

R o u n d t a b l e D i s c u s s i o n

Hypertensive Emergencies

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Following a hypertension symposium in Rochester, NY, in October 2005, a roundtable was convened to discuss hypertensive emergencies. Dr. Marvin Moser, Clinical Professor of Medicine at the Yale University School of Medicine, New Haven, CT, moderated the session, which included Dr. Joseph L. Izzo, Jr., Professor of Medicine at the State University of New York at Buffalo, Buffalo, NY, and Dr. John Bisognano, Associate Professor of Medicine at the University of Rochester School of Medicine, Rochester, NY. (J Clin Hypertens. 2006;8:275–281) ©2006 Le Jacq Ltd.

DR. MOSER: There has been a great deal of discussion about hypertensive emergencies and urgencies, less so in recent years because it is so much less common. Dr. Izzo and I remember when we were house staff officers that, on a given evening, there were always one or more cases of hypertensive emergencies admitted for treatment—patients with renal failure, congestive failure, or strokes. Today, this is uncommon except in big city hospitals, probably because we're treating hypertension earlier and delaying or preventing progression.

There continues to be a debate regarding the definition of a hypertensive emergency. We will agree, I believe, that too many people are being admitted to the hospital with this diagnosis and perhaps being overtreated when they do not truly have an emergency. I'd like to start by asking John how to define a hypertensive emergency and should we continue to use the term urgency in people who do not have an emergency but require fairly urgent treatment?

DR. BISOGNANO: The important first fork in the road that most clinicians come to in the emergency room (ER), is to determine whether the patient with markedly elevated blood pressure (BP) has to have it lowered acutely. When I see a patient like this, the first thing I ask myself is: Is there any specific organ right now that's being damaged by this level of BP? The questions that come to mind

are: Is the patient having chest pain? Is he or she in heart failure? and, Is there an acute cerebrovascular event or renal failure? Lacking an acute aortic dissection and other similar acute organ damage, I will usually not define it as a hypertensive emergency regardless of the level of BP.

DR. MOSER: So, if I came into the ER with a BP of 200/130 mm Hg with headaches but no evidence of heart failure, renal failure, or an impending cardiovascular accident, you would not necessarily consider me a hypertensive emergency?

DR. BISOGNANO: I probably would not. A lot would depend on the degree of the headache. As we all know, many hypertensive patients get headaches. If it were just another mild or moderate headache, I would probably just treat you with medications and suggest an early follow-up. We might insist on a 4- to 6-hour period of observation after an oral medication in the ER, just to verify that the BP is coming down, and then a follow-up in 3 to 5 days in the clinic or an office.

DR. MOSER: Unless I had a severe headache.

DR. BISOGNANO: If it were a severe headache...that's a different story.

DR. MOSER: Joe, is there a BP definition for a hypertensive emergency?

DR. IZZO: No, I don't think there is. There is an age-related issue with regard to levels of BP. For example, in a child who is 8 or 10 years of age, there can be a hypertensive emergency with a systolic pressure of 150 mm Hg but, at the same



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time, there may be no hypertensive emergency in an adult with a systolic pressure of 250 mm Hg. So, I think that John is absolutely right. We have to pair the BP with the level of acute organ damage as the first branch point for thinking. And I would only add to what he said that papilledema and hypertensive encephalopathy would also constitute a hypertensive emergency, along with heart failure, acute myocardial infarction, major bleeds, and central nervous system events.

DR. MOSER: Let's go back to the BP level for a minute. A 55-year-old man with a BP of 250/150 mm Hg and no evidence of an acute myocardial infarction had a creatinine level of 1.4; fundi showing arteriosclerotic narrowing and nicking, but no hemorrhage, exudates, etc.; and an ECG showing left ventricular hypertrophy (LVH). Is this an emergency? What do you do?

DR. BISOGNANO: No, this is not an emergency.

DR. MOSER: Okay. Joe?

DR. IZZO: Not an emergency, but I still like the term urgency because we have to do something relatively quickly for this patient.

DR. MOSER: Why not just call it severe hypertension rather than urgency?

DR. IZZO: You could, but I like urgency because it is motivational.

DR. MOSER: Okay. John, what would you do?

