The characteristics of conflict of interest in the doctor’s pharmaceutical representative Relationship
Les caractéristiques du conflit d’intérêt dans la relation médecin- délégué médical

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Abstract
Introduction: Studies addressed the influence of pharmaceutical representatives in drug prescribing habits, in terms of quality and quantity.
Aim: To describe the representatives’ strategies, assess their impact on medical prescribing, and study the various factors influencing doctors’ prescribing changes.
Methods: We conducted a cross-sectional study including 70 participants. All of them had an anonymous questionnaire to determine their socio-demographic data, the pharmaceutical representative visits details, the influence of gifts on the medical prescription, and the predictive factors of this influence. We also analyzed the solutions to alleviate the conflict of interest.
Results: We found that 52.8% of participants thought that gifts were the source of an ethical dilemma and 85.7% of them thought that the priority of the pharmaceutical representative was the promotion of the product rather than the scientific interest. However, 68.5% of them thought that the gifts were useful and therefore we can continue to receive them. Nineteen participants (27.1% of cases) thought that gifts can modify their medical prescription. However, there were significantly more subjects (p=0.049) who thought that other colleagues would be more influenced (72.8%). Factors that favor the prescription changing by gifts, were age (p=0.002, OR=1.2) and the number of visits per month (p=0.015, OR=8.8).
Conclusions: There is a discrepancy between the growing awareness of this ethical issue and the daily practices of physicians who continue to accept gifts. The absence of training in bioethics explains these results.

Key-words: Medical ethics; prescription; pharmaceutical representative; conflict of interest.
INTRODUCTION

The conflict of interest is a situation that can negatively influence a professional’s submission to the interests he is supposed to serve (1), or “a set of circumstances that creates a risk that professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest” (2). This would be the case of doctors prescribing a drug in exchange for a benefit provided by the pharmaceutical company that produced it. These situations involve their loyalty and their independence. Healthcare professionals are the target of pharmaceutical industry (PI) marketing strategies whose vector is the pharmaceutical representative (PR). Several studies have suggested that this would alter medical prescription qualitative and quantitative aspects, inducing unjustified risks for the patients, and increasing health costs (3,4). To address this problem, some countries adopted legislation to regulate the interactions between PI and physicians (5). We aimed through this study to describe the marketing strategies of the PRs, to evaluate its impact on medical prescription, and to study the different factors, influencing the prescribing behavior changing.

METHODS

We conducted a cross-sectional study including 70 doctors between August and October 2020 in a University Hospital. All participants had an anonymous questionnaire that determined:

Socio-demographic data

Such as age, sex, discipline (medical, surgical, medicosurgical), grade (university doctor, public health doctor, family medicine resident, resident, and intern), and seniority in the grade. University and public health physicians have been grouped into “specialists”, residents and interns have been grouped into “students”.

The pharmaceutical representative visit characteristics

We determined the number of visits per month, the gifts offered during these visits (information cards, free samples, pens, Continuing medical education sessions with coffee breaks, free meals, financial support for a national or an international congress, research funding, or others), and the frequency of their reception (frequently, sometimes, rarely, or never). Information cards, free samples, and pens were grouped as “small gifts”, the rest of the gifts as “expensive gifts”.

Influence of gifts on medical prescription

We have collected physicians’ opinions about receiving gifts by PRs, considered as “necessary”, “useful”, or “inappropriate”, their probable impact on the visits time, and gifts that create an ethical dilemma according to the participant (to be chosen from the list provided or to be added by the participant). We also analyzed the characteristics of the group that was aware that receiving gifts from PRs generates an ethical dilemma (Age, sex, grade, discipline, seniority, number of visits per month, and type of gifts received). The opinion of the participants concerning the reality of the scientific data provided by the PRs was noted, and if they already verified them.

