The influence of alternative medicine in highly active antiretroviral treatment

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Abstract
Objective: Over the last few years, there has been a notable increase in the use of alternative medicine by the general population. The aim of this study is 2-fold. Firstly we will analyse the incidence of the use of medicinal plants in patients with HIV undergoing Highly Active Anti-Retroviral Therapy (HAART). Secondly, with the help of existing bibliographic information, we want to study the existence of possible interactions.

Material and method: We carried out a prospective study with a targeted interview (October to December 2007) on consenting patients with HIV undergoing HAART treatment.

Results: Of the 193 patients that agreed to take part in the survey, 16.6% confirmed they used alternative medicinal therapies. In 46% of the cases there was a potential interaction with the effectiveness of HAART. Forty-six percent of the potential interactions were in the case of the patients who used grapefruit as an alternative medicine, 21% in the case of patients using thistle and Echinacea respectively, 4% for those using omega-3, Chinese herbs, and ginseng.

Conclusion: There is a significant use of natural products by these groups of patients, of which a significant percentage interact with HAART. A better understanding of the possible interactions with HAART and improved information offered to patients with HIV is needed.

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PALABRAS CLAVE
Tratamiento antirretroviral; Plantas medicinales; Interacciones medicamentosas;

Influencia de la medicina alterativa en el tratamiento antirretroviral de gran actividad

Resumen
Objetivo: En los últimos años hemos asistido a un aumento notable en el uso de la medicina alterativa por parte de la población actual. El objetivo de este trabajo es doble. Por un lado, se pretende analizar la incidencia del uso de plantas medicinales en pacientes infectados por el
Introduction

Human immunodeficiency virus (HIV) infection is caused by the HIV virus. Although the eradication of HIV is not currently possible, highly active antiretroviral treatments (HAART) prevents viral replication, re-establishes immunological function, reduces morbi-mortality, and improves the quality of life of the patient infected with HIV.

There are several factors that can have a negative impact on achieving the desired effects. One of these is the interaction of HAART with phytotherapeutic substances. At present, there has been an increase in the use of medicinal plants (alternative medicine) in our environment. The use of medicinal plants has a high risk of interaction with HAART. This risk is increased in drugs with a narrow therapeutic margin, since phytotherapeutic products are complex mixes of organic compounds, they can induce or inhibit the enzymes responsible for metabolism in HAART. As a result, the plasma concentrations of these drugs can be reduced and therefore their efficacy diminished, or, on the contrary, increased, which would exacerbate their toxicity. The aim of this study is to analyse the incidence of the use of medicinal plants in patients infected with HIV and undergoing HAART, as well as analyse the existence of possible interactions with the help of the literature documented.

Material and methods

A prospective study was carried out (October-December 2007) in the outpatient clinic at the Hospital Pharmacy Department at Hospital San Pedro in Logroño. The patients had to be receiving HAART and attending the hospital’s Infectious Disease Department on a regular basis.

A bibliographical search was performed on PubMed for articles published on interactions between antiretroviral drugs and medicinal plants. A search was also performed on the web pages of scientific organisations with databases on interactions, which were considered relevant, between these 2 therapeutic groups.

The following medical terms, extracted from the MeSH database, were used: “herbal medicine,” “herb,” “phytoterapy,” “interactions,” “drug interactions and antiretroviral.” In addition, the following databases were consulted:

a) www.interaccioneshiv.com (Spanish Society of Hospital Pharmacy).
c) www.cofbizkaia.net/COFBI/Publicaciones.nsf/fwContNumeros?OpenForm&rev = Argibideak (Basque Professional Association of Pharmacists).

table 1 summarises the clinical repercussions of the interactions of medicinal plants on the efficacy and toxicity of antiretroviral treatment.

The patients who participated in the study had to complete a targeted questionnaire on the use of alternative medicine, where alternative medicine is understood as “the branch of medicine that compiles non-conventional medical systems, diagnostic methods and therapeutic approaches, both ancient and modern, to understand and validate them and in this way offer them to the public as alternatives or supplements to current conventional medicine,” definition of the 2002 World Health Organization. The interview included aspects such as whether they considered medicinal plants as drugs, whether those interviewed had notified their doctor of their use or whether they had never been specifically asked. The following questions were asked: Do you take medicinal plants, herbs, infusions, or any type of substance as an alternative to antiretroviral medication? In the event of a positive response: Which one(s)? Do you think that these substances could affect the efficacy of the antiretroviral treatment? In the event of a positive response: In what way? Why have these not been recorded in your pharmacistheerapy history? The variables included in the study were taken from the SELENE® computer program, which collects patients’ clinical history (age, sex, how the patient was infected with the HIV virus, the HIV plasma viral load, and CD4 lymphocytes amount). Adherence to HAART was analysed using the calculation in the PRISMA program for dispensing medication to external patients.
The data were codified and entered into a database (Microsoft Access 2007). A spreadsheet (Microsoft Excel Office, 2003) and the SpSS® v12.0 statistical program were used for statistical processing. To find an association between 2 nominal qualitative variables, we used the $\chi^2$ test and when we were working on an association between qualitative and another quantitative variable, we used the non-parametric Mann-Whitney U or Kruskal Wallis tests. There was statistically significant variance when $P$ was lower than .05.

