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Review Article

Standardizing hypertension management in a primary care setting in India through a protocol based model

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ABSTRACT

Hypertension is a leading cause of death in India. Control rates of hypertension are abysmal, even for people on treatment. There are a number of barriers to adequate control of hypertension in India, including therapeutic inertia and the lack of a systematic, simplified approach. Standardizing hypertension management through an evidence based model that sets thresholds for diagnosis, treatment goals, follow up intervals and choice of drugs can lead to improved management of hypertension in an individual hospital or health system. In this paper, we summarize the evidence for such a model, and adapt it to the Indian context, focusing on maximizing effectiveness, safety and ease of use by a non-expert. This model can be utilized by individual practitioners, hospitals, primary health centers (PHCs) and the Health and Wellness Centers (HWCs) under the Ayushman Bharat initiative.
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1. Introduction

In 2010, hypertension was estimated to be the leading risk factor for death and disability worldwide. For ischemic heart disease alone, 53% of disability adjusted life years (DALYs) were attributable to hypertension. In South Asia, hypertension was estimated to be third leading cause of death and disability, after household air pollution from solid fuels and tobacco smoking.[1]

Treatment of hypertension is highly effective, and has been shown to reduce mortality in randomized trials since the 1970s.[2] Despite this knowledge, progress in hypertension control has been slow in low and middle-income countries such as India. In 2014, it was estimated that only 42% of people with hypertension in urban India were aware of their diagnosis, and an even lower 20% had their hypertension well controlled. For rural India, the numbers were worse with only 25% of people aware of their diagnosis and an abysmal control rate of 10%.[3] These numbers are in stark contrast to high income countries such as the United States, where 53% of people with hypertension had their blood pressure well controlled in 2014.[4]

Numerous barriers exist at various levels of the healthcare cascade that account for the low rates of blood pressure control in India. At the health system level, a low political priority given to hypertension, competing healthcare priorities such as infectious diseases and limited financial commitment to hypertension serve as formidable barriers. At a hospital or clinic level, poor healthcare provider education in hypertension management, the lack of a systematic approach and inadequate access to drugs serve to undermine blood pressure control. At a community or individual level, lack of awareness of hypertension, limited capacity to bear out of pocket costs and competing life priorities make control of blood pressure challenging.

However, when considered from the perspective of an individual hospital or healthcare system, there are various measures that can be taken to potentially improve control rates of hypertension in the community served, with a key measure being a protocol based approach to the management of hypertension.

1.1. Benefits of protocol based care

Two major groups of patients benefit from protocol based care. The first group includes patients with undiagnosed hypertension-those who are recognized to have high blood pressure but not

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started on treatment. The second group includes people who are receiving treatment for hypertension but their blood pressure is not controlled. Therapeutic inertia by clinicians has been well documented as a reason for poor blood pressure control.[5] Protocol based care standardizes thresholds for diagnosis and treatment. It enables patient engagement in the treatment plan and standardizes follow up intervals after initiation or intensification of therapy.[6] Furthermore, developing a site specific protocol communicates to other members of the healthcare team that blood pressure control is a priority. It enables non-physician healthcare workers to advance patients along the treatment cascade, and to identify patients that need expert referral.[7] Finally, it contributes to a more efficient inventory management system.

