The pharmacists' and mobile applications' role in the treatment of hypertension

Lorka Tarnovski[1], Stjepan Frkanec[1], Andrea Šarčević[1], Tea Štrbac[1], Fran Rašić[1], Josip Lovaković[1], Bojan Jelaković[1]

[1] School of medicine, University of Zagreb

Abstract:

INTRODUCTION: Poor adherence is the main reason for inadequate blood pressure control. Pharmacists are highly accessible healthcare professionals, and it has been reported that community pharmacist-led interventions improved patients' blood pressure control and health outcomes. Some authors reported on beneficial effects of mobile applications (MA) on better drug adherence. The aim of this study was to identify subjects in general population who are likely to participate in such interventions.

METHODS: A total of 1228 (479 men, average age of 57.6 years, 748 women, average age of 57.2 years) participants enrolled in the EHUH 2 study (a random sample, nation-wide survey) and 424 participants (196 men, average age of 58.8 years, and 212 women, average age of 54.6 years) of the Hunt on the Silent Killer (HSK) (opportunistic screening on islands) were included in these analyses. The same questionnaire was applied containing questions about health issues, therapy, habits and opinion on pharmacists' and MA role in hypertension treatment.

RESULTS: Men of both projects had significantly higher systolic and diastolic blood pressure, BMI and waist circumference. In EH-UH 2 significantly more women had arterial hypertension and dyslipidemia,and more men suffered myocardial infarction. More HSK participants were in favour of pharmacists having a role in hypertension treatment (137 vs 34) than EH-UH 2 participants, and within EH-UH 2 there were statistically more negative answers, with women in majority ($\chi^2 = 4.74$, p = 0.029). The results of the EH-UH 2 pointed out a significant more negative attitude towards MA (403 vs. 823, p < 0.001) with hypertensive participants being the majority against the mobile applications (60.5%, $\chi^2 = 47.6$, p < 0.001).

Education was the most common answer for the role of the pharmacists in hypertension treatment (22.8%). Smartphone ownership was higher in younger age groups in both projects, with a significant difference between the age groups.

CONCLUSION: Pharmacists-led interventions (lifestyle support and adherence increasing programs) have to be individualized. This research showed the need to individualize the hypertension treatment approach to the different areas of Croatia, with less accessible area participants expressing the need for additional interventions in hypertension management.

Keywords: mobile applications, hypertension, adherence

Sažetak:

Uloga ljekarnika i pametnih telefona u liječenju hipertenzije

UVOD: Loša adherencija glavni je razlog za neadekvatnu kontrolu krvnog tlaka. Ljekarnici su vrlo dostupni zdravstveni djelatnici, a istraživanja su pokazala da su intervencije ljekarnika poboljšale kontrolu krvnog tlaka i zdravstvene ishode u zajednicama. Neki autori ukazali su na pozitivan učinak

mobilnih aplikacija (MA) na bolju adherenciju. Cilj ovog istraživanja bio je identificirati pojedince koji bi htjeli sudjelovati u ovakvim intervencijama.

METODE: Ukupno 1228 (479 muškaraca, prosječne dobi 57.6 god, 748 žena, prosječne dobi 57.2 god) ispitanika uključenih u EH-UH 2 projekt (randomizirani uzorak Hrvatske) i 424 ispitanika (196 muškaraca, prosječne dobi 58.8 god i 212 žena, prosječne dobi 54.6 god) Lova na tihog ubojicu (oportunistički screening na otocima) uključeno je u ovu analizu. U oba istraživanja korišten je isti upitnik koji je sadržavao pitanja o zdravstvenom stanju. terapiji, navikama i mišljenju o ulogama ljekarnika i MA u liječenju hipertenzije.