### Results

A total of 193 (44.33%) patients initially participated in the study. Of these patients, the average age (standard deviation) was 43.8 (10.51) years, and 67.3% were male. Of the 193 patients, 32 (16.6%) confirmed that they did consume 1 or more medicinal plants. Table 2 shows their characteristics. Of the 32 patients who consumed some medicinal plant, in 12 (37.5%) there was bibliographic information warning of the toxic potential.
Among the patients who took medicinal plants, 37.5% considered this medication. The same percentage (37.5%) did not know that medicinal plants could produce adverse effects and 100% did not know that these treatments could have a negative effect on their HAART. Among the patients undergoing HAART who consumed some type of medicinal plant, 21.9% were taking nucleoside analogue reverse transcriptase inhibitors, 34.4% protease inhibitors, and 43.7% non-nucleoside reverse transcriptase inhibitors.

There are no statistical differences in any of the variables studied (age, sex, method of contamination, plasma viral load, CD4 lymphocytes amount, adherence, or HAART type) between the group of patients who consumed medicinal plants and the remaining patients.

Figure 1 describes the pharmacological properties of the products used. The results are shown in relation to the total number of patients who confirmed that they consumed some sort of herbal medicine and therefore the sum is greater than 100%. A total of 20 patients (62.5%) confirmed that they consumed just 1 medicinal plant; 9 (28.1%) confirmed that they consumed 2 medicinal plants; and 3 (9.4%) confirmed that they consumed 3 or more medicinal plants. Figure 2 shows the percentage of medicinal plants which are most consumed by patients undergoing treatment with antiretroviral drugs.

Of the total medicinal plants that patients confirmed to consume, no bibliographical references were found for 54% of these in relation to possible adverse reactions with the antiretroviral medication taken. However, information on the influence on the efficacy of HAART was found in the literature for 46% of the medicinal plants consumed (11 cases of grapefruit, 5 cases of Echinacea, and 5 of milk thistle).

Discussion

Patients undergoing HAART regularly use medicinal plants and this often occurs without the knowledge of the doctor or pharmacist. There is evidence that herbal preparations can cause pharmacokinetic and pharmacodynamic interactions.
that represent a potential risk in patients undergoing HAART. Although we found examples of clinically non-significant interactions with antiretroviral agents, there are others that can have serious consequences on the treatment's efficacy.

Despite the fact that the actual prevalence of the consumption of medicinal plants in the Spanish population is not exactly known, it has without doubt increased significantly in recent years. However, some results may help extrapolate these data. A total of 19.6% patients from primary care confirmed consumption; 34.7% from external digestive consultations have consumed some sort of medicinal plant; and 35.7% from anesthetic consultations also confirmed consumption of some sort of medicinal plant. In our study, the results are similar to those observed in primary care (19.6% above and 16.6% in this study).

The population in general and the patients perceive these substances as healthy. The patients are not aware of the adverse effects that these can sometimes produce and that they can even cause HAART to fail. The reasons given for the consumption of medicinal plants is that the patients believe that these increase the efficacy of their treatment, improve their quality of life, reduce the adverse effects of HAART and give them a feeling of control. As observed in this study, a significant percentage of our patients confirm that they are taking some type of medicinal plant, although we found very limited bibliographical information on the possible adverse interactions relating to some of these products. However, other plants do cause interactions, such as grapefruit, milk thistle or Echinacea.

Another interesting aspect is that, in our environment, 62.5% of patients who were taking medicinal plants did not know exactly what type they were taking, could not say what their specific effect was and many had starting using them simply following recommendations from non healthcare individuals. A total of 37.5% of patients taking medicinal plants did not know that these could have damaging health effects. Indeed, none of them informed their doctor or pharmacist in a normal consultation. These results coincide with other studies performed in our environment. One of the reasons cited for not informing their doctors was the lack of awareness that medicinal plants are indeed medication.

Given these data, patients must be directly questioned on the consumption of these products and specifically informed both by the doctors and pharmacists.

There has been little research into the interactions between antiretrovirals and treatment with medicinal plants. However, in some cases there is ample scientific evidence upon which to base recommendations (for example, Hypericum, garlic, Echinacea, marijuana). In order to reduce the risk of interactions, it would be useful to perform targeted questionnaires on the use of medicinal plants, both in the pharmacy and in the medical services. This must be performed by the healthcare professional to improve the efficacy of the antiretroviral treatment, since there are data indicating that patients require better communication to obtain more information on certain habits.

Finally, there is a significant scientific gap in the study of medicinal plants and HAART. In some cases, the studies published are scarce or even contradictory. Knowledge on the potential interactions between many of these medicinal plants and the different HAARTs must be improved.

Conflict of interest
This article has not been previously published and there are no conflicts of interest.

References