1.2. Other protocols

Multiple protocols have been developed for blood pressure management worldwide. The Million Hearts Initiative in the US describes a protocol that starts with a thiazide diuretic and adds an ACEi/ARB as the next step.[8] The Kaiser Permanente Clinical Practice guidelines in the US recommend initiating patients on an ACEI/Thiazide combination.[9] The challenge in using these drugs as first line in the Indian scenario is the need for frequent monitoring of electrolytes and kidney function after initiation and dose uptitration. The National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular diseases and Stroke (NPCDCS), India 2017 flowchart recommends either a CCB, ACEI or Chlorthalidone as first line therapy. As second line, they recommend beta blockers or alpha-blockers.[10] This leaves a certain amount of ambiguity in the choice of a first line agent to treat hypertension, which can lead to sub-optimal choices. A protocol published by the World Hypertension League and Resolve to Save Lives proposes a simple, clear protocol for use of anti-hypertensive drugs in low resource settings.[11] However, it does not elaborate on the frequency of lab testing when starting ACEi/ARB, or the interpretation of its results. Incorporating such information into the protocol, and delineating clear action plans, will allow more practitioners to gain familiarity with using ACEi/ARB. Moreover, it does not incorporate albumin testing in its algorithm, which limits the ability of the protocol to get people with albuminuria on ACEi/ARB, a strong recommendation in this group of patients.[12]

Considering the high prevalence of hypertension in India, and the relative paucity of specialists to treat them, there is a strong need for implementing a hypertension management protocol at the level of the primary health care system. This can be administered by general medical practitioners independently or mid-level health care providers under the supervision of general medical practitioners.

In this paper, we propose a model that addresses the limitations of prior protocols in the Indian context, and customizes the available evidence to an actionable model suitable for India.

1.3. Model components

Given the varying circumstances of different healthcare systems, we divide the model components into essential and add-on features.

1.3.1. Essential features

1) Measuring and recording blood pressure across the hospital system in a standardized manner, while educating all concerned healthcare workers in its correct measurement.
2) Establishing a healthcare system wide protocol for the diagnosis and management of hypertension, with the agreement of all stakeholders.
3) Informing each patient of his current blood pressure, goal blood pressure and his prescribed blood pressure medications at each visit.

1.3.2. Add on features

1) Designating non-physician healthcare workers to provide education regarding hypertension at the time of diagnosis and follow up.
2) A closed pharmacy system that provides hypertension drugs at below typical market prices through bulk purchases.
3) Through such a closed pharmacy system, financially incentivizing 30–90 day drug purchases, rather than shorter periods.

We will describe these model components in detail.

1.3.3. Essential features

1) Measurement of blood pressure

Measurement and recording of blood pressure across the healthcare system should be done in a standardized manner, while educating all concerned healthcare workers in its correct measurement. All adults (>18 years) should be screened for hypertension as a part of their routine assessment irrespective of their presenting symptoms. Healthcare systems can use either an automated BP monitor (preferred) or the auscultatory method with a sphygmomanometer. Automated BP monitors are preferred because of their ease of use, low level of training required and higher reproducibility. All BP monitors should be calibrated periodically.[13]