DR. BISOGNANO: I agree, I think urgency is a good term because it implies something has to be done fairly soon. We want to verify that things are going in the right direction in a matter of hours and chronically after a number of days. There is another thing that we should look at: Is today's BP a major change from previous baseline BPs?

Given this case with LVH and evidence of possible renal insufficiency, it suggests that BP has been elevated for quite a period of time and there is some chronic target organ damage. In this instance, a BP of 250 mm Hg may only be a 30% or 40% increase from what pressures have been previously.

DR. MOSER: But what if I told you that the systolic BP had been about 140–150 mm Hg 3–4 months ago?

DR. BISOGNANO: That's a different story. This would suggest a hypertensive emergency with more target organ damage on top of a chronic less severe elevation of BP. In the same way that a young woman who may have a BP of 110 mm Hg or 120 mm Hg during pregnancy comes in with a headache and a BP of 180 mm Hg, this may be a patient with a hypertensive emergency.

DR. MOSER: Alright, so we've said that the BP itself isn't the criterion for an emergency unless it's

a sudden BP increase, which can be documented. Generally, we would have to have not only some symptoms but some evidence of acute target organ involvement, not just evidence of LVH to diagnose a hypertensive emergency.

DR. BISOGNANO: Right, and some evidence that the BP represents a substantial change from what it is chronically.

DR. MOSER: Alright, what do you do, Joe? A patient comes into your office, he had gone to work this morning but didn't feel well. You find a few basilar rales and some peripheral edema. In retrospect, the patient admits to being a little tired getting on the train this morning and having shortness of breath. His BP is 180/120 mm Hg.

DR. IZZO: This is the early phase of what we'll call acute target organ damage. That would define a hypertensive emergency. In this case, when symptoms are not severe, you could quibble and call it an urgency. But what you can't do is delay treatment.

DR. MOSER: Well, would it matter to you if the pressure was 220/130 mm Hg instead of 180/120 mm Hg?

DR. IZZO: No, not at all, because urgent treatment is required on the basis of target organ damage. Classifying emergency/urgency, as John did earlier, gives you a time frame in which BP has to be lowered. I would put this case in the emergency category: the person needs BP-lowering treatment right now.

DR. MOSER: Alright, John, what would you do? Are you going to do any tests? Are you going to check for a specific etiology or are you just going to treat?

DR. BISOGNANO: I think the first step will be to initiate some treatment and not do a lot of tests. Once we've defined a hypertensive emergency, some treatment that's going to bring the BP down within hours must be started. There are some orally acting medications like short-acting captopril that we can use in the office.

DR. MOSER: Why not send the patient right over to the ER?

DR. BISOGNANO: If I believed that very rapid BP lowering and close monitoring were necessary, I would. It might not be good enough just to give a pill and see the patient the next day.

DR. MOSER: Alright, so even with a BP of 220/130 mm Hg, with a mild headache and LVH but only minimal signs of heart failure, you might not send him over to the ER?

DR. BISOGNANO: Probably not. There really has to be some sign that the BP levels are resulting in acute target organ damage. There is no evidence of acute

renal failure or acute cerebrovascular symptoms, so I would be inclined to just begin oral therapy in my office. I would likely use an angiotensin-converting enzyme (ACE) inhibitor, such as lisinopril 2.5 or 5 mg, or an angiotensin receptor blocker (ARB) as initial therapy along with a low dose of a β blocker, such as 25 mg of metoprolol twice a day. A dihydropyridine calcium channel blocker (CCB) such as felodipine or amlodipine would also be a reasonable choice.

DR. MOSER: What about a diuretic?

DR. BISOGNANO: Some patients at this point may be actually intravascularly dry, so a diuretic may not be the first choice in all cases. Given the markedly elevated BP, I suspect that a diuretic will be needed to maintain long-term BP control and, with evidence of heart failure, it may be a drug of choice in this patient.

DR. MOSER: So, you would send this patient home on a small dose of a β blocker, an ACE inhibitor, and possibly a diuretic.

DR. BISOGNANO: Or as an alternative, labetalol or a CCB.

DR. MOSER: Orally.

DR. BISOGNANO: Orally.