REZULTATI: Muškarci oba projekta imali su značajno viši sistolički i dijastolički talk, BMI i opseg struka. Žene su značajno češće imale hipertenziju i dislipidemiju, dok su muškarci češće imali infarkt miokarda u EH-UH 2 projektu. Više ispitanika Lova nego EH-UH 2 projekta bilo je za ulogu ljekarnika u liječenju hipertenzije (137 vs 34), a unutar EH-UH 2 projekta bilo je statistički više negativnih odgovora, od kojih je većina bila u skupini žena ($\chi^2 = 4.74$, p = 0.029). Rezultati EH-UH 2 pokazali su značajno negativniji stav prema MA (403 vs. 823, p < 0.001), većinom kod hipertoničara (60.5%, $\chi^2 = 47.6$, p < 0.001). Edukacija je bila najčešći odgovor kod pitanja koja se uloga ljekarnika očekuje u liječenju hipertenzije (22.8%). Posjedovanje pametnih telefona bilo je značajno češće u mlađim dobnim skupinama oba projekta sa značajnom razlikom među dobnim skupinama.

ZAKLJUČAK: Intervencije ljekarnika (podrška životnom stilu i programi podizanja adherencije) moraju biti individualizirni. Ovo istraživanje pokazalo je potrebu da se pristup liječenju hipertenzije individualizira prema različitim područjima Hrvatske, ukazujući također na to da stanovnici područja koja imaju manje dostupnu skrb izražavaju potrebu za dodatnim intervencijama u liječenju hipertenzije.

KLJUČNE RIJEČI: mobilne aplikacije, hipertenzija, adherencija

INTRODUCTION

1. EPIDEMIOLOGY AND GLOBAL BURDEN OF HYPERTENSION

Hypertension is one of the leading contributors to cardiovascular diseases (CVD). Because of its major role in the global burden of diseases, it is considered as one of the greatest public health problems in the world (1). According to the World Health Organization (WHO), CVD accounts for one-third of all deaths worldwide, with an estimated 17.9 million people dying in 2019. At the European level, they are responsible for 4.1 million deaths per year, which represents 43% of all deaths. Unfortunately, Croatia is also not behind the dark world statistics. According to the Croatian Yearbook of Health Statistics, CVD were the cause of 40% of deaths, and a total of 22,817 people died in 2020. The prevalence of hypertension shows an increasing trend in most countries of the world (2). According to WHO, an estimated 1.4 billion people in the world suffer from hypertension, meaning that the global prevalence of hypertension is about 31%. Although hypertension is associated with reversible risk factors and effective treatment is available, research shows that it is poorly controlled in the general population. The devastating fact is that only 14% of patients have satisfying regulation of arterial hypertension (3). One of the problems is that hypertension is a silent, insidious disease, often asymptomatic for years – and is therefore known "the silent killer".

Hypertension is also a major economic burden on health care systems. Notwithstanding the global health care savings from effective treatment of hypertension alone are estimated at $100 billion per year according to the World Heart Federation, too little priority continues to be given to investment in the management and prevention of hypertension.

Since the management and treatment of hypertension occur primarily in primary care, it is important to provide enough healthcare professionals capable to cope with this problem. In 2021, the Croatian Medical Chamber declared that they have identified a shortage of 207 primary care physicians in Croatia.

2. MEDICATION ADHERENCE

The long-term use of pharmacotherapy for chronic diseases is an ongoing challenge. The efficacy of these medications often does not meet the expected level, as approximately 50% of patients do not adhere to the prescribed therapy (4). The known factors contributing to poor adherence to therapy are the patient-physician relationship and the patient's health status. Patients' medical illiteracy and denial of their condition are often the barriers to adequate treatment, but physicians' lack of time and willingness to explain the mechanism of action and benefits of medications also promote poor adherence. Interventions that can improve adherence fall into the following categories: patient education, improving patient-physician communication, making physicians

more accessible to patients, and improving dosing schedules (5). Poor adherence and the rapid digitalization of everyday life have raised awareness of potential new ways to prevent poor adherence. The aim is to reduce the burden on primary care and increase patient independence – by involving pharmacists and smartphone technology in the chronic disease management.