2) Protocol for diagnosis and management of hypertension

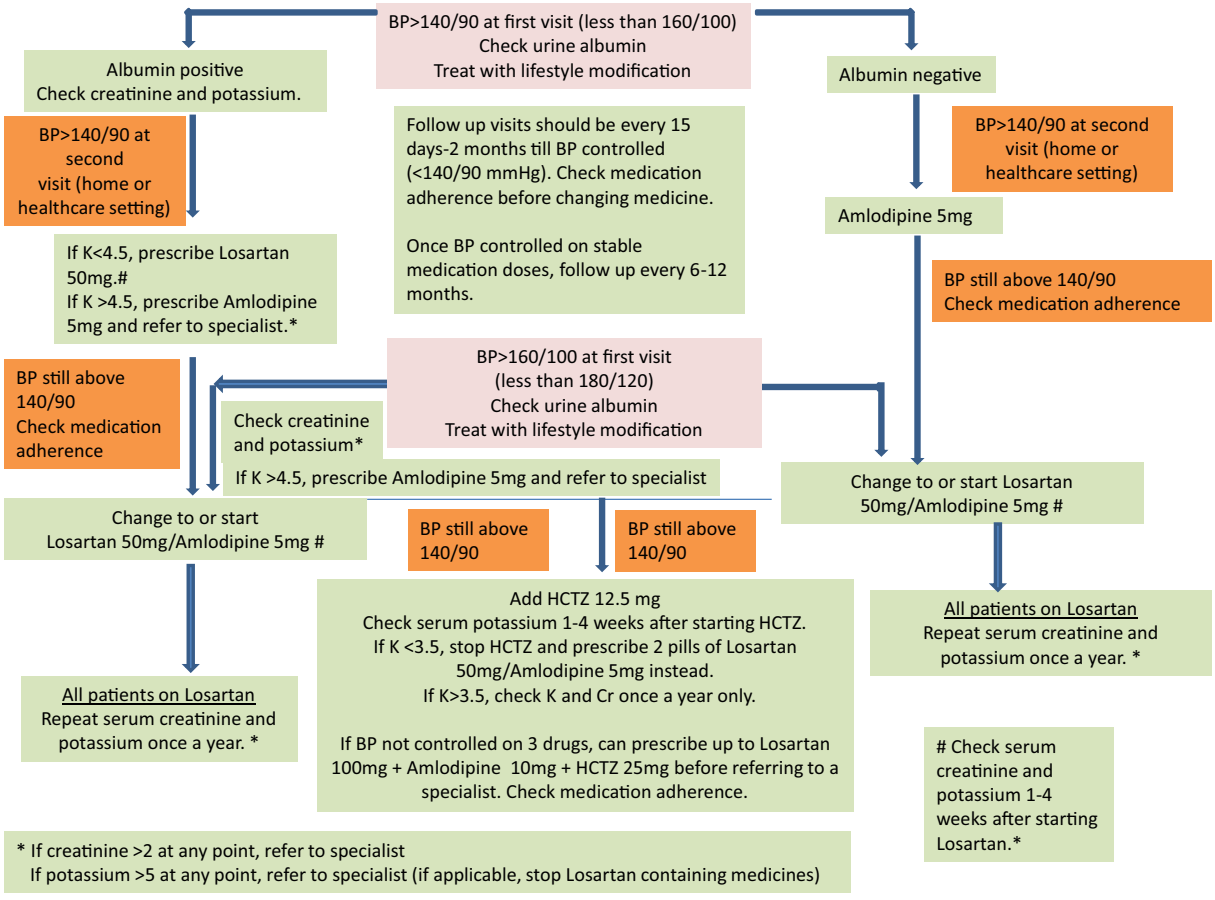
India has a strong tradition of using well defined protocols to manage complex diseases, through a primary health care approach. For tuberculosis, a clearly defined drug strategy through the DOTS model has led to impressive progress.[14] For children, the IMNCI (Integrated Management of Neonatal and Childhood Illnesses) model is widely used.[15] Through these models, complex diseases are simplified, sharpening focus on the most important elements of a disease and shutting out the noise.

For hypertension, the high costs of the absence of such a model is obvious. Most healthcare providers are faced with a plethora of choices in treating hypertension, ranging from thresholds at which to start drug therapy, choice of antihypertensive agent and goal blood pressure. The presence of co-morbidities and the elderly present further choices to be made. While existing guidelines can help, there is substantial variation between the guidelines on all the above parameters.[16] Moreover, most guidelines seek to guide, and still leave practitioners with considerable choice. In the absence of a clearly defined protocol to use, there is substantial variation in practice, likely leading to overuse of unnecessary investigations, underuse of necessary investigations and suboptimal choice of drugs-all leading to high cost and suboptimal outcomes.

In order to improve outcomes and simplify the choices that healthcare providers have to make, a health system wide protocol that is locally adapted and acceptable is crucial. Such a protocol should have the approval of all relevant stakeholders, including all physicians involved in prescribing drugs for hypertension (general practitioners, specialists and sub-specialists), the hospital pharmacy and relevant hospital administrators. This work can be

accomplished through a committee, and the protocol can be updated as needed. The committee will also be in charge of publicizing the protocol in the health system, and taking steps to monitor and improve adherence to the protocol.

