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ORIGINAL ARTICLE

The UrgeRe (Urgenze Ipertensive: Un Progetto Educazionale Fondato Sulla Vita Reale, Hypertensive Urgencies: A Project in the Real World) Project

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Abstract
The approach to hypertensive emergiencies (HE) and urgencies (HU) may be different according to local clinical practice, despite recent guidelines and position papers recommendations. The Italian Society of Hypertension (Società Italiana della Ipertensione Arteriosa, SIIA) developed an online survey, in order to explore the awareness, management and treatment of HU in Italy, sending by e mail a 12 items questionnaire to the members of the SIIA. The results show that the definition of HU was correctly identified by 62% of the responders. Most physicians identified the role of pharmacological therapy or legal/illegal substances abuse as possible cause of BP elevation; the use of a benzodiazepine drugs was considered worthwhile by 65% of responders. The prescription of diagnostic test and drug administration significantly differed from guidelines recommendations and only 57% of the physicians reported to treat HU with oral drug administration. Sub-lingual nifedipine was prescribed by 13% or responders. This survey shows the need to further spread the updated scientific information on the management and treatment of HE and HU, along with the improvement of the interrelationship with the general practitioner health system in Italy.

1 Introduction

In most recent years the diagnostic approach and the treatment of hypertension have gained interest by patients and physicians. Acute elevations in blood pressure (BP), usually defined as ≥ 180/110 mmHg, may present with highly heterogeneous profiles ranging from absence of symptoms to life-threatening target organ damage [1–3]. The rate of hospitalization has significantly increased in the last 10 years while the related mortality has declined in USA [4], while few epidemiological data have been collected in Europe [5–9].

Increased BP (above 140/90 mmHg) was found in more than 30% of patients admitted to the Emergency Departments (EDs) [10]. The association of an acute and severe rise in

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blood pressure with an acute end-organ damage, influences patients' prognosis and is usually defined as hypertensive emergency (HE). However, the same amount of BP increase may be observed in the absence of acute end-organ injury in a larger number of patients/subjects and has been recently renamed by the term hypertensive urgency (HU) or uncontrolled hypertension [3, 11]. Because of pain and/or anxiety frequently present in patients admitted to the ED, elevated BP levels are commonly observed, although the value of increased BP measurements is usually not adequately taken into account and the influence of different stressors is overlooked [12]. Oras et al have recently shown that raised BP in the ED is significantly associated with increases in incident ASCVD, MI, or stroke in the long-term [13], reinforcing the paramount importance of a correct recognition and therapeutic approach in these different groups of clinical conditions.

The American Heart Association statement has given some recommendations, guiding the appropriate management of acutely elevated BP [1], the 2018 European Society of Hypertension/European Society of Cardiology Guidelines [2] and a focused statement of the European Society of Cardiology [3] gave appropriate attention to hypertensive emergencies and urgencies.

The GEAR (Gestione delle Emergenze e urgenze in ARea critica) project [14] reported the results of a questionnaire, prepared by the group of Young Investigators of the Italian Society of Hypertension (SIIA) aimed to evaluate the awareness, diagnosis and treatment of hypertensive emergencies and urgencies in Italy. Overall the results have underscored the incomplete knowledge, some wrong beliefs and behaviors in the treatment of hypertensive urgencies, including the use of intravenous administration of drugs and an excessive use of sublingual (s.l.) nifedipine [15].

We therefore considered worthwhile to administer another questionnaire to physicians members of the SIIA, after having conducted educational initiatives in national and local meetings, aimed to improve both the management of hypertensive emergencies and urgencies and the interrelationship with the general practitioner health system.

2 Methods

SIIA developed a survey on HU and HE called UrgeRe (Urgenze ipertensive: un Progetto educazionale fondato sulla vita Reale, Hypertensive urgencies: a project in the Real world). This survey was administered between June 10th 2020 and September 20th 2020 through a web platform to the members of the SIIA. The invitation to join the survey was sent by an email describing the purpose with a direct link to the questionnaire. The participation was voluntary and confidential and each responder could withdraw at any point. The questionnaire consisted of 12 different items regarding diagnosis, management, treatment of HU and HE, methodology for BP measurements, eventual patients' admission and follow-up after discharge; some were multiple choice questions, while others required only one answer (supplemental material). The survey was developed according to the 2018 ESH/ESC hypertension guidelines [2].

2.1 Statistical Analysis

We reported continuous variables as mean ± SD. Categorical variables, were expressed as frequencies and percentages. The chi-square distribution was used to compare categorical variables. Differences between continuous variables were calculated by Student's t-test. Data were analyzed using excel system, and Statistical Package for the Social Sciences version 25 (SPSS Inc., Chicago, IL). A two-tailed p-value < 0.05 was considered statistically significant in all analyses.