3. PHARMACISTS' AND MOBILE APPLICATIONS' ROLE
Pharmacists develop expertise in medications with an emphasis on safe prescribing and dispensing and are able to share the burden of hypertension with physicians (6). Collaboration between physicians, pharmacists, and patients should be established to treat hypertension well. Pharmacists have insight into each patient's medication record and educate patients about medication use. The advantage of the pharmacists' role is also that they are easily accessible as health care professionals and the pharmacological knowledge they can provide is important for both patients and physicians (7,8). In the literature, common pharmacist interventions have included education about medications and lifestyle, feedback to physicians, and medication management (8). In their meta-analysis Santschi et al. reported that pharmacist interventions resulted in greater reductions in systolic and diastolic blood pressure, triglycerides, and LDL cholesterol in participants than in those who did not have pharmacist-led hypertension management (8). Pharmacists frequently identify problems with drug therapy. Hirsch and al. reported that about half of patients required a dose increase and/or additional therapy (9). Potential side effects and drug interactions could be identified and avoided more frequently by pharmacists rather than physicians. Telemedicine is another health care strategy, cost-effective and always available, but only to those familiar with the technology. The increasing use of mobile applications worldwide has proven to be a convenient way to deliver healthcare services to patients. The mobile applications could provide daily, weekly, monthly and any period data to the physicians, and 24-hour monitoring could offer a tremendous potential to improve the patient adherence and health. Mobile applications should also remind and encourage patients to take the initiative for their health. Along these lines, some authors have reported the benefits of using mobile applications for treatment adherence (10)therefore, they have the potential benefits of lowering blood pressure. Despite this, there is currently a lack of evidence for their effectiveness, usability, and patient satisfaction with their use. Objective: A systematic review was conducted to assess the effectiveness of apps in lowering blood pressure, as well as their usability and patients' satisfaction with their use. Methods: We conducted searches in the following databases: MEDLINE (OVID. Specifically, on the benefits in hypertension management, Indraratna and al. conducted a meta-analysis that included all relevant randomised control trials featuring smartphone technology from 2000 to 2019 (11). They reported significantly lower systolic BP

and fewer hospitalisations in patients exposed to mobile phone interventions.

4. THE HUNT ON THE SILENT KILLER AND EHUH-2 PROJECTS
Despite the fact that hypertension is widespread, there have been no consistent data on the prevalence, awareness, treatment, and control of hypertension in our population. To change this, a cross-sectional study entitled The Epidemiology of Arterial Hypertension in Croatia, part one (EH-UH 1) was conducted in the early 2000s. The aim of this study was to collect data for the entire territory of the Republic of Croatia. The study lasted two years and analysed, among other things, the so-called new indicators of cardiovascular risk - isolated systolic hypertension, heart rate, pulse pressure. In addition, therapeutic response was monitored in individual subgroups, taking into account the applied therapy.

After the end of the EH-UH 1 project, no similar studies were performed. This was an incentive to use the same methodology to organise EH-UH 2 research, which finally started in 2018. The main objectives of this follow-up project were to determine the new prevalence, awareness, treatment and control of arterial hypertension (current status and comparison with EH-UH 1), to determine salt intake (potassium, iodine) and to determine the prevalence of chronic kidney disease in Croatia, including the stages of the disease.

On the other hand, in order to monitor the epidemiology of hypertension in less accessible areas, the public health campaign "The Hunt for the Silent Killer" (HSK) began in the summer of 2021. The primary mission of HSK was to familiarise the target population with the concept of arterial hypertension and the risk factors that lead to it. The action so far was based on the inhabitants of the islands of Vis, Korčula, Hvar and Brač, as it was assumed that the island population had different lifestyle habits and less availability of secondary and tertiary health care facilities. Participants were recruited by volunteering to participate in the project, which took place on a boat in different locations on the mentioned islands.

