Letter to the Editor Regarding the Brazilian Guidelines of Hypertension – 2020

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Dear Editor

Initially, the Brazilian Society of Cerebrovascular Diseases (SBDCV) congratulates the Department of Arterial Hypertension of the Brazilian Societies of Cardiology, Hypertension, and Nephrology for the Brazilian Guidelines on Arterial Hypertension 2020 publication.[1] Our aim is to raise some issues related to stroke care and BP management in acute setting, an important topic of discussion and controversy. The guideline correctly attributes arterial hypertension as the main cause of ischemic stroke and intracranial hemorrhage. We would like to point out some issues regarding managing blood pressure (BP) in these patients.

Regarding BP control in patients with intracranial hemorrhage (ICH), the guidelines mentioned that "robust studies suggest that reducing BP (within 6h) to values <140/90 mmHg does not decrease important primary events, including mortality" (item 10.6.1), according to INTERACT-2 study.[2] The physiological response of increased BP levels in ICH is correlated with worse prognosis and hematoma expansion, as demonstrated in the INTERACT-1 study.[3] Subsequently, the INTERACT-2 trial compared intensive BP control [target systolic blood pressure (SBP) <140 mmHg] versus the guidelines-recommended levels (SBP <180 mmHg) in acute setting, and the primary outcome of death or functional dependence (modified Rankin Scale, mRS: 0-3 versus 4-6) were similar (55.6% in conventional treatment versus 52% with aggressive BP treatment, p=0.06).[2] Further, there was no significant difference in the shift distribution pattern in mRS. However, the ordinal analysis revealed a lower disability (mRS 0-2) with intensive BP treatment, with an odds ratio of 0.87 (95% confidence interval, 0.771.00; p=0.04), and additional better physical and mental quality, measured by EQ-5D scale.[2] Contrary to the 2020 Brazilian Arterial Hypertension Guidelines recommendation, and based on the results of this ordinal analysis, the current recommendation of the American Heart and American Stroke Association,[4] endorsed by the SBDCV, is to achieve an acute reduction of SBP in patients with ICH who present with high SBP (150-220 mmHg) without contraindications for intensive BP control. The SBP target is <140 mmHg, which can improve functional clinical outcomes. There is no sufficient data to systematically support the safety and effectiveness of the acute management of BP in patients with SBP >220 mmHg; however, a more aggressive reduction of BP in this profile of patients is reasonable, using intravenous drugs, dose titration and strict BP control in the acute phase.[4] Based on this trial and the recommendation of the societies mentioned above, we would like to suggest the correction of items 10.6.1 and 13.7 of the brazilian hypertension guideline, that states no benefit in reducing severe disability with intensive BP control.[1] We also emphasize that the proposed reduction in BP is safe.[2-4] The SBDCV does not recommend the proposed target of SBP <180 mmHg for acute ICH management.

Regarding the management of BP in acute ischemic stroke (IS), topic 10.6.2, we emphasize that BP reduction in patients who are candidates for thrombolysis should be performed when the values are >185/110 mm Hg in the first hour. After the end of thrombolysis, the recommended BP value is <180/105 mmHg in the first 24 h, as indicated in the hypertension guideline.[1]

Regarding topic 13.7.1, the recommended BP for the indication of thrombolytic treatment is <185/110 mmHg, and intravenous antihypertensive medication should be started immediately above this level. A contraindication to thrombolysis occurs only if refractory elevated BP occurs in three consecutive measurements, with an interval of 5 min, despite optimized treatment.

We are also unaware of the reference that suggests immediate BP reduction in patients with a transient ischemic attack (TIA), as suggested in Table 10.2.[1] In contrast, TIA is considered an equivalent to acute IS, and must be managed with the same parameters of a non-thrombolysed IS, or a IS not submitted to thrombectomy, that is, BP tolerability up to 220/120mmHg and suspension of oral antihypertensive drugs in the hyperacute phase of care, unless there are other impeding cardiovascular conditions to allow these blood pressure levels (e.g., acute myocardial infarction, aneurysm, or aortic dissection).[5] Thus, it is also worth reviewing the topic and table of recommendations

Keywords

Hypertension; Intracranial Hemorrhage; Isquemic Stroke; Risk Factors; Mortality; Acute Treatment; Blood Pressure.

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DOI: https://doi.org/10.36660/abc.20210873

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for immediate BP reduction in TIA, as well as no reduction of BP in all types of IS (Table 10.2).

The denomination of stroke in our country is quite diverse, depending on the state or region of the country (use of terms "AVC - Acidente Vascular Cerebral" and AVE - Acidente Vascular Encefálico"), a fact that has been demonstrated in a Brazilian study.[6] For this reason, recently, the portuguese term "AVC" have been widely recommended by specialists in the field, patient organizations, together with the SBDCV and the Scientific Department of Cerebrovascular Diseases of the Brazilian Academy of Neurology, as well as in academic research, campaigns, educational activities, press releases and interviews, with the purpose of better educate the population regarding the disease, and to avoid using other terms that may confuse and hinder the rapid recognition, essential for immediate stroke treatment and better prognosis. Thus, for future hypertension guidelines, we suggest the use of this recommended standardized portuguese terminology: "AVC - Acidente Vascular Cerebral", instead of other terms, like "AVE".