3 Results

We collected 245 questionnaires: 53% from Internal Medicine Departments, 12% from Cardiology Departments 9% from EDs and from Emergency and Urgency Medicines, 24% from other departments and 1% from Intensive Care or Stroke Units.

Among participants (18–35 years 29.4%, 35–55 years 30.3%, 55–65 years 30.2% and > 65 years 10.2%; 64% males) 73% were physicians with different specialties, 20% were residents, 7% were general practitioners or private practice doctors.

The definition of HU, according to ESH/ESC 2018 guidelines [2] was correctly identified by 62 % of the responders (Fig. 1). Most physicians (84%) declared a low estimated annual rate of HU (between 0 and 25%) among all patients followed by each of them.

Physicians reported to repeat at least 2 office BP measurements (35%) or more than 2 BP measurements (22%) while few adopt unattended office BP measurements (10%) and none accepted to rely on a single measurement. The prescription of benzodiazepines was considered a reasonable therapeutic choice by 65% of participants.

When participants were asked about BP cuffs availability, most of the responders (94%) used of standard cuffs (24–32 cm), while large (32–42 cm) or extra-large (> 42 cm) cuffs were less frequently available (70% and 63% respectively). BP measurement was performed in both arms by 34% of participants.

The role of pharmacological therapy or legal/illegal substances abuse as possible cause of BP elevation was investigated: (87% of participants identified illegal substances abuse, steroids, vasoconstrictor agents or steroidal anti-inflammatory drugs as the most frequent causes, while 112

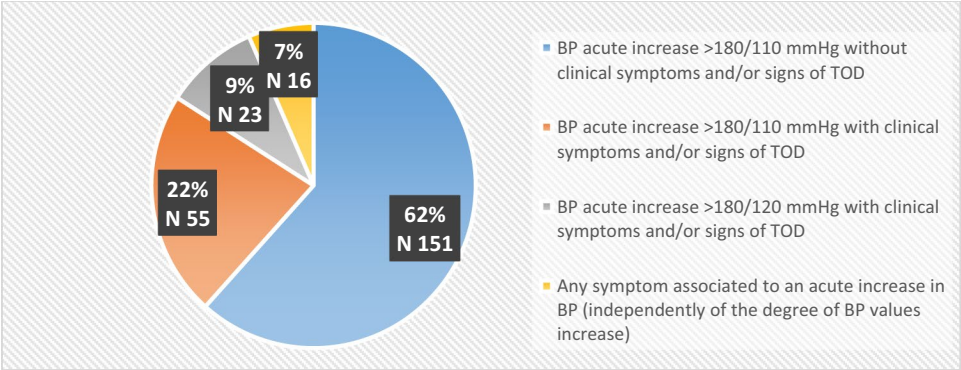

Fig. 1 Distribution of different answers regarding the definition of hypertensive urgency. BP, blood pressure; TOD, target organ damage

Table 1 Causes of acute increase in blood pressure (BP)

	% of positive answers
Steroids	87
Vasoconstrictor substances	86
Non steroid anti-inflammatory drugs (NAIDS)	84
Abuse substances	87
Oncology therapies	46

responders suggested that antineoplastic drugs could induce an acute BP elevation. One-hundred fifty-four responders identified all 4 causes (abuse substances, steroids, vasoconstrictor agents and non-steroidal anti-inflammatory drugs) as most frequent drugs responsible for an acute BP elevation (Table 1).

The diagnostic tests most frequently prescribed to exclude an hypertensive emergency were: an electrocardiogram (77%), urine and blood samples for proteinuria and creatinine (58%), a fundus oculi examination (49%) blood samples for BNP and troponin evaluation (27%), echocardiography (18%), 24 h blood pressure monitoring (18%), brain CT scan (17%), chest X-ray (15% or chest ultrasound (4.5%). No laboratory or instrumental tests were suggested by 14% of responders to differentiate a HE from an HU.

Only 57% of the physicians reported to treat HU with oral drug administration, although in 30% of the cases the use of intravenous (i.v.) administration was indicated; intramuscular (i.m.) and s.l administration was preferred in 2% and 11% of the cases. The use of a benzodiazepine drugs was considered worthwhile by 65 % of responders (Fig. 2b).

