PREDICTING NON-ADHERENCE TO MEDICATION REGIMEN AMONG PATIENTS WITH HYPERTENSION: TAKING STEPS TOWARD ECOLOGICAL APPROACH

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Summary

Medication non-adherence among patients with hypertension is one of the main reasons for poor treatment efficacy, higher healthcare costs, increased patient morbidity and mortality. Despite numerous attempts to explain and improve adherence to long-term treatment regimen, the prevalence of non-adherence is still very common. Moreover, treatment adherence research rarely includes environmental variables as proposed by the ecological model. The aim of this study is to analyze the role of patient-level and micro-level variables in predicting medication non-adherence among patients with hypertension. Method. 101 hypertensive outpatients aged 33-93 (M = 60.13; SD = 11.85) volunteered to participate in the study. A self-report questionnaire was constructed to assess subjects' adherence to medication regimen. Pivotal socioeconomic variables were recorded as well as treatment-related information, illness-related beliefs, perceived social support and satisfaction with the healthcare provider. Results show that perceived longer illness duration and higher satisfaction with the healthcare provider predict lower levels of intentional medication non-adherence. Younger age, higher intensity of side effects and lower levels of perceived social support predict higher unintentional medication non-adherence. Amount of prescribed medication has no direct effect on unintentional medication non-adherence, but is mediated through intensity of side effects. Results of this study emphasize the importance of environmental variables and recognition of various patterns of medication non-adherence, which provide additional understanding of the complexity of this health-related behavior.

Introduction

Hypertension can be considered one of the major challenges in the health care system worldwide. Rarely accompanied by any symptoms, this disease is attributed to approximately half of all strokes or ischemic heart disease [1] and is estimated to cause 12.8 percent of all deaths [2]. What is more, according to Lithuanian National health insurance fund, expenses on reimbursement of antihypertensive medication are the highest compared to other chronic diseases. Although researchers and practitioners agree that proper blood pressure control can prevent stroke and other cardiovascular events among patient with hypertension [3], poor adherence to antihypertensive therapy may result in 3 times higher odds of mortality [4] and persistence of antihypertensive treatment is important for clinical treatment results [5], still the lack of adherence to medication regimen in patients with hypertension is very common.

The level of non-adherence varies across different diseases. Usually non-adherence to treatment regimen is present among half of the patients treated for chronic diseases [6]. In case of hypertension, however, the prevalence of non-adherence reaches up to 80 percent [7]. Moreover, up to two thirds of patients with presumed resistant hypertension were non-adherent to treatment regimen [8]. Despite the prevalence of non-adherence and the role of adherence for the clinical outcomes, healthcare practitioners rarely consider this issue when working with patients and it rarely becomes the focus of research in Lithuania.

Having in mind that adherence to treatment regimen

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has enormous impact on patients' health, it is crucial to identify variables influencing medication adherence, since modifiable variables can be targeted for intervention [9]. There is a number of health behavior theories that contribute to understanding adherence behavior, however these theories are often supported by fragmented or contradictory evidence [10] and the effectiveness of commonly used interventions aiming to improve adherence is lacking [11]. Mentioned theories are predominantly focusing on the patient-related variables, but fail to encompass a broader approach and examine environmental factors proposed by the ecological model [12-13]. Of course, it is impossible to disregard the relevance of patient-related variables such as complexity of the regimen or side effects of medication [6, 14], various illness beliefs [10, 15] and self-efficacy [16-17]. Nevertheless, support from the immediate social environment and relationship with the healthcare professional, which are attributed to the micro-level [12], are also suggested to have a tangible impact on patients' disease management behavior [6, 18].

This is why the aim of this study is to analyze the role of patient-level and micro-level variables in predicting medication non-adherence among patients with hypertension.

Material and method

The study was carried out in a sample of 101 hypertensive outpatients (M age = 60.13, SD = 11.85, range: 33-93) that volunteered to fill out the confidential questionnaire. Subjects were recruited using a non-probability convenience sampling technique (Table 1).

