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Original Research

# The Use of Herbal Products/Dietary Supplements and Affecting Factors in Patients Applying to a Pediatric Neurology Outpatient Clinic: A Descriptive Questionnaire Study

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## ABSTRACT

**Objective:** The use of herbal products/dietary supplements (HP/DS) in the pediatric population is increasing day by day. The interaction of HP/DSs with drugs with a narrow therapeutic index such as phenytoin, phenobarbital, and valproic acid, may cause problems in treatment. In this respect, it is very important to determine the use of HP/DS in children with neurological diseases and/or complaints. In this study, it was aimed to determine the use of HP/DS and the factors affecting the use of these products in individuals with a neurological complaint and/or disease who applied to the pediatric neurology outpatient clinic.

**Methods:** Parents were questioned face-to-face as part of the descriptive questionnaire research. 174 questionnaires with appropriate data quality were included in the study. The statistical software tool SPSS 23.0 was used to analyze the data.

**Results:** 44.6% of the parents stated that they gave HP/DS to their children. The findings of the analysis showed that kids whose parents use HP/DS are more likely to utilize these items themselves ($p<0.001$). The most commonly used products are linden (70.1%), bee products (26.0%), carob (18.2%), chamomile (13.0%), and lemon (13.0%). It has been determined that the reasons for parents to have their children use HP/DS are to strengthen the immune system (51.9%), improve general health status (40.3%), and supplement normal nutrition (27.3%), respectively.

**Conclusion:** This study revealed a high frequency of HP/DS use in children with pediatric neurological diseases/complaints in Türkiye. The frequency of HP/DS use was higher in children whose parents tended to consume HP/DS. Considering the high use of these products, healthcare professionals need to inform parents to prevent adverse effects caused by HP/DS.

**Keywords:** epilepsy, herbal products, dietary supplements, herb-drug interaction, pediatric neurology

## INTRODUCTION

The use of herbal products for various purposes such as curing diseases, preventing diseases, or improving general health is as old as human history [1]. According to World Health Organization (WHO), the term "herbal product" includes raw drugs, teas, and pharmaceutical-formulated products obtained from plants [2]. Similar to the European Union regulations, herbal products on the market in Türkiye are classified as food

supplements or traditional herbal medicinal products. If the herbal product is presented with therapeutic properties, the registration application, evaluation, and approval procedures are carried out by the Republic of Türkiye Ministry of Health [3]. On the other hand, dietary supplements that have an important place in the market are defined as "the products for which the daily intake dose is determined by being prepared alone or in mixtures, in capsules, tablets, drops, disposable powder packs, liquid ampoules, dropper bottles, and other similar liquid or powder forms consist of nutrients such as vitamins, minerals, proteins, carbohydrates, fibers, fatty acids, amino acids or concentrates or extracts of the plants, plant, or animal originated substances, bioactive substances, and similar substances that have nutritional or physiological effects to supplement the normal diet" [4].

Herbal products/dietary supplements (HP/DS) are widely used in children and the frequency of use is increasing day by day. HP/DS use rate in children is 85% in Germany, 23% in Scotland, 15% in Denmark, 5% in England, 4.8% in Italy, and 3.9% in the United States [5]. In a study conducted by the United States Food and Drug Administration, Center for Disease Control and Prevention, with 2653 healthy mothers, it was revealed that 9% of parents use HP/DS for their babies in the first year of life [6]. In a study, it was discovered that in Türkiye, the frequency of use of herbs and herbal products in pediatric patients was 74.4% [7].

**Main Points;**

- There is a high frequency of HP/DS (44.3%) use in children with pediatric neurological diseases/complaints in Türkiye.
- The frequency of HP/DS use is higher in children whose parents tended to consume HP/DS.
- There is a positive relationship between the usage of HP/DS in children and the experience of parents using these products.
- No relationship is found between the duration of diagnosis of the disease and the use of HP/DS.
- There is no correlation between parental sociodemographic and personal characteristics and HP/DS usage in children.