When the treatment of an HU occurring at patients' home was investigated, the drug most frequent prescribed was a calcium channel blocker, given by oral administration (59%), followed by the increase of daily therapy regimen dosages (49%) or the association of another drug (45%). The use of an oral administration of an ACE-inhibitor, of an angiotensin 2 receptor antagonist or of oral furosemide was suggested by 40%, 22% and 30% of physicians, respectively. Thirty-two physicians suggested the administration of s.l. nifedipine (13%) and 21 (9%) would have sent the patient directly to the ED.

For patients with an HU admitted to the ED or seen in the hospital, the use of intravenous or oral therapy was selected by 37% and 40% of responders, respectively, while 49 physicians would have used both oral and intravenous drug administration. Among intravenous administered drugs, furosemide (n = 94), and/or nitroglycerin (n = 89) and/or labetalol/urapidil (n = 99) were chosen by in 35 % of physicians. The oral administration of a calcium channel blocker was the preferred choice by 48% of responders (n = 118), followed by the use of an oral administration of an ACE-inhibitor, of an angiotensin 2 receptor antagonist or of oral furosemide; 36 physicians would have used a fixed combination. Twenty-seven (11%) physicians would have used s.l. nifedipine and 57 would have used a pain-killer drug in the presence of any painful clinical condition (Table 2).

When the target BP to be reached and the time needed to decrease BP were explored, 52% of physicians suggested a target BP < 140/90 mmHg in 24–48 h, while 21% suggested a reduction below 160/100 mmHg in 30 min, 15% considered a target of 140/90 mmHg in 60 min and 29 (12%) of participants selected to consider a target below 160/100 mmHg in 48 h (Fig. 2a).

Among the management options after the occurrence of an HU, 109 physicians asked for a 24 h BP monitoring, while 104 physicians suggested a short term (2–3 days) follow-up visit and 92 considered a hypertension specialist consultation. An increase in the dosage of patients' drug therapy or a general practitioner re-evaluation were less frequently recommended.

After the occurrence of an HU, several options were given, including a 24 h BP monitoring, suggested by 109 physicians, 104 responders suggested a short term (2–3 days) follow-up visit and 92 considered a hypertension specialist consultation (with short term visit in 22 cases). An increase in the dosage of patients' drug therapy or a general practitioner re-evaluation were less frequently recommended.

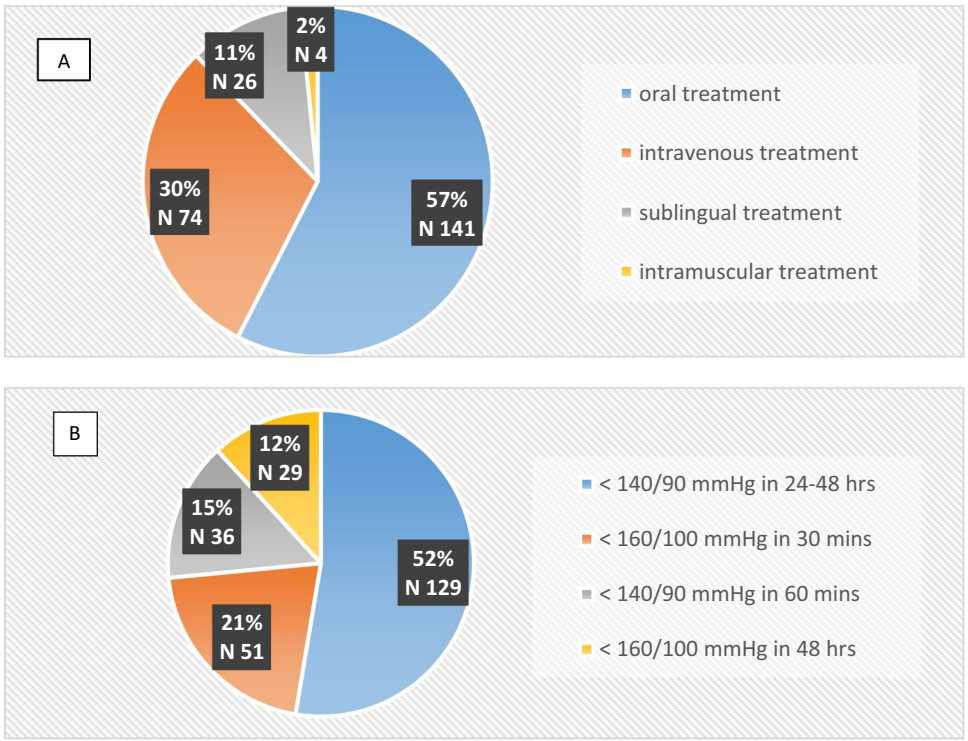

Fig. 2 **a** Frequency of different ways of administration of antihypertensive drugs in patients with a hypertensive urgency. **b** Frequency of target BP and time needed to reach the BP target in patients with a hypertensive urgency