Non-adherence to medication regimen scale was constructed for the purpose of this research and measured 2 types of medication non-adherence: intentional and unintentional. Sample items include the following: "It happens that I forget to take my medication on time" and "It happens that I make a longer break from taking my medication." These were rated on a 4-point scale from *never* (1) to *all the time* (4). Higher scores indicate higher levels of non-adherence.

Confirmatory factor analysis (CFA) confirmed 2 factor model for the non-adherence to medication regimen scale ($\chi2$ = 25.746; df = 19; p = 0.137; CFI = 0.970; TLI = 0.955; RMSEA = 0.060). Both subscales have satisfactory reliability in the current sample, as Chronbach's internal consistency α was 0.67 and 0.82.

Patient-level variables: Pivotal socioeconomic variables including age, gender, area of residence, level of education, vocational status and income were recorded. Subjects also reported specifics of their regimen as well as incidence and intensity of side effects. Psychological variables included self-efficacy and perceived illness duration.

Patients' *self-efficacy* was measured using General Self-Efficacy Scale [19]. Using CFA one factor model was confirmed ($\chi2$ = 41.687; df = 28; p = 0.046; CFI = 0.975; TLI = 0.959; RMSEA = 0.070). The scale also showed good reliability in the current sample, as Cronbach's internal consistency α was 0.91.

Perceived illness duration was rated on a 10-point scale from 1 (*very short*) to 10 (*for the rest of my life*).

Micro-level variables included perceived social support as well as patients' satisfaction with the healthcare provider.

Perceived social support was specifically designed for this study and measured through 5-item scale, with the sample item, "My family members and / or friends fully support me." These were measured on a 5-point Likert-type scale ranging from *not true at all* (1) to *very true* (5). Scale has good psychometric characteristics. CFA confirmed one factor model ($\chi2$ = 2.882; df = 3; p = 0.410; CFI = 1.000; TLI = 1.000; RMSEA < 0.000). The scale has satisfactory reliability in the current sample, as Chronbach's internal consistency α was 0.70.

Satisfaction with the healthcare provider was specifically designed for this study and measured using 9 items, with the sample item, "The doctor devoted enough time to provide the best care possible." These were measured on a 5-point Likert-type scale ranging from completely *disagree* (1) to *completely agree* (5). CFA confirmed one factor model ($\chi2$ = 37.024; df = 24; p = 0.414; CFI = 0.975; TLI =

Table 1. Characteristics of the sample

		N	%
Gender	Male	31	30.7
	Female	70	69.3
Level of education	Primary or basic	12	11.8
	Secondary	35	34.7
	Higher non-university	24	23.8
	Higher university	30	29.7
Vocational status	Employed	55	54.5
	Unemployed / retired	45	44.6
	No responce	1	1.0
Area of residence	Urban	47	46.5
	Rural	54	53.5

0.962; RMSEA = 0.074) The scale also showed good reliability in the current sample, as Cronbach's internal consistency α was 0.90.

Data analyses

Initial data analysis was conducted using SPSS 22 statistical package. Further analysis was conducted using structural equation modelling (SEM) with AMOS 22.

Results

Initial analysis showed that there no significant differences in intentional medication non-adherence between gender (male M (SD) = 6.40 (2.04); female M (SD) = 5.95 (2.27); t = 0.960, df = 99, p = 0.340) and residential groups (urban M (SD) = 5.74 (2.26); rural M (SD) = 6.39 (2.13); t = -1.502, df = 99, p = 0.136). Also no differences were found between gender (male M (SD) = 6.84 (1.80); female M (SD) = 6.57 (1.93); t = 0.643, df = 99, p = 0.522) and residential groups (urban M (SD) = 6.36 (1.90); rural M (SD) = 6.91 (1.85); t = -1.474, df = 99, p = 0.136) in unintentional medication non-adherence. Therefore these variables were not included in SEM analysis.

Figure 1 presents final structural model and standardized coefficients. The fit statistics of the model met the multiple criteria for adequately fitting model (χ2 = 9.745; df = 10; p = 0.634; CFI = 1.000; TLI = 1.000; RMSEA < 0.001).