In Fig. 1, we have proposed such a protocol. We believe this protocol will be suitable to a wide variety of systems of care in India. However, a given hospital system can also adapt and modify the protocol according to its needs. The algorithm should be printed on two sides of a laminated card for distribution within the hospital system. To complement the treatment algorithm, we added a four page handout (supplementary appendix) that focuses on benefits of blood pressure control, measurement of blood pressure, diagnosis of hypertension, blood pressure thresholds to initiate drug treatment, goal blood pressure, preferred medications and non-pharmacological treatment of hypertension. The handout also has a reference list of oral antihypertensive drugs with their dose ranges and dosing frequency. Guidance regarding additional laboratory testing, seeking specialist opinion and other points not covered otherwise are listed in a 'Things to keep in mind' section. To implement the model, providers need to be adequately trained to perform medication titration and/or lifestyle counselling, as per their qualifications. To this end, we have attached a one day training



Lifestyle modification

Salt restriction (up to 5mmHg SBP reduction)

Increase in physical activity (5mmHg reduction)

Weight loss (1mmHg SBP reduction per kg weight loss)

Increased intake of fruits/vegetables/dairy products (up to 10 mmHg SBP reduction)

Smoking cessation/restricting alcohol intake

For frail individuals >70 years of age, with BP>160/100 at first visit, consider starting one drug (either Losartan 50mg or Amlodipine 5mg, depending on urine albumin) instead of Losartan 50mg/Amlodipine 5mg combination.

Fig. 1. Protocol for management of hypertension.

guide that can be used as a template for providing this needed training. The two sided laminated card and four page handout can be distributed to all relevant physicians-electronically as well as in print. The same information can be posted on the hospital website. In addition, the laminated cards can be posted in clinics where people with hypertension are seen.

3) Informing each patient of his current blood pressure, goal blood pressure and his prescribed blood pressure medications at each visit.

Since hypertension is usually a lifelong condition, patient engagement is vital to successful management. There should be an established process to provide each patient with a written record of his current blood pressure, goal blood pressure and his current list of anti-hypertensive medications (such as through a patient card or prescription). This information should also be communicated verbally to patients during their physician encounter.

1.3.4. Add on features

1) Designating non-physician healthcare workers to provide education regarding hypertension at the time of diagnosis and follow up.

Non-physician health workers such as nurses, pharmacists, AYUSH practitioners or community health workers can be trained to provide education for hypertension. These workers can be trained through a weeklong course totaling 15–20 h, covering essential aspects of hypertension.[17] It is recommended that workers employ an education tool such as a flipbook or online presentation to communicate with patients, as it helps standardize education delivery and maintain a minimum quality of instruction.

At the time of diagnosis, initial education can be delivered in a 20–30 min slot. For pharmacists, the education can be delivered at the time of medication pick up. Nurses can educate patients (individually or in groups-in a designated room) as patients wait for their appointments. Community health workers can deliver it in community based settings or in patients' homes.[18]

2) A closed pharmacy system that provides hypertension drugs at below typical market prices through bulk purchases.

A closed pharmacy (such as in government or trust hospitals) is integrated with the healthcare system, and drug purchases are made directly by the healthcare system for its patients. By bulk purchasing common anti-hypertensive drugs such as Amlodipine and Losartan (or Telmisartan), considerable savings can be achieved. This can lead to lower drug prices for patients, and make obtaining medication more convenient for patients.

3) Incentivizing 30–90 day drug purchases, rather than shorter periods.

At initiation of drug therapy, it is reasonable to prescribe medicines for a short duration of 2–4 weeks, as therapy will likely be titrated. However, patients on a stable medication regimen should be encouraged to buy medicines for 30–90 days, rather than a shorter duration. Frequent medication refills increase the chances of skipped doses and poor blood pressure control.[19] For health systems that have a closed pharmacy, systems should be put in place to provide longer prescription duration for people with hypertension. Additionally, patients should be financially incentivized to buy longer prescriptions of 30–90 days, rather than shorter durations. This can be achieved by cross-subsidizing longer term prescriptions with more expensive short term prescriptions.

