The safety role of gap junctions: A new perspective on atrio-ventricular nodal reentry

In the normal heart, the atrio-ventricular node (AVN) is responsible for the appropriate atrio-ventricular delay. Most of the slow conduction in AVN is probably caused by the small number of gap junctions connecting the myocytes [1].

Experimental and theoretical studies show that although conduction velocity decreases by reducing gap junctions, in such conditions safety factor increases [2].

Disorderly arranged gap junctions in myocytes might contribute to alterations in conduction that are capable of precipitating reentry arrhythmias. Some evidences approve the dissimilar distribution of gap junction in different parts of AVN during AVN reentry. For example, some reports indicate the presence of few gap junctions between cells within the region of slow conduction through the AVN [3].

Previously we proposed that gap junctions are dynamic structures, which open and close in the diverse moments of each normal heart cycle, rather than being continuously open [4].

According to the aforementioned evidences, we suggest that besides the disordered distribution of gap junctions in AVN as a root of reentry, abnormal opening or closing of these gap junctions helps to generate a very low resistance pathway as a fast source for abnormal action potential propagation. According to previous results, we think that disordered distribution of gap junction in AVN provides a background for preparing two different pathways with different resistances. In this background, opening and closing of gap junctions may seriously affect the resistance of the two pathways. We assume that opening of gap junctions in the compact region, which is assumed to be the low resistance pathway, may be the main cause of AVN reentry. We assume that this view on gap junctions in the compact region, which is assumed to be the low resistance pathway, may be the main cause of AVN reentry. We assume that this view on gap junctions in the compact region, which is assumed to be the low resistance pathway, may be the main cause of AVN reentry. We assume that this view on gap junctions in the compact region, which is assumed to be the low resistance pathway, may be the main cause of AVN reentry. We assume that this view on gap junctions in the compact region, which is assumed to be the low resistance pathway, may be the main cause of AVN reentry.

In such condition, closure of gap junctions in the AVN may not cause disorders because:

1. In the normal heart, the amount of AVN gap junctions is not too high [1].
2. The reduction of gap junctions also can increase the safety of action potential propagation [2].
3. Closure of gap junctions occurs during normal cardiac cycle and is not a pathological state [4].
4. Myocardial cells may not require low-resistance connections for successful propagation of the action potential. Some other mechanisms such as electric field are capable to propagate the action potential [6].
5. The closure of gap junctions in the normal heart has been observed. Some experimental evidences show that the number of available gap junctions is much larger than needed for propagation of action potential in normoxic conditions [7]. In those cases, most of the gap junctions may be closed [6].
6. The propagation of action potential is observed in the absence of gap junction in the ventricular myocardial cells of some vertebrate hearts [6].

We think that our hypothesis on the mechanism of cardiac action potential propagation may have exciting advantages and consequences, especially in introducing new drugs. Of course, this novel view needs to be confirmed with experimental and clinical studies.

References

[4] Somayeh Mahdavi, Mostafa Rezaei-Tavirani, Shahrar Towhidkhah, Farzad Towhidkhah. Dynamic behavior of gap junctions during reentry, such as cardiac glycosides (with adequate concentrations) and nitric oxide, may be helpful for treating AVN reentry [5].
Endo-abdominal hypertension complicating pregnancy & fetal development

I discovered abdominal disproportion and hypertension [1,2] the hard way. As a kid, I survived a strangulated sciatic hernia with every complication [2]. Later, I realized that when pressure in my belly rose post-operatively (as with advancing pregnancy in an eclamptic), I became comatose. Pneumonia kept me coughing, so I burst my incision open. That decompression, like delivery in an eclamptic, cured the coma. In 1933, abdominal wound dehiscence was wrongly considered a highly lethal complication requiring immediate secondary closure, but I was prohibitively moribund, until the decompression revived me. Days later, still expecting me to croak momentarily my surgeon could stand it no longer, he closed the wound, sealing in the peritonitis. Then, with the surgical pneumoperitoneum and bugs making more gas, I was really set back. Coughing over several dying days saved me again by bursting the incision subcutaneously. The hernia was repaired later. So I learned about abdominal hypertension, celiotomy, their implications and complications.

As a physician, to see that big tense bellies gave some gravida similar complications was easy. Furthermore, the same disorders afflict corpulent males, coming as “single spies” spread over years, rather than crowding into weeks as when abdominal hypertension complicates pregnancy... especially with multiple fetuses/primips.

The causes of pre-eclampsia, puerperal psychosis, hyperemesis, gestational diabetes, high blood pressure are widely unknown. But they are all just complications of pregnancy, actually, manifestations of abdominal hypertension and disproportion. The fundamental disorder of pregnancy is expansion of the gravid uterus exceeding that of the tummy, making endo-abdominal hypertension (my hypothesis).

I noticed some patients coming to laparotomy with distended-bellies, i.e., ileus or intestinal obstruction, having had the expanding pneumoperitoneum superimposed would not wake up. Their deaths were attributed to presenting illness/anesthesia. Realizing [3] that abdominal hypertension and disproportion is a common and sometimes fatal clinical entity, I started using prostigmine/neostigmine to treat or prevent it. This decompression worked as verification, e.g., reducing pregnancy/fetal problems/wound dehiscence to vanishing point, and curing distended-belly comas [4,5].

In my limited experience, but definite opinion, prostigmine is invaluable in surgical and pregnant patients. This Cinderella of wonder drugs is neglected because the dose, like that of digitalis, must be tailored to the individual.

Fetal evidence of endo-abdominal hypertension includes miscarriage, premature delivery, endo-uterine fetal impaction, uterine rupture, webbed fingers, sirenomelia, Siamese twins, etc.

Obscure disorders of endo-abdominal organs, liver, spleen, pancreas, kidneys, adrenals, bowels,