of AVL leads and we did not see any of other T wave inversions also some we have seen in case of V 4 leads T wave inversions. And also we could see few Q waves, we could see few Q waves in case of lead V 2 and V 3, we could see Q waves in case of lead V 2, V 3. So, we do not have any other Q waves, which I am not able to see right now, so ST segment elevations in case of lead 1 AVL, V 2 to V 6 with T wave inversion, I have seen in AVL T wave inversion is present. Q waves are seen in V 2 and V 3, so which means this is acute ST segment elevation is there, so definitely it is acute anterior leads as well as lateral leads.

So, it is acute enterolateral stemy or acute enterolateral ST elevated myocardial infarction, so this is the diagnosis of this patient with the presenting with such symptoms with severe chest pain as well as this ECG. . So, with this next we will move on to the autonomic nervous systems, now with the references or with the lectures, so far we have covered in abnormal ECGs. It is not very easy to become a pro in ECG unless and until you practice seeing the ECGs regularly. So, with if you just go through various ECGs regularly and with the concepts, then you could easily make out like what are the changes in the ECG very fast.

So, nervous system we have central nervous system, peripheral nervous system, central nervous system consists of brain and spinal cord. And peripheral nervous system we have autonomic nervous system, somatic nervous system through somatic nerves supply the skeletal muscles. And autonomic nervous system through autonomic nerves that is sympathetic nerves and parasympathetic nerves, they usually supply the various target organs like glands, cardiac muscles and we have various blood vessels, so these are the target organs. Now, what is the autonomic pathway, generally the autonomic pathway consists of two neurons and this neurons usually make a synapse in the autonomic ganglion. Now, the post ganglionic neurons the activity of the post ganglionic neurons is actually regulated by the pre ganglionic neurons, whose cell bodies are present in the central nervous system.

So, this is the pre ganglionic neuron, the cell bodies are present in the central nervous system, this is making an synapse that is autonomic ganglion. And from here the dendrites which we are getting that is post ganglionic neuron and this post ganglionic neuron is making the synapse with the target tissues, whichever target tissues like glands, cardiac muscles and the blood vessels. Now, this autonomic pathway the morphology is different in case of sympathetic nerve fibres and the parasympathetic nerve fibres. In case of sympathetic nerve fibres the pre ganglionic neurons are usually shorter, now before that I would like to say that all pre ganglionic neurons are cholinergic. You have to remember this that all pre ganglionic neurons are cholinergic that means, they secrete the acetylcholine.

And post ganglionic neurons depending on the nerve whether it is sympathetic or parasympathetic the neurotransmitter will be secreted. So, in case of sympathetic nerve fibres the cholinergic neuron, the pre ganglionic cholinergic neuron you can see this is very short. And the post ganglionic nerve fibres this is very long. So, sympathetic fibres have short pre ganglionic neuron and long post ganglionic neuron. The reverse is occurring in case of parasympathetic fibres we can see there is a long pre ganglionic neuron and there is a short post ganglionic neuron.

Now, the cholinergic nicotinic receptors the receptors for the acetylcholine that is nicotinic receptors and the muscarinic receptors. So, the nicotinic receptors are present in the autonomic ganglion here generally we get the N 2 nicotinic receptors N 1 receptors are present in the skeletal muscles. So, N 2 nicotinic receptors are present and the cholinergic muscarinic receptors obviously, in case of parasympathetic pathway the post ganglionic neurons will secrete acetylcholine. So, when it will secrete acetylcholine this usually bind to the muscarinic receptors present in the target tissue. If the fiber is sympathetic it will secrete norepinephrine and this will bind the adrenergic receptors present in the target tissues that can be alpha and beta.

Also epinephrine which is secreted from adrenal medulla they also bind to this adrenergic receptors that is alpha and beta. So, what we are seeing in autonomic innervation of the heart and vasculature the parasympathetic or the vagal fibers this is the long pre ganglionic fibers which are coming from the central nervous systems. And in the heart itself it is a synapsing and the post ganglionic fibers are very short. Whereas, the sympathetic fibers are travelling all along the spinal cord and the sympathetic ganglion they are synaptic and the sympathetic ganglion this have the pre ganglionic fibers which are short and the post ganglionic fibers are long. And these are terminating both in the heart as well as in the blood vessels.