1.3.5. Rationale of the protocol

A) A urine albumin first approach

At the initial visit for a patient with a blood pressure >140/90 mmHg, the goal of the treating physician is threefold. Firstly and most importantly, the prescribed therapy should be the most effective, maximizing improvement in cardiovascular outcomes while maintaining safety. Second, the prescribed investigations should be the bare minimum needed to achieve the first goal, again while maintaining safety. Third, the entire approach should aim to minimize cost, without sacrificing any effectiveness or safety.

In otherwise healthy patients (without coronary artery disease or heart failure) with a BP > 140/90 mmHg, urine albumin is the only test that changes choice of drug therapy. For patients who have albuminuria, ACEi/ARB therapy has been shown to be superior to calcium channel blockers, and this is reflected in nearly every guideline.[20] For all other patient groups, including people with non-proteinuric CKD, there is no strong evidence that a particular drug class leads to superior outcomes.[21] Due to the primacy of urine albumin in determining choice of drug therapy, our protocol employs a urine albumin first approach. An additional advantage of urine albumin is that it is inexpensive and a point of care test, which allows it to be delivered in non-traditional settings with immediate results-thus optimizing patient convenience. Urine dipstick testing has also been shown to be comparable to more expensive tests such as urine albumin to creatinine ratio and albumin excretion rate.[22] However, care needs to be taken to use standardized urine albumin kits.

To maximize safety, patients who have a positive urine albumin test undergo a serum creatinine and potassium check, before proceeding with ARB therapy. On the other hand, given that the risk of hyperkalemia is exceedingly low in people with a normal urine albumin, these patients can start ARB without a serum creatinine and potassium check, and can get it checked 1–4 weeks after starting the ARB instead.

B) Choice of drugs

In patients with a normal urine albumin, Amlodipine is our drug of first choice and its dose is maximized before adding a second drug. Amlodipine is inexpensive, well tolerated, has no serious side effects and requires no lab monitoring, making it an ideal drug for these patients. Multiple studies comparing CCB to other antihypertensive agents have shown that CCBs are equivalent to other drugs when equal blood pressure reduction is achieved in each arm.[23]

After maximizing Amlodipine, there is a choice of three major drug classes-beta blockers, ACEi/ARB or diuretics. Our protocol chooses an ARB over the other drugs for four reasons. First, ARB is preferred over ACEi because of a lower incidence of cough and angioedema. Second, beta blockers have been shown to be a suboptimal choice in multiple studies, showing no difference in overall mortality when compared to placebo, despite producing a significant lowering of blood pressure.[24] Moreover, the most commonly used beta blocker in India, Atenolol, has been associated with a significant increase in stroke, cardiovascular mortality and overall mortality when compared to other drug classes.[25] In addition, treatment discontinuation due to adverse effects is more common with beta blockers, as compared to RAS inhibitors.[24] Third, ARBs decrease the lower extremity edema associated with Amlodipine, making Amlodipine more easily tolerated. Additionally,

since patients with a positive urine albumin use an ARB first strategy, physicians will be comfortable overall with using ARBs. Third, diuretics have little advantage over ARBs, as both drug classes require lab monitoring. Moreover, given that India is a tropical country with a hot climate and has a high incidence of acute diarrheal illnesses, there is a risk of hypokalemia during the summer and periods of acute illness that may be more challenging to monitor and treat.

Once a patient is on an ARB and Amlodipine, with blood pressure still above goal, a thiazide diuretic is added as a third drug. With the concomitant use of a thiazide and an ARB, the risk of hypokalemia with a thiazide is considerably minimized, ameliorating the above concerns. The cost of thiazide diuretics and beta blockers are about the same, creating no reason to prefer beta blockers at this stage, especially given the latter's inferior effectiveness profile.