It has been reported that different traditional treatment methods are used in the treatment of various neurological diseases including epilepsy, headaches, traumatic brain injury, neuromuscular disorders, developmental delay, and degenerative brain diseases in children [8-12]. The main purpose of these studies, which were mainly carried out under the umbrella of complementary medicine, was to determine the use of traditional treatment methods such as massage, acupuncture, chiropractic, prayer, and yoga. Even though the use of HP/DS included in traditional treatment methods has been questioned, no detailed evaluation has been made about these products. There is only one study in the literature that determines the frequency of HP/DS use and the factors affecting its use in children with neurological diseases. This study, which interviewed the families of 378 children with epilepsy, showed that the frequency of use of herbal products was 17.2% [13]. This study aims to determine the frequency of HP/DS use, the products used, and the factors affecting the use of these products in patients who applied to the pediatric neurology outpatient clinic.

## MATERIALS AND METHODS

### Research Population

The population of this descriptive study consists of children and their families who applied to Karadeniz Technical University (KTU) Farabi Hospital Pediatric Neurology Outpatient Clinic between 10.05.2021 and 10.06.2021. It was seen in previous hospital data that the average number of patients admitted to the pediatric neurology clinic was approximately 750 patients per month. Lee et al. reported that the prevalence of herbal product use in patients with epilepsy was 17.2% [13]. As a result of the power analysis using the OpenEpi Version 3.01 program according to the prevalence of herbal product use and the number of patients who applied to the clinic monthly, the minimum number of patients planned to be reached with a 5% error level and 95% confidence interval was determined as 170 people [14]. Children who were at least 3 months after the diagnosis of their neurological disease and/or complaint, who were citizens of the Republic of Türkiye, and who agreed to participate in the study and/or their families, were included in the study. Newly diagnosed and/or patients who refused to participate in the study were excluded. All patients who met the inclusion criteria between the specified dates were tried to be reached without sampling. During this period, a total of 205 people participated in the research. Researchers checked the obtained data, and 174 questionnaires with sufficient data quality were assessed.

## QUESTIONNAIRE FORM

The questionnaire forms were created with the data obtained from the current literature review and applied using the face-to-face interview method. Prior to data collection, a pre-test was carried out by conducting the questionnaire to fifteen people. The input was taken into account, the questionnaire was finished, and the unclear expressions and inconsistencies were corrected. All of the patients or parents of the patients were informed about the content and purpose of the study. Only participants above 15 years were interviewed themselves and their responses were supported by their parents. For the other participants, information was obtained from their parents as their ages were not suitable to answer. Informed consent was obtained from each participant and each interview took approximately 10 minutes.

The questionnaire form which contains a total of 12 questions, was divided into three sections: "sociodemographic and personal characteristics", "characteristics of the participants regarding their diseases and treatments" and "features related to the use of herbal products/dietary supplements". The question types of the questionnaire consisted of two-choice, multiple-choice, and open-ended questions. In the sociodemographic and personal characteristics section, parents who participated in the study were questioned on parents' educational status, the gender of the child, and the child's age. In the section about the diseases and treatment characteristics of the participants, the disease diagnosis, presence of additional diseases, long-term/regular drug use associated with the disease, and drugs used were asked. In the section where information on the use of herbal products is researched, the use of these products, the types of products used, the reasons for using HP/DS, and the use of HP/DS by parents were investigated.

Patient statements formed the foundation for this study. No plant samples were obtained from the participants and no botanical description was made.

### Statistical Analysis

The statistical package program IBM SPSS 23.0 was used to analyze the data. In descriptive statistics, mean, standard deviation, minimum and maximum are provided for numerical variables, whereas numbers and percentages are provided for categorical variables. To compare categorical variables in independent groups, the Chi-square test family ($\chi 2$ test, Yates Continuity Correction, Fisher's Exact test) was utilized. The statistical significance threshold of $p<0.05$ was approved.

## RESULTS

140 (80.5%) of the parents participating in the study were mothers, and 95 (54.6%) of the parents were primary school graduates or did not graduate from a school. While the mean age of the patients was 9.1±4.7 years (min: 6 months, max: 17.5 years), 102 (58.6%) of them were male. 108 (62.1%) of the children were followed up with the diagnosis of epilepsy. The mean duration of diagnosis was calculated as 4.4±3.4 years (min: 3 months, max: 15 years). The sociodemographic and main characteristics of the participants were given in Table 1.