The influence of marketing strategy on medical prescription

We noted physicians’ opinions concerning the ability of gifts to influence their prescriptions. The importance of this influence was graded on a scale of 0 to 10. In the group claiming that receiving a gift modifies their prescription, we analyzed the factors that would influence this behavior such as: age, sex, grade, discipline, seniority in the grade, number of visits per month, type of gifts received, and marketing strategy adopted by PRs (more visits, more gifts, persuasiveness, clothing, gender, and the laboratory). The doctors’ opinion about the ability of gifts to influence the prescription of other colleagues, which reflects the “illusion of unique invulnerability” was also noted.

The solutions proposed to overcome conflicts of interest

We searched whether participants opted for stopping PRs visits. We noted their opinion about the importance of declaring the conflict of interest in all scientific works and the level of accomplishment of this task in current practice. The participants could suggest other solutions for this ethical dilemma.

Data were analyzed using IBM SPSS Statistics version 23 software.

RESULTS

Socio-demographic data

Seventy doctors were included, their characteristics were summarized in Table 1.

Table 1. Socio-demographic characteristics of our participants

| Socio-demographic characteristics | Results       |
|-----------------------------------|---------------|
| Age (years)                       | 36.63 ± 9.15  |
| Sex ratio (F/M)                   | 1.8           |
| Discipline                        |               |
| medical                           | 28 (40 %)     |
| surgical                          | 15 (21.4 %)   |
| Medico-surgical                   | 27 (38.5 %)   |
| Grade                             |               |
| university doctor                 | 29 (42 %)     |
| public health doctor              | 12 (16 %)     |
| family medicine resident          | 4 (6 %)       |
| resident                          | 18 (26 %)     |
| intern                            | 7 (10 %)      |
| Groups                            |               |
| Specialists                       | 41 (58.6%)    |
| Students                          | 29 (41.4%)    |
| Seniority                         | 7.72 ± 8      |
The visit of the pharmaceutical representative
The average number of visits per month was 4.23 with a median of 3 visits (from one visit to 20). Small gifts were the most distributed: information cards (55 participants or 78.57%), pens (37 participants or 52.85%), and free samples (53 participants or 75.71%). Twenty-seven participants (38.57%) got all of them at once. These gifts were received “frequently” by eight participants (11.4%), “sometimes” by 21 participants (30%), and “rarely” by 41 participants (58.6%).

Opinions regarding gifts received during visits
Only ten participants (14.2%) thought that receiving these gifts was “inappropriate” while 48 participants (68.5%) thought it was “useful”. There were no statistically significant differences between specialists and students. However, according to 56 participants (80%), the time allocated to the PRs will not be reduced in the absence of gift distribution.

Opinions regarding the relationship between gifts and ethical dilemma
Thirty-seven participants (52.8%) believed that gifts are the source of an ethical dilemma, although only 10 participants (14.2%) said their reception was inappropriate. Thirty-one participants (44.2%) believed that gifts do not represent an ethical dilemma and two subjects did not answer the question. Among these gifts, free meals, expenses for national or international congresses were thought to induce an ethical dilemma with respectively 41.4%, 21.4%, and 37.1%. Small gifts such as the information cards, pens, and free samples were only involved in four cases (7.5%). Pens were significantly more mentioned by the students’ group compared to specialists. On the other hand, free meals were significantly more mentioned by the group of specialists. Seven participants proposed other types of gifts such as travels, internships, training, and valuable gifts such as expensive watches.

Characteristics of the group recognizing the link between PRs gifts and ethical dilemma (table 2)
These participants were significantly from a surgical specialty (p=0.008, OR=0.2). Age, sex, grade, seniority in the grade, number of visits, and type of gifts received did not influence this response.

Particularities of the relationship with the pharmaceutical representatives
Sixty participants (85.7%) corresponding to 87.8% of specialists and 79.3% of students thought that the priority of the PR representative was the promotion of the product rather than scientific interest. There was no statistically significant difference between the two groups (p=0.336). Among these participants, only 40 (66.6%) verified the information that was stated during the visit. Specialists were more likely to verify this information [28 specialists (70%) versus 12 (30%) students, (p=0.03)].