DR. MOSER: And you would tell the patient that you would like to see him tomorrow or the next day?

DR. BISOGNANO: I would do that, if there is no evidence of an ongoing acute organ event.

DR. MOSER: Joe, let's look at another scenario. One of your patients whom you have been treating had continued to have BPs of 150–160 mm Hg/90–95 mm Hg. Possibly suffering from physician inertia, you decided that a 75-year-old person is okay with these pressures and continued him on 12.5 mg hydrochlorothiazide and 5 mg enalapril. Now the patient comes in with pressures of 210–220/110 mm Hg, without acute target organ change. What do you do? The patient, by the way, is not happy with his care.

DR. IZZO: Because I've not given enough therapy?

DR. MOSER: That's right. He had read in the newspaper that he should always ask his doctor why he hasn't gotten his pressures below 140 mm Hg.

DR. IZZO: In this partially treated hypertensive, the doses that are being used are woefully inadequate. There is no excuse to give just 5 mg of enalapril daily in any patient for the treatment of hypertension. I guess that I may not have been as conscientious as I should have been.

DR. MOSER: But is it possible that 5 mg would be sufficient along with the thiazide?

DR. IZZO: At no time in my career have I given a persistent dose as low as 5 mg daily of enalapril as monotherapy.

DR. BISOGNANO: Even on initiating therapy in what might be a patient with grade I hypertension or someone with fluctuating BPs?

DR. IZZO: As a general rule, John, no. This gets back to the question that was posed to you earlier. You correctly identified the fact that the higher the BP, the greater the chance of clinically significant volume contraction and therefore enhanced ACE inhibitor responsiveness. Vasodilator therapy, in general, is very powerful in patients with very high pressures, so you may want to start with a single agent. But remember, as now suggested, and as the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) recommends, if the BP is higher than 160 mm Hg systolic, serious consideration should be given to starting with two agents.

DR. MOSER: Alright, this patient is already on two medications.

DR. IZZO: Coming back to this case. First you must use appropriate doses. This patient is not on an appropriate dose of the ACE inhibitor or a diuretic if BPs are still high. The second ought to be obvious: use appropriate combinations of agents.

DR. MOSER: An ACE inhibitor/diuretic is appropriate, isn't it?

DR. IZZO: Yes, but you may want to add something else if a dosage adjustment of either of these agents isn't effective.

DR. MOSER: Shall this patient be sent to the hospital?

DR. IZZO: No, absolutely not.

DR. MOSER: But the systolic pressure is higher than 200 mm Hg and may represent a relatively acute change in BP.

DR. IZZO: The pressure was not well controlled and obviously kept going up. But again, if there is no acute evidence of target organ damage, i.e., heart, brain, or kidneys, you would consider this to be an urgency, not an emergency necessitating acute care in a hospital. Have we looked for evidence of acute target organ change?

DR. MOSER: You checked the urine. There was no evidence of an acute nephritic process, and the fundi didn't show hemorrhage and exudates. An ECG shows LVH with no evidence of ischemic changes, and there is no evidence of anemia.

DR. IZZO: So, we have to treat the patient now and ask additional questions later. I would increase the dose of the ACE inhibitor to 20 mg of enalapril daily.

DR. MOSER: What about the dosage of the diuretic?

DR. IZZO: The diuretic dose is important. The long-term control of BP in patients on an

ACE inhibitor or ARB is highly dependent on the dose of diuretic. One way to think of drugs that block the renin-angiotensin or sympathetic nervous system is that they convert the patient into a “salt-sensitive” individual who will respond in a dose-dependent fashion to a diuretic.

DR. MOSER: So, you would double the dose of the diuretic right away?

DR. IZZO: That’s step two.

DR. MOSER: You would just increase the ACE inhibitor dosage as a first step.

DR. IZZO: I would, and then see where the situation settles out. The next step is to go to 25 mg hydrochlorothiazide.

DR. MOSER: John, what would you do?

DR. BISOGNANO: I think we’re alluding to a patient who we frequently see in the clinic. The patient shows up with a systolic BP that’s 200–220 mm Hg. It may also be useful to start a CCB in this kind of patient because, in the long run, they are probably going to need 3 or 4 or 5 medications. A CCB is a medication you can give in most patients without knowing much about them.