Table 2. Medications prescribed to reduce blood pressure elevation in the hospital in patients with hypertensive urgencies

Drugs	Yes (n/245 responders, %)
Oral Calcium-antagonist	118, 48%
Oral Furosemide	26, 11 %
Oral ACE-inhibitor	91, 37%
Oral Labetalol	99, 40%
Oral fixed combination	36, 15%
i.v. Nitrates	89, 36%
i.v./i.m. Clonidine	59, 24%
i.v. Furosemide	94, 38 %
s.l. Nifedipine	27, 11%
t.d. Nitrate	7, 3%
Pain killer if presence of pain	59, 24%

Yes, means that the physician was keen to prescribe the drug

i.v. intravenous, *i.m.* intramuscular, *s.l.* sublingual, *t.d.* transdermal

Some differences in the definition of HU were observed, being GPs the group with the lowest percentage (33%) of correct identification of clinical characteristics associated with a HU. We did not observe any significant difference in most of laboratory and instrumental examinations and in the therapeutic approach for BP reduction. The prescription of 24 h ABPM was less frequently prescribed by emergency physicians (7%) than other specialists (45 to 50%), despite the difference did not reach statistical significance.

4 Discussion

The UrgeRe survey was directed to physicians members of the SIIA, more deeply involved in the management of hypertensive patients, in order to investigate the clinical approach to HU and HE in daily clinical practice. This survey represents an update of previous data collected in the framework of the GEAR project [14], which included healthcare providers working mainly in the ED and intensive care units throughout Italy. A slightly lower proportion of residents participated to the UrgeRE survey as compared to the GEAR one (20% vs 27%, respectively); this suggests an older age of responders to the UrgeRE questionnaire, although data on GEAR participants' age is not currently available.

Altogether, a substantial proportion (80%) of the sample was able to correctly identify an HU, while about 90% of the interviewed gave a correct definition for HE. This result may be influenced by the publication of the recent ESH/ESC guidelines [2] and by the position paper by the ESC Council on hypertension [3]. In this document it is suggested to abandon the term "HU", since there is no clear evidence that treatment in patients who lack acute clinical evidence of hypertension-mediated organ damage should be different from that usually proposed to patients with asymptomatic uncontrolled hypertension [3], and consider the presence of an uncontrolled hypertension. The results of the previous GEAR survey, conducted before the release of the ESC Position Paper, found superimposable results, underscoring the need of a more precise definition and management of HU.

Most of the participants recognized the use of drugs including steroids, vasoconstrictor agents and NAIDS or toxic substances (cocaine/meth) as related to acute BP increase [1–3], while a slightly lower portion of physicians indicated anticancer drugs as possible cause of an HU [16, 17]. Therefore, the awareness of drug-induced hypertension is high among hypertension specialists, leading them to ask about any drug /substance use to properly identify possible causes of acute BP rise.

In addition, anxiety or acute pain were recognized as possible conditions contributing to the acute rise of BP and about a half of participants agreed on the use of an anti-anxiety drug such a benzodiazepine. Moreover, in the presence of acute pain, at least 24% of physicians would prescribe a pain killer drug. It is well known that patients with HU/HE, even when managed at home, are exposed to a stressful condition, which could itself raise BP levels [12]. In a small number of patients admitted to the ED and presenting with an HU, it has been shown that oral diazepam was associated to a SBP decrease SBP of more than 40 mmHg 3 h after administration [18]. Therefore, treatment with benzodiazepine may reduce the anxiety related to the clinical condition and associated adverse consequences.

As far as treatment options were investigated, only two thirds of participants correctly preferred oral BP lowering drugs for HU while were keen to use intravenous drugs in 30% of cases, confirming the lack of an homogeneous approach to the treatment of HU [19]. This was further shown when several drugs options were proposed, including both oral and i.v. administration; again, an oral calcium channel blocker was proposed by only 59 and 48% % of participants for the treatment of an HU at home or in the ED/hospital, respectively. Other reasonable options, such as the increase of the dosage of current antihypertensive treatment or the combination with another drug were also suggested by nearly half of participants.

The rate of physicians choosing the use of sub-lingual nifedipine for the control of BP in an HU was unacceptably high, and against the recommendations of guidelines [1, 2, 20] or expert consensus documents [3, 21]. Sub-lingual nifedipine, as well as the inappropriate prescription of i.v. drugs for HU might induce a reduction in BP levels which is too fast and possibly dangerous because of the risk of cerebral hypoperfusion [21]. Almost 25 % of responders considered appropriate the administration of clonidine in HU, despite its use by i.v. route has been suggested for the treatment hypertensive emergencies only, with caution on side effects such as sedation and rebound hypertension [3].