The final model indicates that perceived longer illness duration and higher satisfaction with the healthcare provider predict lower levels of intentional medication non-adherence. Younger age, higher intensity of side effects and lower levels of perceived social support predict higher unintentional medication non-adherence. Even though the amount of prescribed medication has no direct effect on unintentional medication non-adherence, it has indirect effect and is mediated through the intensity of side effects. General self-efficacy, educational level, financial and vocational status showed no significant impact on either type of medication non-adherence. Correlation between intentional and non-intentional non adherence is insignificant.

Discussion

Results of this study suggest that

medication non-adherence should not be viewed as unidimensional construct, but rather as a construct including at least two types of non-adherence behavior, i.e. intentional and unintentional. This notion is supported not solely by the results of the factor analysis, but also by the fact that different types of medication non-adherence are predicted by different variables. Various researchers also recognize the importance of distinguishing different types of adherence [20-22]. De Geest and colleagues [8] proposed that comprehensive investigation of various medication-taking patterns is needed. Focusing research on different types of medication non-adherence will help understand the clinical significance of adherence and in addition provide with the evidence-based guidelines for developing targeted adherence promoting interventions.

The findings of this research show that intentional medication non-adherence can be predicted by patients' beliefs regarding illness duration. Even though hypertension is a long-term disease, not all patients see it as such. Since intentional medication non-adherence is an active decision-making process [20], patients' knowledge about the disease, as well as seeing the illness as more permanent, promotes a better understanding of the necessity of persistent antihypertensive treatment. Furthermore, results indicate that intentional medication non-adherence can
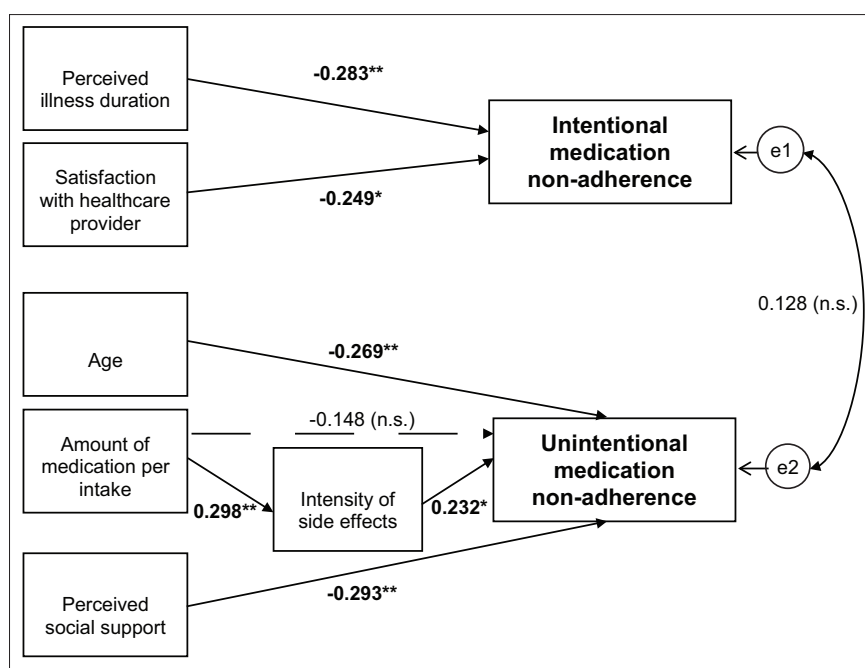

Figure 1. Final structural equation model for the predictive impact of personal- and micro-level variables on intentional and unintentional medication non-adherence
*p < 0.05; ** p < 0.01; n.s. – non-significant.*

be predicted by satisfaction with the healthcare provider. Considering that satisfaction with the healthcare provider is closely related to patient-provider communication [23], information-giving and quality of communication contribute to patients' understanding of illness and benefits of treatment [7], shaping more constructive attitudes and beliefs along with modifying the inaccurate ones. Therefore, improvement of communication between the patient and the healthcare provider through training physicians to communicate better might have a positive effect on intentional adherence behavior.