MATERIALS AND METHODS
This study included 424 participants of the HSK, including 196 men, 212 women and 16 participants of unknown sex, and 1228 participants of the EH-UH 2 project, including 479 men, 748 women and 1 participant of unknown sex. The participants of the HSK were recruited within the framework of "street-epidemiology" – that is, the participants were recruited when they voluntarily entered the project, which took place in several places of the Croatian islands (Vis, Vela luka, Korčula, Stari grad, Jelsa and Pučišća). The EH-UH 2 sample was randomized from general practices in several towns across Croatia. Each participant received a structured questionnaire with questions about

their health problems, therapy, habits, and opinions about the role of pharmacists and smartphone technology in treatment of hypertension.

Each participant's weight, height, and waist circumference were also noted, and body mass index (BMI) was calculated. A BMI 25-30 kg/m² was considered overweight, and a BMI over 30 kg/m² was considered obese. An increased waist circumference was above 88 cm in women and above 102 cm in men.

STATISTICAL ANALYSIS

The distribution of variables was analysed using the Shapiro-Wilk test. Continuous variables were presented as mean and standard deviation. Differences in quantities between groups were analysed with the Mann-Whitney test for parametric and Kruskal-Wallis test for nonparametric variables. The Chi-square and binomial test were used to analyse differences in categorical variables between groups. Values of P less than 0.05 were considered statistically significant. The programme used for statistical analysis was JAMOVI, vers. 2.2.5.

RESULTS

A total of 1652 participants were included, 424 participants of The HSK project, including 196 men with an average age of 58.8 years and 212 women with an average age of 54.6 years, and 1228 participants of the EH-UH 2 project, including 479 men with an average age of 57.6 years and 748 women with an average age of 57.2 years. Table 1 shows the general information and differences between the participants of the HSK and EH-UH 2 project.

Table 2 shows clinical information regarding to the sex of the participants of the HSK, and Table 3 of the participants of the EH-UH 2 project. Both tables highlight the significantly higher systolic and diastolic blood pressure, BMI and waist circumference in men in both projects.

Personal history of hypertension, kidney disease and cardiovascular diseases did not differ between the genders among HSK participants, but did among participants in the EH-UH 2 project. In the EH-UH 2 project significantly more women had arterial hypertension (400 vs. 247, p < 0.001) and dyslipidemia (201 vs. 99, p < 0.001) than men, and men were more likely to have personal history of myocardial infarction (24 vs. 9, p = 0.014). When asked, participants in the HSK project were more likely to believe that pharmacists should play a greater role in treating hypertension than those in the EH-UH 2 project (137 vs 34). However, within the projects, the difference between positive and negative answers was statistically significant in the EH-UH 2 project (yes: 34 vs. no: 82, p < 0.001), and women were generally less supportive of pharmacists playing a role in AH treatment (women: yes - 19 vs. no - 47, men: yes – 15 vs. no – 35, χ^2 = 4.74, p = 0.029). Table 4 shows responses by gender and hypertension diagnosis to the questions "Should pharmacists play a role in hypertension treatment?" and '' Could mobile applications be useful in the hypertension treatment?" in the HSK and EH-UH 2 project.

Positive attitudes toward the benefits of mobile applications in the treatment of hypertension were enhanced in the HSK (Table 4) (yes; 269 vs. No; 109, p < 0.001), with normotensive participants being the majority of mobile applications advocates (65.8% of positive responses, χ^2 = 11.0, p < 0.001).

On the other hand, the results of the EH-UH 2 (Table 4) project pointed out a significant negative attitude towards mobile applications (yes; 403 vs. no; 823, p < 0.001) with hypertensive participants being the majority against the mobile applications (60.5% of negative responses, χ^2 = 47.6, p < 0.001).

When asked about their opinion of what the role of pharmacists should include in the treatment of AH, the majority of HSK participants responded with education (22.8%) (Figure 1). Participants in EH-UH 2 were also asked if they had ever measured blood pressure at a pharmacy (Figure 2).