Other 2 important items investigated BP measurements, including the available equipment and the number of BP measurements. Concerning BP measurement technique, only two-thirds of the responders had universal or large/extra-large cuffs. It is well known that the use of a cuff with a bladder too narrow or too short for the arm circumference, may lead to an overestimation of BP levels, with inappropriate diagnosis or overtreatment of the patients; the opposite is true when a too large or to long bladder are used. Several guidelines and consensus documents, including the one released by the Italian Society of Hypertension, have highlighted the importance of a correct size of cuffs and bladders [1, 2, 22, 23]. Therefore, a wider use of different cuffs was expected being participants all members of the Italian society of Hypertension, while in the GEAR survey participants were mostly physicians working in EDs [13].

Participants suggested the use of several measurements of BP, in 25 % of cases on both arms. It is encouraging that none declared to rely on a single BP detection, since it could lead to overestimation of risk and that a small proportion of interviewed physicians have adopted the unattended BP measurement, especially if the patient is clearly alarmed.

Among the diagnostic tests, a detectable proportion of participants indicated fundus oculi examination as an important clue for the diagnosis of an HE, as malignant hypertension or hypertensive encephalopathy [24]; nowadays the lack of fundoscopy perfomed by an ophtalmologist may be overcome by the use of smartphone-based devices for ocular fundus photography, proven to be feasible and reliable in the ED [25]. Creatinine and urine dipstick were performed frequently prescribed, representing “standard tests” for all hypertensive patients, according to guidelines [1, 2]. Few participants indicated the use of lung ultrasound, possibly related to the higher sensitivity in the diagnosis of lung congestion [26].

Recent evidences suggest that the adequate approach to patients with HU is based on a strict outpatient-clinic visits. A retrospective cohort study including patients with HU showed that both patients sent home and those sent to the ED had the same, very low, incidence of major adverse cardiovascular events at 30 days [27]. Other more recent data have shown that even one single measurement of elevated BP taken in the ED, in the absence of acute organ damage, may predict an unfavorable event free survival during the following 10 years [12]. Very few data are currently available in order to differentiate the long-term clinical outcome of patients with HE or with HU or with uncontrolled hypertension. [27, 28].

The importance of the follow-up of patients with a HU, even after discharge by ED or hospital, is confirmed by the high proportion of physicians (71%) suggesting either a Hypertension Center visit or a short term outpatient visit or both. In a recent study, early follow-up after leaving ED with a diagnosis of hypertension, was associated with an improvement of long-term outcome [29] and the assessment by an hypertension specialist may represent the proper follow-up for these patients [12, 30, 31]. Hypertension reference

centers are widely distributed in Italy, with a regular activity 3 to 5 days/week, and easy contacts in order to improve clinic schedule appointments (https://siia.it/centri-e-ambulatori/) [30]. In all Excellence Centers and in most Hypertension Outpatients Clinics endorsed by the Italian Society of Hypertension, an ABPM, prescribed by 44% of participants to the survey may be performed, during all the weekdays. This result differs from the GEAR survey, in which very few ED physicians prescribed ABPM, despite its crucial role in confirming the diagnosis of hypertension or BP control under treatment [13, 30]. It would be therefore desirable to update protocols for improving access to an outpatient hypertension center after an HU.

4.1 Limitations

First of all, this is a descriptive analysis, being based on a survey, and we cannot extrapolate any causative relationship of the results. Data based on physician self-reporting, in the absence of more objective measures or quantifications, may have potential biases, although it may truly reflect the practice of HU management in Italy, being the questionnaire answer anonymous. In addition, the answers given to the questionnaire may not represent the opinion of a larger number of physicians members of the SIIA. No data related to the management of acute BP increase in pregnant women were collected, being pregnant women usually managed by gynecologists. Finally, the response rate (40%), despite a good distribution of the Italian country, was lower than expected.

5 Conclusion

In conclusion, this survey adds new information about the management of HU in Italy. The survey was directed to members of the SIIA, in order to evaluate the effect of new scientific statements and of some educational initiatives conducted in national and local meetings, aimed to improve the management of HE and HU. The results show the need to further spread the updated scientific information on the management and treatment of HE and HU, even among members of the SIIA, along with the improvement of the interrelationship with the general practitioner health system.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40292-021-00433-1.

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Declarations

Conflicts of interests Nothing to declare.

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