It was demonstrated that 77 (44.3%) of the patients were using HP/DS. In addition, the HP/DS usage habits of the parents of the patients were questioned. 58 (75.3%) of parents who let their children use HP/DS also used these products themselves. The use of HP/DS according to the basic characteristics of the participants is presented in Table 2. Accordingly, no correlation was found between the use of HP/DS and the parent, the parent's educational status, the gender of the child, the child's age, long-term/regular drug use associated with the disease, and the presence of additional disease (each $p>0.05$). A statistically significant relationship was shown between the use of HP/DS and the use of these products by the family ($p<0.001$). It has been determined that children whose families use herbal products use these products more.

The most used products were linden (n=54, 70.1%), bee products (n=20, 26.0%), carob (n=14, 18.2%), chamomile (n=10, 13.0%), and lemon (n=10, 13.0%). The HP/DS variety used by the participants is presented in Table 3.

Parents or patients were asked about the reasons for using HP/DS. It has been determined that the most common reasons for using HP/DS were strengthening the immune system (n=40, 51.9%), improving general health status (n=31, 40.3%), and supplementing normal nutrition (n=21, 27%). The reasons for the participants to use HP/DS are presented in Table 4.

## DISCUSSION

The use of HP/DS in children is growing day by day, just as that is in adults. The results of the studies show that the usage of traditional therapy procedures in children has grown due to some chronic diseases and attention deficit hyperactivity disorder [8-10,15]. In these studies, the use of HP/DS was discussed together with the application of traditional treatment techniques. The number of studies examining the use of HP/

**Table 1.** Main characteristics of the participants (N=174)

| | N | % |
|---|---|---|
| **Parent** | | |
| Mother | 140 | 80.5 |
| Father | 30 | 17.2 |
| Other* | 4 | 2.3 |
| **Parent's educational status** | | |
| Primary school and below | 95 | 54.6 |
| Middle school | 18 | 10.3 |
| High school | 41 | 23.6 |
| College, faculty and above | 20 | 11.5 |
| **Gender of the child** | | |
| Girl | 72 | 41.4 |
| Boy | 102 | 58.6 |
| **Child's age (years, mean ± sd)** | 9.1±4.7 | |
| <10 | 91 | 52.3 |
| ≥10 | 83 | 47.7 |
| **Disease diagnosis[a]** | | |
| Epilepsy | 108 | 62.1 |
| Non-epileptic seizure | 14 | 8 |
| Cerebral palsy | 7 | 4 |
| Headache/migraine | 17 | 9.8 |
| Genetic diseases | 8 | 4.6 |
| Developmental delay-autism | 22 | 12.6 |
| Other[b] | 31 | 17.8 |
| **Duration of diagnosis (years, mean ± sd)** | 4.4±3.4 | |
| <5 | 125 | 71.8 |
| ≥5 | 49 | 28.2 |
| **Long-term/regular drug use associated with the disease** | | |
| Yes | 116 | 66.7 |
| No | 58 | 33.3 |
| **Medicines used[a]** | | |
| Levetiracetam | 48 | 41.4 |
| Valproic acid | 42 | 36.2 |
| Carbamazepine | 17 | 14.7 |
| Phenobarbital | 9 | 7.8 |
| Clobazam | 7 | 6.0 |
| Oxcarbazepine | 6 | 5.2 |
| Lamotrigine | 6 | 5.2 |
| Other[c] | 29 | 25 |

| **Presence of additional disease** | | |
|---|---|---|
| Yes | 33 | 19.1 |
| No | 140 | 80.9 |