To the contrary, unintentional medication non-adherence is viewed as a more passive and irrational behavior [22], linked to forgetfulness [24], limited financial resources [6, 25], and increased by the presence of unpleasant side effects [12, 26] that make patients avoid medication. Since forgetfulness is often attributed to the older age, it is often believed that older patients would have poorer medication adherence due to possible limited cognitive resources or cognitive decline [27], however, results regarding age in the context of medication non-adherence are often contradictory [6, 22]. Current study shows that older patients report lower levels of unintentional medication non-adherence. As suggested by other researchers, older adults have less busy everyday routines, which makes it easier to keep track of their medication schedules [27], moreover, taking medication is a more habitual task for older compared to younger adults [28]. Besides age, lower levels of unintentional medication non-adherence are predicted by higher levels of perceived social support. Social support is often associated with physical health outcomes, morbidity and mortality [29-31], and it is reasonable to expect that social support has significant ties with medication non-adherence. Assistance and encouragement of immediate social environment not only can alleviate emotional burden associated with the illness [18], but also can help the patient keep up with the medication schedule more accurately. Which is why patients' family members and close friends are a valuable resource that should be involved when necessary.

In addition, results of this research showed that relationship between the amount of medication per intake and unintentional medication non-adherence is mediated by the reported intensity of side effects. Complexity of medication regimen is repeatedly reported to have negative effect on medication adherence [6, 32-33]. The higher the number of different drugs or number of daily dosing, the more difficult it becomes for the patient to follow the regimen. What is more, interventions aimed at simplification of medication regimen were found to be the most effective in improving adherence [11]. The findings of this research not only provide some insight on the link between regimen complexity and adherence, but also support the relevance of regimen simplifying interventions, e.g. reducing the number of pills when tackling the problem of unintentional medication non-adherence among patients with hypertension. However, monotherapy produces the desired effect only in limited number of patients, whereas majority of hypertensive patients require the combination of at least two drugs [34-35]. Thus, achieving balance between proper medication adherence and maintaining target blood pressure may seem challenging. On the other hand, when prescription of multiple agents is needed in order to achieve effective control of blood pressure, replacing multiple-pill antihypertensive combinations with single-pill or otherwise called fixed-dose combinations provides treatment simplification and benefits medication adherence [36]. Moreover, drug combinations may also lessen the intensity of adverse side effects that are induced by high-dose monotherapy [35], while reduction of side effects is likely to promote better medication adherence.

Although self-efficacy is strongly associated with various health related behaviors [16-17], in this research self-efficacy was insignificant in predicting medication non-adherence. While it is suggested that self-efficacy plays the important role in the process of both initiating and maintaining of health behavior, it is also probable that, due to the novelty of the behavior, initiation requires believing in the capability to perform courses of action, whereas maintaining practice over a period of time may be more dependent on self-regulatory processes than it is on perceived self-efficacy [37]. Moreover, it can be assumed that the role of self-efficacy may vary depending on the type of behavior, since different behaviors require varying amount of planning and deliberation [38]. Compared to a variety of self-care activities, including weight control, low-salt diet, regular physical activity, limited alcohol and tobacco use, that are recommended in cases of hypertension, medication taking can be viewed as a routine behavior that does not require as much effort or competence for most patients. Therefore, self-efficacy in the context of maintaining proper medication adherence might only become important when obstacles arise.

In order to modify adherence behavior, practitioners developing interventions should take into account the type of medication non-adherence that they are aiming to improve. In addition, interventions should not be limited to patient-level variables. Based on the results of this study, simplification of medication regimen through fixed-dose or single-pill combinations, addressing patient's concerns with side effects along with prompting the engagement of family and

friends should be used for the subgroup of non-adherent patients who regularly forget to take their medication. On the contrary, aiming to decrease medication non-adherence among patients that deliberately alter the dosing or take "drug holidays" without consulting their physician, practitioners should try forming a collaborative partnership with the patient, which could facilitate identification and discussion of inaccurate beliefs regarding patients' illness or treatment.

Results of this study stress the importance of a broader perspective focusing on environmental micro-level variables in the context of adherence behavior, as satisfaction with the healthcare provider and perceived social support predict medication non-adherence. However, results of this research do not undermine the importance of patient-level variables such as health-related beliefs and attitudes. Further investigation of patients' beliefs, especially in relation with satisfaction with the health care provider, is needed. Also, future research should not be limited to medication adherence, but should include other self-care activities, since simultaneous analysis of various hypertension management behaviors may give a deeper understanding into the matter of adherence to long-term treatment regimen.