C) Threshold to start treatment and goal blood pressure

In order to maximize ease and effectiveness, our threshold for starting drug treatment and goal of drug treatment is 140/90 mmHg. This threshold and goal is constant across all age groups, including the elderly. This is consistent with evidence from the SPRINT trial and updated guidelines, that clearly show a benefit of lower blood pressure goals in the elderly.[26]

While a lower goal of 130/80 mmHg may benefit people at high cardiovascular risk, we did not recommend that in our protocol to maximize simplicity. However, it is mentioned in the handout as an additional consideration for people who have achieved the goal blood pressure of <140/90 mmHg.

D) Additional lab testing

Testing for urine albumin, serum creatinine and serum potassium-essential tests for managing hypertension, is outlined in our protocol as described. Additional testing recommendations are laid out in the handout that is provided to the physicians. Similar to the Government of India protocol, all patients with hypertension are recommended to be screened for diabetes, though this does not have to be done at the time of the hypertension diagnosis. Due to ease and low cost, screening can be safely done with a random blood sugar; those with a value > 140 mg/dL are to be tested with fasting blood sugar or HbA1C to confirm diagnosis of diabetes.[27]

Lipid profile testing is recommended on follow up visits only, once patient is adherent with his anti-hypertensive medication regimen with controlled blood pressure. This is to minimize testing that will not affect treatment decisions, as barriers to blood pressure control need to be addressed prior to considering initiation of a statin. Given that statin initiation is guided by overall cardiovascular risk, and not just the lipid profile, patients with concurrent diabetes or LDL >160 mg/dL should be started on a statin. Patients with established atherosclerotic vascular disease are also recommended to be on a high dose statin.

An ECG and thyroid function test are left to provider discretion (and depending on available resources), since there is no good evidence to recommend them on a routine basis.

E) Frequency of follow up

After the initial visit, the first follow up visit should be scheduled in 2–4 weeks to monitor labs (if needed per protocol), blood pressure response and titrate drug therapy. Subsequent follow up visits should be tailored to the level of blood pressure control. It is advisable to follow up every 2–4 weeks till blood pressure control is obtained. Once a patient's blood pressure is well controlled on a stable regimen, follow up can be scheduled at 6–12 month intervals.

2. Discussion

We have proposed a model to strengthen the institutional management of hypertension in India. We believe that given India's successful history of using protocols (in addition to guidelines) to treat complex diseases, instituting such a protocol-based approach in institutions will have wide acceptability. Going forward, we propose that the NPCDCS should also consider adopting a similar approach. It can also be useful for management of patients with hypertension by Mid- Level Health Providers (MLHP) at the Health and Wellness Centers (HWCs) under the Ayushman Bharat initiative, under supervision.

Recently, the World Hypertension League and Resolve to Save Lives published treatment protocols to improve management of hypertension globally.[11] Our model is consistent with the basic principles of their treatment protocols, prioritizing use of Amlodipine and an ARB. However, effective management of hypertension at a system wide level will require measures beyond treatment protocols. Clear guidance regarding choice and frequency of laboratory testing, optimizing pharmacy usage and instituting systems to enhance patient education are equally important components of a hypertension care model.

The primary limitation of our model is the lack of demonstrated real world evidence for its effectiveness and challenges in its implementation. However, this is a general limitation of most treatment protocols. Towards, this end, we plan to evaluate the effectiveness of our model at Shree Krishna Hospital, Gujarat through a quality improvement framework. We encourage other Indian institutions to employ a similar model and share their experiences. A protocol driven approach to treating hypertension, within a larger model that focuses on optimizing blood pressure control, has the potential to substantially decrease the mortality and morbidity from hypertension in India.

Declaration of competing interest

All authors have no conflict of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ihj.2019.11.257.

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