*4 participants (>15 years) were interviewed themselves and their responses were supported by their parents. For the other participants, information was obtained from their parents as their ages were not suitable to answer. [a]More than one option is marked. [b]hydrocephalus, Post-traumatic seizure (n=5), vertigo, trauma (n=3), intracranial mass, ocular deviation (n=2), medulloblastoma, post-infectious ataxia, craniostenosis, brachial plexus, corpus callosum adenosis, SVO, tic disorders, microcephaly (n=1) [c]methylphenidate (n=5), topiramate, clonazepam, diazomid (n=4), baclofen, sertraline, risperidone (n=3), sultiam, aripiprazole, piracetam, zonisamide (n=2), haloperidol, phenytoin, ethosuximide, amitriptyline, atomoxetine (n=1)

**Table 2.** Herbal products/dietary supplements use according to the main characteristic of the participants (N=174)

| | **Using (77, 44.3%)** | | **Not Using (97, 55.7%)** | | **p** |
|---|---|---|---|---|---|
| | **N** | **%** | **N** | **%** | |
| **Parent** | | | | | |
| Mother | 65 | 46.4 | 75 | 53.6 | 0.536[a] |
| Father | 11 | 36.7 | 19 | 63.3 | |
| Other | 1 | 25.0 | 3 | 75.0 | |
| **Parent's educational status** | | | | | |
| Middle school and below | 46 | 40.7 | 67 | 59.3 | 0.200[b] |
| High school and above | 31 | 50.8 | 30 | 49.2 | |
| **Gender of the child** | | | | | |
| Girl | 35 | 48.6 | 37 | 51.4 | 0.331[b] |
| Boy | 42 | 41.2 | 60 | 58.8 | |
| **Child's age** | | | | | |
| <10 | 41 | 45.1 | 50 | 54.9 | 0.824[b] |
| ≥10 | 36 | 43.4 | 47 | 56.6 | |
| **Duration of diagnosis** | | | | | |
| <5 | 55 | 44.0 | 70 | 56.0 | 1.000[c] |
| ≥5 | 22 | 44.9 | 27 | 55.1 | |
| **Long-term/regular drug use associated with the disease** | | | | | |
| Yes | 52 | 44.8 | 64 | 55.2 | 0.829[b] |
| No | 25 | 43.1 | 33 | 56.9 | |
| **Presence of additional disease** | | | | | |
| Yes | 15 | 45.5 | 18 | 54.5 | 1.000[c] |
| No | 62 | 44.3 | 78 | 55.7 | |
| **Family HP/DS use** | | | | | |
| Yes | 58 | 92.1 | 5 | 7.9 | **0.000**[a] |
| No | 19 | 17.1 | 92 | 82.9 | |

$p < 0.05$; [a]: Fisher's Exact Test, [b]: $\chi 2$ test, [c]: Yates Continuity Correction

**Table 3.** Herbal products/dietary supplements used by the participants (N=77)

| Herbal products/dietary supplements | N | % |
|---|---|---|
| Linden | 54 | 70.1 |
| Bee products | 20 | 26.0 |
| Carob | 14 | 18.2 |
| Daisy | 10 | 13.0 |
| Lemon | 10 | 13.0 |
| Sage | 7 | 9.1 |
| Rosehip | 6 | 7.8 |
| Ginger | 6 | 7.8 |
| Turmeric | 6 | 7.8 |
| Mint | 6 | 7.8 |
| Fish oil | 5 | 6.5 |
| Mulberry/grape molasses | 4 | 5.2 |
| Oregano | 4 | 5.2 |
| Unknown product | 4 | 5.2 |
| Other[a] | 24 | 31.2 |

[a]Fennel (n=3), olive oil, coenzyme Q10, anise, lemon balm, walnut, cinnamon, apple cider vinegar, mallow (n=2), St. John's Wort, black pepper, udihindi, blueberry, date extract, cloves, cranberry, broccoli sprouts, cannabinoids, β-glucan, inositol choline, melatonin, menthol, uridine, cytidine, zinc, vitamin B12, pyridoxal phosphate (n=1)

**Table 4.** Reasons for participants to use herbal products/dietary supplements (N=77)

| Reason for use of herbal products/dietary supplements | N | % |
|---|---|---|
| Strengthening the immune system | 40 | 51.9 |
| Improvement of general health | 31 | 40.3 |
| To supplement normal nutrition | 21 | 27.3 |
| Sedative | 9 | 11.7 |
| Relieving symptoms associated with the disease | 5 | 6.5 |
| Other[a] | 12 | 15.6 |

[a]: In diseases other than pediatric neurological diseases (as antipyretic, and abdominal pain, gas pain, anemia, menstrual pain, and stomach disorders) (n=9), For healthy brain development (n=2), To eliminate the side effects of epilepsy drugs (n=1)

DS in children with neurological diseases and/or complaints is limited. In our study, we evaluated the use of HP/DS in children with pediatric neurological disease without the advice of a healthcare professional and factors affecting the use of these products.