Conclusions

Intentional medication non-adherence can be predicted by perceived illness duration and the level of patients' satisfaction with the healthcare provider. Whereas unintentional medication non-adherence can be predicted by patients' age, intensity of medication side effects and perceived social support. No common predictors of intentional and unintentional medication non-adherence were identified, therefore, when aiming to improve medication adherence among patients with hypertension, distinguishing between intentional and unintentional medication non-adherence will allow more targeted interventions, which in turn may yield better results.

Statement of conflict
The authors state no conflict of interest.

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HIPERTENZIJA SERGANČIŲJŲ MEDIKAMENTINIO GYDYMO NURODYMŲ NESILAIKYMO PROGNOSTINIAI VEIKSNIAI: EKOLOGINIO POŽIŪRIO LINK

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Raktažodžiai: medikamentinio gydymo nurodymų nesilaikymas, socialinė parama, pasitenkinimas sveikatos priežiūros specialistu, suvokta ligos trukmė, hipertenzija

Santrauka

Medikamentinio gydymo nurodymų nesilaikymas hipertenzija sergančiųjų grupėje yra viena pagrindinių prasto gydymo efektyvumo priežasčių ir siejamas su padidėjusia neįgalumo bei mirtingumo rizika. Nepaisant mokslininkų ir praktikų susidomėjimo šiuo sergančiųjų elgesiu bei bandymų paaiškinti ir pagerinti medikamentinio gydymo nurodymų laikymąsi, su vaistų vartojimu susijusių gydymo rekomendacijų nevykdymas hipertenzija sergančiųjų grupėje yra vis dar labai dažnas. Be to, analizuodami medikamentinio gydymo nurodymų nesilaikymo prognozuojančius veiksnius, tyrėjai retai atsižvelgia į socialinės aplinkos veiksnius, kurių svarbą pabrėžia ekologinis požiūris. Taigi, šio tyrimo tikslas – išanalizuoti sergančiojo lygmens ir mikrolygmens veiksnių reikšmę hipertenzija sergančiųjų medikamentinio gydymo nurodymų nesilaikymui. Metodai. Tyrime sutiko dalyvauti 101 hipertenzija sergantis asmuo. Tiriamųjų amžius buvo nuo 33 iki 93 metų (M = 60.13; SD = 11.85). Siekiant įvertinti sergantiesiems būdingą medikamentinio gydymo nurodymų nesilaikymą, buvo parengtas klausimynas. Be to, papildomo klausimyno pagalba buvo surinkti duomenys apie pagrindinius sergančiųjų sociodemografinius rodiklius, medikamentinio gydymo ypatumus, sergančiojo įsitikinimus apie ligą, suvokiamą socialinę paramą ir pasitenkinimą savo sveikatos priežiūros specialistu. Rezultatai. Šio tyrimo rezultatai rodo, kad sergantieji, kurie savo ligą suvokia kaip ilgiau besitęsiančią ir yra labiau patenkinti savo sveikatos priežiūros specialistu, rečiau apgalvotai sumažina vartojamų vaistų dozę ar nutraukia vaistų vartojimą. Jaunesni, dažniau šalutinį vaistų poveikį patiriantys ir mažiau socialinės paramos gaunantys sergantieji dažniau pamiršta ar dėl kitų nenumatytų priežasčių neišgeria jiems paskirtų vaistų. Paskirtų vaistų kiekis neturi tiesioginio ryšio su netyčiniu vaistų nevartojimu, tačiau šis ryšys yra medijuojamas vaistų šalutinio poveikio dažnumo. Šio tyrimo rezultatai taip pat pabrėžia tyčinio ir netyčinio medikamentinio gydymo nurodymų nesilaikymo išskyrimo svarbą bei pademonstruoja aplinkos veiksnių vaidmenį, kas savo ruožtu suteikia papildomų žinių apie tokį sudėtingą reiškinį kaip hipertenzija sergančiųjų gydymo nurodymų laikymasis.

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