So, the receptors what we see usually the vagal fibers they are terminating in the acenode and the AV node they modulate usually the sine atrial node and the atroventricular node. And usually the sympathetic fibers they innervate the myocardial fibers as well as the blood vessels. So, the heart usually the receptors adrenergic receptors we get beta 1 adrenergic receptors we get beta 1 and beta 2 M 2 musculinic receptors is usually present in the heart. Adrenergic receptors which we get in the blood vessels that is alpha 1 and alpha 2 and M 3 receptors usually we get in the blood vessels. So, what are the functions of this receptors? Generally, the adrenergic receptors alpha 1 beta 1 beta 2 alpha 2 is very generally it is located vastly in the central nervous system and the brain.

And in some junctional blood vessels, but alpha 1 and beta 1 and beta 2 that is very important over here. So, alpha 1 the agonist is norepinephrine beta 1 and beta 2 is epinephrine. So, alpha 1 causes vasoconstriction there will be constriction of the blood vessels atriolar constrictions as well as venoconstrictions. The epinephrine binds to the beta 1 receptors that will cause increase in the heart contractility increase in the heart contractility increase in the heart rate will come to the mechanisms later. Beta 2 receptors epinephrine also binds to the beta 2 receptors and cause vasodilatations or bronchodilatations.

So, the actions of beta 2 is just opposite to that of the beta 1. The beta 1 epinephrine causes increase in the heart rate increase in the contractility, but beta 2 epinephrine causes vasodilatation bronchodilatations in the lungs. The muscarinic receptors or the cholinergic receptors they bind to the acetylcholine and they causes the vasodilatation and decreased heart rate and decreased contractility force of contraction as well as vasodilatation. So, what are the general or overall effects on the heart? So, chronotropy is the increase in the rate, ionotropy is the contractility, ionotropy coming from the ions calcium ions, lucitropy means relaxation rate, dromotropy means conduction velocity. All this will get increased in the under the sympathetic stimulation.

And the parasympathetic stimulation we usually will decrease all this specifically the ionotropy and lucitropy effect is related to the atrial musculature or atrium. And in case of blood vessels usually parasympathetic does not have any innovations except the major dilatory effects are seen in specific organs like penis genitalia. Besides that the blood vessels arterial the vasoconstrictions which includes arterial constructions and the venous constructions the sympathetic innovations usually play a very important role in that with the vasoconstrictions. Now, what is the cardiac signal transduction mechanism? The cardiac signal transduction mechanisms is usually linked with G protein. Now, G protein is G stimulatory protein and G inhibitory protein.

So, whatever actions G stimulatory protein will have the opposite role G inhibitory protein will occur. So, G proteins are usually attached to a molecule that is adenylcyclase. So, adenylcyclase usually what happens whenever non epinephrine or epinephrine is binding to the receptors present in the which related to the G stimulatory proteins. For example, beta 1 and beta 2, so beta 1 and beta 2 receptors. So, this non epinephrine and epinephrine will bind to the G stimulatory proteins and stimulate the adenylcyclase enzyme.

Now, this beta 2 I am talking about the heart which will cause which will increase the contractility. This is the cardiac receptors I am talking about. So, adenylcyclase will get stimulated there will be formation of cyclic AMP. So, increased cyclic AMP because of

this adenylcyclase enzyme stimulation will cause increased formation of protein kinase. This protein kinase will cause increased calcium influx.

This increased calcium influx will cause more contraction. This is exactly reverse reversal occurs in case of G inhibitory protein. And the receptors are one we already know the muscarinic receptors acetylcholine. The muscarinic receptors also we have adenosine which binds to the A 1 receptors. They bind to the G inhibitory proteins and the adenylcyclase enzyme will be inhibited.