A questionnaire study was conducted in Canada in which the use of traditional treatment methods was evaluated in children (n=206) with neurological disorders in two separate centers. In this study, the frequency of herbal product use was found as 25.2% [16]. In a survey study conducted with 352 parents in Saudi Arabia, it was determined that the participants applied various traditional treatment methods to their children with neurological disease, and the frequency of herbal product used among these methods was 30% [17]. Lee et al. reported that the frequency of use of medicinal plants in children with epilepsy was 17.2% in Korea [13]. In a survey study conducted with

parents (n=832) of children with chronic neurological disease in Türkiye, it was revealed that parents resorted to traditional methods for their children's disease. Among these methods, the frequency of using herbal products has been reported as 25% [18]. We found a higher rate of HP/DS use (44.3%) than in previous studies in the literature.

At the beginning of this study, we thought that the use of these products may be higher in children whose parents tend to use HP/DS. Previous studies have revealed that parents' experience of using traditional treatment methods affects their children's use of these practices [16,19-21]. Similar to the hypothesis we established at the beginning and the literature findings, the result of our study showed that there is a positive relationship between the use of HP/DS and the experience of parents using these products. Parents who have positive experiences with these products may also be inclined to use them for their children.

Previous studies have shown different results for the relationship between parents' educational status, child's gender and child's age, and HP/DS use. In some studies, these parameters were found to be associated with the use of HP/DS, while in others, the relationship could not be established [15,18,22-28]. Our results suggest that there was no relationship between sociodemographic and personal characteristics and HP/DS use.

In this study, we evaluated the relationship between participants' disease and treatment characteristics and HP/DS use. Jeong et al. reported that as the duration of diagnosis of the disease increases, the frequency of use of traditional treatment methods increases [20]. Hanson et al. did not find a significant relationship between the duration of diagnosis of the disease and the use of traditional treatment methods [26]. We found no relationship between the duration of diagnosis of the disease and the use of HP/DS. The rate of using traditional treatment methods was high in children with comorbidities [29]. Contrary to this finding, our study showed that the presence of the additional disease did not affect HP/DS use. In studies, no significant relationship was demonstrated between antiepileptic drug use and HP/DS use [19,21]. Our study supported this finding.