Finally, we are grateful for the opportunity to present our observations. On behalf of the Brazilian Society of Cerebrovascular Diseases and the Scientific Department of Cerebrovascular Diseases of the Brazilian Academy of Neurology, our goal as a stroke society is to help and contribute with other partners in future discussions of topics involving managing patients with stroke.

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Reply

Response to the Brazilian Society for Cerebrovascular Diseases and the Scientific Department on Cerebrovascular Diseases of the Brazilian Academy of Neurology.

First, we would like to express our respect and gratitude to the reviewers for the careful reading of the 2020 Brazilian Guidelines on Arterial Hypertension (DBHA2020)[1] and for the comments on Chapter 10, more specifically on the topic 10.6 that addresses arterial hypertension (AH), and hemorrhagic and ischemic stroke.

It is worth pointing out that the DBHA2020[1] was developed by the collective effort of the Brazilian Society of Cardiology through the Department of Arterial Hypertension, the Brazilian Society of Hypertension, and the Brazilian Society of Nephrology, represented by 97 specialists chosen by scientific criteria. During the entire year of 2020, these experts worked together to construct this document, which was achieved by weekly meetings of the directive committee, two meetings with 18 chapter coordinators, and two plenary sessions of all members involved in the elaboration of the DBHA2020. The final text represents the opinion of the majority of this work group.

We will now discuss the questions raised by the authors of the Letter to the Editor, by first making the following considerations:

The question about the treatment target for HA, the time when treatment should be initiated, and the drugs of choice in cerebrovascular events is certainly a complex and challenging issue.

In January 2021, a narrative review summarized the main studies on ischemic and hemorrhagic stroke and pointed to a conservative approach in the acute phase, in addition to associated limitations that cannot be overcome even when strategies proposed by systematic reviews and meta-analyses are used.[2]

Regarding the item 10.6.1 of the DBHA2020,[1] which describes recommendations on the treatment of AH in the acute phase of hemorrhagic stroke: "In case of an increase in blood pressure, the odds of hematoma expansion, death and worse prognosis may increase. Robust studies have suggested that the reduction of blood pressure (within six hours) to levels < 140/90mmHg does not reduce important primary events, including mortality. Therefore, the immediate reduction of blood pressure in case of hemorrhagic stroke is not recommended, unless systolic blood pressure is > 220 mmHg ". We reinforce that the text states that there is no evidence of reduction of primary events, which is in accordance with the Letter to the Editor submitted by the Brazilian Society of Cerebrovascular Diseases and by the Scientific Department of Cerebrovascular Diseases of the Brazilian Academy of Neurology, which affirms: "the phase 3 INTERACT-2 study evaluated the strict control of blood pressure in these patients, with a target systolic blood pressure below 140 mmHg *versus* the target recommended by guidelines (<180mmHg). Considering the primary outcome of death or functional dependence (modified Rankin Scale – mRS: 0-3), no statistically significance was found in this outcome by reducing blood pressure levels in the acute phase".

In our opinion, it is not appropriate to adopt guidelines' recommendations based on results obtained from secondary objectives, when the primary objective was not achieved. In Chart 10.2, the suggestion of reducing blood pressure (within six hours) in the acute phase after a hemorrhagic stroke was in line with the decision of the general coordination, chapter coordination and the plenary session, that this approach was in accordance with current scientific evidence.

As for the acute phase of ischemic stroke (item 10.6.2), the recommendation of the DBHA2020 is to reduce systolic blood pressure to values below 180 mmHg and diastolic blood pressure to values below 105 mmHg only for patients candidate for thrombolysis, with no evidence of clinical benefit for other patients. (Chart 10.2). Based on the close reading of the Letter to the Editor, we understand that there is a consensus on this recommendation, which coincidently is the same of the recently published European Stroke Organization (ESO), guidelines[3] and of the American Heart Association and American Stroke Association.[4]

In response to the comment on the management in the acute phase following a transient ischemic attack, we are in line with recommendations of other scientific societies, like the last European guidelines on arterial hypertension published in 2018 which recommends the same approach (see page 3086).[5]

In the ESO guidelines,[3] whose 11 authors work in the field of Neurology, the first sentence expresses the constructive possibility of divergence: "The optimal blood pressure (BP) management in acute ischemic stroke (AIS) and acute intracerebral hemorrhage (ICH) remains controversial". The document concludes that further randomized controlled studies are needed to support treatment targets, time and strategies to reduce blood pressure levels in the acute phase in different subgroups of patients with stroke.[6]

Finally, concerning the nomenclature used in the DBH2020[1] – stroke – it was considered by most specialists as the most appropriate to be used in the current document. We understand that this is a semantic rather than an anatomic issue, and that cerebrovascular disease may involve any encephalic structure. Curiously, the descriptor brain vascular accident has 28 alternative synonyms, including its abbreviation, BVA, recognized by the virtual health library.[6] However, this suggestion should be further discussed in a new update of the guideline, because of the arguments presented, and the familiarity with the term stroke by physicians in general.

Once again, we are grateful for the opportunity to have this technical and intellectual debate, and we hope that we have clarified the questions raised.

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