So, the cyclic AMP will be inhibited there will be less protein kinase and there will be less calcium influx. And thus relaxation or the less contraction of the muscle. So, that is how the cardiac signal transduction occurs. This I am repeatedly telling because beta 1 and beta 2 beta 2 I have already told it is very important in case of vatsudialitations. Now, that is beta 2 for the vessels blood vessels.

Here I have said the beta 2 increasing the contractions contractility in case of heart rate in case of cardiac receptors. So, beta 1 and beta 2 G stimulatory protein and acetylcholine or muscarinic that is G inhibitory protein. Now, coming to the vascular signal transduction mechanisms. In case of vascular signal transduction mechanisms beta 2 receptors which bind to the G stimulatory proteins. What are the G cycle enzymes? What it will cause again the same it will stimulate the adenylcyclase enzyme.

Now, this vascular signal transduction means it is occurring in the blood vessels. And blood vessels are nothing but the smooth muscles. But here the mechanism of contraction of the smooth muscles is bit different compared to the other muscles. Now, because of the adenylcyclase enzyme activation there will be increased formation of cyclic AMP. Now, this cyclic AMP is actually a inhibitor of myosin light chain kindness.

What is this myosin light chain kindness? Now, in case of smooth muscle contraction to occur whenever calcium binds with calmodulin. The calcium calmodulin complex and the myosin light chain kindness activated this will cause the contraction of the smooth muscles. Here in case of vascular smooth muscles, but this happens this myosin light chain kindness this gets activated in presence of ATP. Now, whenever we are utilizing the ATP in the formation of cyclic AMP. That means, the ATP is decreased which means actually the cyclic AMP is an inhibitor of myosin light chain kindness.

So, in there will be no calcium influx and there will be no contraction of the muscles. So, that means, the beta 2 is actually causing through g stimulatory protein relaxation in case of vascular smooth muscles it will be vasodilatations. Now, similarly the opposite occurs in case of alpha 2 receptors, where alpha 2 receptors bind to the g inhibitory

protein. Now, when alpha 2 receptors are binding to the g inhibitory protein which means ATP will be more adenylcyclase is inhibited. So, ATP will be more and cyclic AMP will be less which means the myosin light chain kindness will be activated and there will be contraction.

So, they know vasoconstrictions occurs because of the alpha 2 receptors, but usually the action of the alpha 2 receptors is balanced or counter balanced rather with the beta 2 vasodilatations in our body. The next is the alpha 1 adreno receptors, the GQ proteins present in the vascular smooth muscles are coupled with alpha 1 adreno receptors. And a specialty of the GQ proteins is they act through the second messengers inositol phosphate and diacylglycerol. So, IP3 and diacylglycerol again this will cause increase in the protein kinases and this will cause calcium influx. And this calcium influx will cause contraction hence contraction of the vessels occurs because of the alpha 1 adreno receptors, but alpha 1 adreno receptors specifically bind to GQ proteins which is acting not by a adenylcyclase, but IP3 and DAG mechanisms.

Now, in case of vascular smooth muscles we have M 3 receptors M 2 receptors we have seen in case of cardiac muscles and the action is just binding to the G inhibitory protein. But in case of M 3 receptors in the vascular smooth muscles they act via binding to the act via releasing the nitric oxide. So, nitric oxide it is the vascular endothelial relaxing factor which causes relaxation or the vasodilatations of the vascular blood vessels. So, this is the mechanism of G protein coupled signal transduction. So, here we have seen what are the autonomic pathway the sympathetic pathways and the parasympathetic pathways the various receptors present in the heart along with the innervation the cardiac receptors and the vascular receptors beta 1 beta 2 receptors in the heart and alpha 1 alpha 2 receptors in the blood vessels M 2 receptors in the heart M 3 receptors in the blood vessels.

So, and we have seen how the signal transduction occurs through various cardiac receptors and vascular receptors this much you have to know in the cardiac autonomic regulation. Thank you.