Plants contain many phytochemicals that show various pharmacological effects in their composition. The type and amount of these compounds vary according to the plant's growing conditions, geographical conditions, harvest time, and processing method [2]. Herbal medicinal products whose standardization and quality-control processes have been completed should be prepared. These products should be offered for sale through pharmacies. Herbal products are used in society by collecting them from nature or by purchasing them from other platforms such as herbalists, uncontrolled media channels, and the internet. This leads to some problems, including the collection of the wrong plants, adulteration, risk of contamination, and errors in product labels [2]. In the clinic, undesirable effects are encountered due to the effects of contaminants, heavy metals, substances added as a result of adulteration, toxic effects of plants, and allergic reactions [30]. Another problem that may arise due to the use of herbal products is herb-drug interactions. It has been proven in clinical studies that herbs *Andrographis paniculata* (Burm.f.), *Cimicifuga racemosa* (L.), *Citrus paradisi* Macfad., *Echinacea purpurea* (L.) Moench, *Hypericum perforatum* L., *Paeonia lactiflora* Pall., *Silybum marianum* (L.) Gaertn. and *Vaccinium macrocarpon* Aiton interact with midazolam, diazepam, carbamazepine, valproic acid and phenytoin [31-35]. There are case reports in the literature showing that the simultaneous use of herbal products with conventional drugs causes toxic effects in individuals with neurological diseases. In one of these cases, it was stated that the phenytoin and valproic acid levels of a patient who used an unknown dose of nutritional supplements containing Ginkgo and Saw palmetto extracts for about 1 year, decreased to the subtherapeutic level and consequently had a fatal seizure [36]. A male patient with a diagnosis of epilepsy and a history of 200 mg/day carbamazepine use simultaneously used ten grams of carbamazepine and one liter of pure grapefruit juice. Two hours after the use, he applied to the emergency service with unconsciousness and coma. The serum carbamazepine level of the patient was determined as 41.5 mg/L. Despite the treatment applied, it was observed that the carbamazepine level was still high (31.8 mg/L) in the measurements taken after 12 hours. High plasma concentration of carbamazepine despite the treatment applied in this case report was associated with the use of the drug together with grapefruit juice [37]. In a case series, four patients with a history of sertraline use were reported to develop serotonin syndrome within 2 to 4 days following the use of 300 mg St. John's wort two or three times a day [38]. In the literature, there are cases of severe sedation, mania, and serotonin syndrome resulting from the simultaneous use of St. John's Wort with other antidepressants such as fluoxetine and paroxetine [39]. According to our research, the five products that participants used most frequently were linden, bee products, carob, chamomile, and lemon. In this study, the interaction

between the HP/DS most commonly used by the patients and their conventional drugs was evaluated based on the literature data. We could not find sufficient data revealing the interaction between the products that patients prefer to use frequently and conventional drugs. It's conceivable that the use of these products has not been associated with any side effects or drug interactions that have not been documented. Determining the diversity of use of HP/DS is important in terms of detecting possible adverse effects and/or herb-drug interactions. Even if the effects and risks of using dietary supplements or herbal products have not been established, it is essential that you keep in mind that they could have a negative impact on your health. Depending on the herb-drug interactions, the increase in the pharmacological effects of the drugs may result in toxic effects or the desired response may not be obtained in the treatment due to the decrease in the effect. This is clinically important, especially for individuals in the pediatric population. If the blood concentration levels of drugs such as phenytoin, phenobarbital, carbamazepine, valproic acid, ethosuximide, and lamotrigine whose therapeutic levels are followed in the clinic, are at unexplained subtherapeutic or supratherapeutic levels, the use of HP/DS should be considered. HP/DS usage status should be questioned while taking anamnesis from the patients.

As with other studies measuring the tendency to use herbal products, this study has limitations. Our research is susceptible to selection and recalls biases due to the use of questionnaires. The study was single-center therefore, the results cannot be generalized to all pediatric neurology patients in Türkiye. It is impossible to draw conclusions about a particular plant or a product since botanical identifications of the plant species used are not made. However, our study is the first study on the use of herbal products in pediatric neurology patients in our country and its results support the results of studies conducted in other countries. However, our study contributes to the limited literature in terms of directly evaluating the use of HP/DS in pediatric neurology patients.

## CONCLUSION

In conclusion, this study revealed that the prevalence of HP/DS use is common in children with pediatric neurological disease/complaints in Türkiye. It has been determined that the children of parents using HP/DS are more likely to use HP/DS. For this reason, health personnel, especially doctors and pharmacists, should take a role in creating social awareness on this issue and inform parents about this issue. In order to prevent cases that may arise from non-medical use, herbal medicinal products should be prepared after standardization and necessary quality control processes and presented to the market through pharmacies. Herbal medicinal products should be used under the control of health personnel.

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**Conflict of Interest:** The authors declare that there is no conflict of interest.

**Ethical Approval:** Ethical approval was obtained from the obtained from the Scientific Research Ethics Committee of Karadeniz Technic University, Faculty of Medicine to conduct the study (Date: 05.05.2021 No: 2021/110).

**Authors Contributions:** The authors confirm contribution to the paper as follows: study conception and design: All authors; data collection: İG, TS, NY; analysis and interpretation of results: İG, TS; draft manuscript preparation: All authors. All authors reviewed the results and approved the final version of the manuscript.

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