DR. MOSER: So, you might increase the ACE inhibitor dosage as Joe did, but you’d also add a CCB right away.

DR. BISOGNANO: The ACE inhibitor is probably the best drug to use and I would probably just focus on one drug, make the dosage change, and then monitor the patient several days later.

DR. MOSER: So, you would just increase the ACE inhibitor?

DR. BISOGNANO: As an initial step, yes.

DR. MOSER: And neither of you would increase the dosage of the diuretic as an initial step.

DR. IZZO: That’s correct. I think the risk of lowering the BP too much is significant.

DR. MOSER: I don’t believe that would happen on hydrochlorothiazide. It might happen if we used furosemide.

We apparently differ here. I would double or triple the dose of the ACE inhibitor and double the dose of the diuretic and I’d see the patient in 2 or 3 days.

DR. BISOGNANO: That’s okay, too.

DR. MOSER: Now, neither of you said that you’ve got to rule out a pheochromocytoma or renovascular disease in this person who seems to have become severely hypertensive after just having stage I hypertension. Should we pay some attention to these diagnoses?

DR. BISOGNANO: It is certainly something that we would consider in a patient who is presenting with a recent increase in BP. This involves taking a history to see if the rise in pressure is recent or gradual.

DR. MOSER: Alright, I can tell you that at a fair 2 months ago, pressures were similar to those obtained by Dr. Izzo: about 140–150/90–95 mm Hg.

DR. BISOGNANO: If that history is accurate, then it is something that we need to consider. This may be a good time to start a 24-hour urine collection for metanephrine as a clue for a pheochromocytoma or to look at blood chemistries as a clue to renovascular disease.

DR. MOSER: But the pressure is well over 200 mm Hg, and the patient doesn’t want to wait 24 hours and doesn’t want to bother collecting urine. Do symptoms help you triage?

DR. BISOGNANO: The symptoms do help you triage, but a pheochromocytoma is so rare that it is low on the differential list.

DR. MOSER: But what if the answer is yes to the three key questions? Do you get palpitations? Yes, I sweat like a pig, not just on a hot day, and I get severe headaches all the time.

DR. BISOGNANO: I think that increases the probability of a pheochromocytoma from almost none to something that we may need to evaluate but, still, it is rare.

DR. MOSER: Would you do a phentolamine test on the spot to rule it in or out?

DR. BISOGNANO: I wouldn’t. I think that it’s too dangerous.

DR. MOSER: And BP might be lowered in a patient with severe hypertension without a pheochromocytoma.

DR. BISOGNANO: Right.

DR. MOSER: So would you try and start a 24-hour urine collection but treat the BP without waiting for an answer?

DR. BISOGNANO: If the history were very compatible with a pheochromocytoma, and I felt that the probability of a pheochromocytoma was great, I might treat empirically with a β and an α blocker to see what happened to the BP—but again, this is very, very rare.

DR. MOSER: Although, it should not be lost track of because it is treatable. Okay, we probably would all go ahead and treat even if we thought there was a possibility of a renovascular lesion. Get the pressure down and worry about the diagnosis later. You both agree that you would either double the dose of the present medication or add a CCB to the ACE inhibitor and the diuretic. And you would see the patient in 2 or 3 days. Obviously, if the pressure isn’t down, more medication, such as doubling the dosage again, would be appropriate.

Well now, what about the patient with acute organ changes whom you admit to the ER?

Residents used to give a little nifedipine under the tongue and BPs would come down, but there was a risk from this type of therapy. Joe, what would you do? There is some congestive heart failure, some headaches, but you don't interpret them as being the beginning of a hemorrhagic stroke?

DR. IZZO: Well, in the case of heart failure, it's wise to consider some hemodynamic needs of the patient before you choose medication. Just lowering the pressure, and cardiac afterload, is a pretty good idea most of the time, but you really ought to consider balanced preload–afterload reduction in all of these patients. And one way to do that if you want to commit the patient to the intensive care unit is to use nitroprusside. But it is by no means the only way to treat this individual.