Smartphone ownership (Table 5) was higher in younger age groups in both projects, with a significant difference between the groups (HSK; χ^2= 67.8, p < 0.001, EH-UH 2; χ^2 = 377, p < 0.001).

DISCUSSION

The global and Croatian burden of cardiovascular disease, for which arterial hypertension is the main risk factor, has overwhelmed the healthcare system at all levels. The estimated disability-adjusted life years (DALYs) for CVD in Croatia in 2019 (12) totaled 346.7, with 181.6 for men and 165.1 for women.

To be successful, treatment of hypertension should achieve common goals in the areas of prevention, screening, diagnosis, and management of hypertension. Many well-known strategies are used in the treatment of hypertension. During the pandemic, the constant lack of time in health care has unsurprisingly increased. Patient education could be provided in the primary care physician's office, but not all physicians have time and not all patients are willing to follow the therapeutic protocol. In the age of digitalization, all the information patients are looking for can be found on the Internet. The problem, of course, is that medical laypeople cannot always distinguish false from true statements. Treatment of arterial hypertension has also been improved to meet the needs of patients, but why is it not working? Dosing regimens often complicate treatment adherence, especially for those who take numerous different tablets daily. The solution to this problem is offered by pharmaceutical companies, which tend to combine different active ingredients in a single pill.

Statistical data from the Croatian Institute of Public Health for 2020 show that the number of general practitioners is 2327 and the number of pharmacists is 3029. Since the Croatian Medical Chamber indicates a shortage of general practitioners of 207 for 2020, these figures suggest that pharmacists are more available to the population than general practitioners.

The idea of involving pharmacists in the management of AH was equally accepted or not accepted by both genders in the HSK, while EHUH 2 participants were generally not in favour (82 vs. 34, p < 0.001), with females predominating (women: 47 (57.3%) vs. men: 35 (42.7%)). The fact that HSK participants represent the population that has less access to medical care might have an impact on the increased tendency to use pharmacists' help in AH management. On the other hand, when opinions were divided into groups according to the diagnosis of hypertension, it appeared that HSK participants who had hypertension were more supportive of the role of pharmacists. This is consistent with the lack of medical care on the Croatian islands. Both in the literature and in the HSK, the educational role of pharmacists is expected, which is consistent with the fact that one of the main reasons for poor adherence is the medical illiteracy of patients (8).

On the other hand, smartphones and tablets, including mobile applications, have become an integral part of people's lives, with usage rates increasing significantly since their introduction. In the literature, many studies report significant improvements in behaviour and related health outcomes from mobile application use (13–15).

Logan et al. used an automatic BP transmission procedure in hypertensive patients, that alerted the patient's primary care physician in the event of abnormal values (16). Potential automatic data transmission, which could be enabled by mobile applications, would reduce the patient workload and could improve compliance with the system and treatment (11).

Smartphone technology was well approved by the residents of the Croatian islands represented by the HSK participants, but was not in the general population of Croatia represented by the EHUH 2 participants. The possible reason behind these opinions might be that the Croatian population is getting older, and both of these projects showed that generally, the participants above 65 years did not own a smartphone, making them unable to use or understand the option of mobile applications in the hypertension management.

Although the discussed solutions to the adherence should be implemented to improve the medication adherence, in the end, it is up to patients to follow the therapy regimen. Self-management is considered an important element of chronic care management and demands an active role of patients in managing their symptoms, treatment, psychosocial and physical effects, and changing lifestyle (17).

CONCLUSION

The Hunt on the silent killer and EHUH 2 project showed that the HSK participants were more in favour of pharmacists' and smartphone technology taking place in arterial hypertension management, possibly because of the lesser availability of healthcare services across the Croatian islands. The need to educate the population about arterial hypertension, as well the pharmacists' abilities to participate in the AH treatment, has been enhanced through both of these projects. Poor medication adherence has many causes, and as much as possible solutions should be implemented to keep the patients motivated to follow the treatment protocol.

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