DR. MOSER: But the intensive care unit is booked, you've got an ER bed, and there are nurses, etc. Can you still use a nitroprusside drip?

DR. IZZO: I like labetalol in these patients as well. This can be given as an IV drip, orally, or as a repeated IV injection. You're rarely going to get into trouble using labetalol.

DR. MOSER: Can the patients take medication by mouth to save the problem of monitoring carefully?

DR. IZZO: If they are able to swallow, there is no reason that there will be a problem. Yes, you could do that. But most of the time, with some evidence of failure, I would probably give medication parenterally.

DR. MOSER: Would you use a diuretic parenterally?

DR. IZZO: No, I would not. In fact, I think there's too much diuretic use early in heart failure. That's the second drug once the peripheral circulation and the heart have been treated with specific agents.

DR. MOSER: John, what's your first choice of drug in a true hypertensive emergency?

DR. BISOGNANO: I think the most practical drug to use is labetalol. And even though nitroprusside may be the fastest-acting drug pharmacologically, there are always barriers to giving nitroprusside, whether it's mixing up the drug, the effect of the light in the ER, or the speed of the infusion. It's a drug that has barriers. In the time that it takes to get the nitroprusside into the patient, one can usually open a vial of labetalol and begin to control the BP.

DR. MOSER: So, would you give it as an IV bolus?

DR. BISOGNANO: I would.

DR. MOSER: And then start it orally at the same time?

DR. BISOGNANO: Either start labetalol orally or start whatever medication you ultimately intend to have the patient on.

DR. MOSER: You'd start it at the same time though, you wouldn't just keep labetalol IV going intermittently unless the patient is unable to swallow?

DR. BISOGNANO: Oh, I may treat the patient with serial labetalol doses for the first hour or two, but at that point we would start oral medication.

DR. MOSER: So, you start them on a program that they would use when they leave the hospital?

DR. BISOGNANO: Absolutely, because this will save hospital days. There won't have to be a transition of medication on hospital day 2 or 3. If I intend to send the patient home on an ACE inhibitor or a CCB, I can start it early on and then 2 days later when the patient is ready to go home, those drugs will have already begun to have a stable effect.

DR. MOSER: That's a good point. Too many people are kept on IV therapy for days and then changed over to oral therapy, wasting a lot of time, effort, energy, and money.

DR. BISOGNANO: And I'm very careful, as is Dr. Izzo, not to overdiurese them.

It's awkward when a patient comes in with a BP of 240 mm Hg and 12 hours later has a BP of 140 mm Hg and isn't feeling well. Often that's the result of aggressive volume contraction while vasodilating.

DR. MOSER: What's your target systolic pressure? What's your target in the first 3–4 hours of treatment in a truly emergent situation?

DR. IZZO: I would not have a BP target primarily; I'd have targets related to heart rate and other parameters of heart failure.

DR. MOSER: You wouldn't worry about a decrease from 240 mm Hg to 140 mm Hg in 2–3 hours?

DR. IZZO: Oh, I see what you're saying. Yes, it's hypothetically possible that a patient could have some kind of perfusion problem with a rapid drop in pressure. The majority of the time that doesn't occur, but everyone seems to remember a case where it may have occurred. So I don't think you want precipitous BP lowering; it's not absolutely necessary, and with drugs like labetalol parenterally or nitroprusside, with all its caveats, one can be very careful in adjusting the BP downward in a metered way.

DR. MOSER: What about all the other drugs that are listed in textbooks and definitive articles—nitroprusside is listed as the first drug, labetalol is certainly listed as a possibility, but diazoxide, hydralazine, phentolamine, and others are also listed. Are these agents that we should sort of forget about? Let them be listed in textbooks but, from a practical point of view, ignore them? John?

AGENT	DOSAGE	ONSET/DURATION OF ACTION (AFTER DISCONTINUATION)	PRECAUTIONS
Sodium nitroprusside	0.25–10 µg/kg/min as IV infusion	Immediate/2–3 min after infusion	Nausea, vomiting; may cause thiocyanate intoxication with prolonged use; bags, bottles, and delivery sets must be light resistant
Labetalol	20–80 mg as IV bolus every 10 min; up to 2 mg/min as IV infusion	5–10 min/2–6 h	Bronchoconstriction, heart block, orthostatic hypotension

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AGENT	DOSE	ONSET/DURATION OF ACTION (AFTER DISCONTINUATION)	PRECAUTIONS
Captopril	25 mg p.o., repeat as needed SL, 25 mg	15–30 min/6–8 h SL, 15–30 min/2–6 h	Hypotension, renal failure in bilateral renal artery stenosis
Clonidine	0.1–0.2 mg p.o., repeat hourly as required to total dose of 0.6 mg	30–60 min/8–16 h	Hypotension, drowsiness, dry mouth
Labetalol	200–400 mg p.o., repeat every 2–3 h	30 min–2 h/2–12 h	Bronchoconstriction, heart block, orthostatic hypotension

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DR. BISOGNANO: I think from a practical point of view, one needs to have only a few drugs at their disposal to treat hypertensive emergencies because it is really a short-term treatment. If patients are still on these drugs a day or two later, too much time has been wasted in transitioning them to the oral regimen that you intend to send them home on. A few drugs, perhaps nitroprusside, labetalol, and hydralazine on occasion, or in patients who for some reason you suspect a lot of adrenergic stimulation, a β blocker such as metoprolol might be of use. Beyond that, there are certainly other drugs that will work, but are probably not necessary to use routinely (Tables I and II).

DR. MOSER: It's really not necessary to list a great many possibilities and give too many choices. This may just confuse.

DR. IZZO: Yes. The only medication that we didn't mention that might be added to the list is oral clonidine. For the most part, this is pretty safe and, if you don't have access to anything else, could be an alternative.

DR. MOSER: Good point. So, 0.1 mg, then an hour later, 0.2 mg, etc.?

DR. IZZO: Oh, you might start with 0.2 mg and then every 1–2 hours supplement it with 0.1 mg up to about 0.6 mg as a total dose. Then rethink what you're doing if it hasn't worked.

DR. MOSER: If you happen to have some samples of clonidine or an ACE inhibitor for a patient in your office with severe hypertension but not in

an emergency situation, would you just give it to them right on the spot?

DR. IZZO: I've done it.

DR. BISOGNANO: I think it can be useful as a bridge, as long as it's not used as an end in itself.

DR. MOSER: To summarize, we should keep the term hypertensive urgencies to let people know that if BPs are very high, even without acute target organ damage, the BP should be lowered within a few days to a week. With an emergency where there is evidence of acute organ damage, it is probably best to treat these people as inpatients at least for a few days.

DR. BISOGNANO: Correct, I think you could say minutes to hours for emergencies and hours to days for urgencies.

DR. MOSER: Fair enough. And the patient with an urgency, with high pressures, even as high as 220–230 mm Hg/130–140 mm Hg, with evidence of chronic but not acute target organ involvement might be treated as an office patient. If they are on medication, it should be increased. There seems to be some difference of opinion whether you would start out with an ACE inhibitor or an ARB and a diuretic or a CCB in addition or even a β blocker in some patients if they had not been on medication. There also seems to be a difference of opinion on diuretics. I still think that these should be part of the treatment in almost everyone.

In emergencies in the hospital, the practical thing to think about is that there basically are two or, at

most, three options for treatment. One is IV nitroprusside titrated to a level of pressure that is lower but not dramatically lower than it had been. Perhaps aim for a systolic BP decrease of 30 or 40 mm Hg in an hour or two and then gradually decrease BP further. This may require a lot of nursing time and some problems with setting up the infusion. The other option is IV labetalol or labetalol by mouth or a short-acting ACE inhibitor by mouth with other drugs to get you started. Clonidine is an option. The important point that everyone believes is to start oral medication as soon as possible if the patient

is able to do so, so that within a few days they are titrated up to an effective dosage and able to go home. Tables I and II summarize the approach that is appropriate in most cases.

DR. IZZO: And the only thing I'd add is that you're not going to do this with one drug.

DR. MOSER: John?

DR. BISOGNANO: That's exactly what I was about to add. These are patients who ultimately will require four or five medications, including a generous dose of a diuretic.

DR. MOSER: Thank you.