The influence of marketing strategy on medical prescription
Nineteen participants (27.1% of cases) said that gifts received by the delegate can change their prescription. Among them there were 12 students (63.1%) and 7 (36.8%) specialists, the students were significantly more influenced (p=0.029). However, 49 participants (70%) denied this influence, and two of them did not answer the question.

Table 2. Univariate analyses of characteristics of the group thinking that gifts induce an ethical dilemma.

| Studied factors       | p     |
|-----------------------|-------|
| Age                   | 0.739 |
| Sex                   | 0.455 |
| Grade                 |       |
| University doctor     | 0.634 |
| Public health doctor  | 0.745 |
| Resident              | 1     |
| Family medicine doctor| 0.337 |
| Intern                | 1     |
| Specialists           | 0.873 |
| Students              | 0.873 |
| Seniority             | 0.123 |
| Discipline            |       |
| Medical               | 0.334 |
| Surgical              | 0.08  |
| Medical surgical      | 0.223 |
| Number of visits      | 0.124 |
| Types of gifts received|      |
| Dosage sheet          | 0.403 |
| Pen                   | 0.811 |
| Free sample           | 1     |
| Staff with coffee break| 1    |
| Lunch dinner          | 1     |
| National congress      | 1     |
| International congress | 0.361 |
| Small gifts           | 1     |
| Expensive gifts       | 0.531 |

The gifts that would have the most influence on the medical prescription were summarized in table 3. For the subjects who said they were influenced by the PRs gifts, the payment of international congress charges (63.1%) and research funding (63.1%) were the most influential gifts. Free meals were significantly more involved according to the specialists (p=0.05). Small gifts were not involved.

Table 3. Gifts that influence medical prescription.

| Gifts                                | Participant number (%) |
|--------------------------------------|------------------------|
| Information cards                    | 1                      |
| Free samples                         | 5                      |
| Pens                                 | 0                      |
| Continuing medical education sessions with coffee breaks | 0 |
| Free meals                           | 2                      |
| Financial support for a national or an international congress | 17 |
| Research funding                     | 12                     |
| other                                | 3                      |
**PRs behavior and modification of the medical prescription**

Forty-three subjects (61.4% of cases) said they would prescribe more products from the PR who visits them the most. Fourteen subjects (20%) would prescribe more products from the PR who gives more gifts. Fifteen subjects (21.4%) would prescribe more products from the friendliest and the more persuasive PR with whom contact is easier. Twenty-nine subjects (41.4%) would prescribe more the products of the most eloquent PR. There was no significant difference in the responses between the student and specialists (p=0.371, p=1, p=0.772, p=0.221, respectively). Twelve participants (17.1%) believed that the originating laboratory may influence the prescription. There was no significant difference in responses between the student and specialists (p=0.745). Only seven participants (10% of cases) believed that the gender of the delegate could influence their medical prescription. There was no significant difference in responses between the student and specialists (p=0.628).

**Predictors of prescription modification by gifts reception**

In the group claiming that receiving a gift can modify their prescription, the univariate study showed that factors that would influence this behavior were age (p=0.01), student's grade (p=0.031) especially the intern grade (p=0.014), seniority in the grade (0.012) as well as the number of visits received per month (p=0.05). The multivariate study retained age (p=0.002, OR=1.2), and the number of visits per month (p=0.015, OR=8.8).

**The illusion of unique invulnerability**

Nineteen participants (27.1%) said that gifts received by the delegate can change their prescription. However, 51 participants (72.8%) thought that it was the prescriptions of other colleagues that could be influenced (p=0.049). There was no significant difference in responses between the students and specialists (p=0.159).

**The solutions proposed (table 4)**

Fifty-five subjects (78.6% of cases) did not agree to stop seeing the PR. Thirty-nine participants (55.7% of cases) believed that conflict of interest should be always declared. Forty percent (28 participants) believed that it should be declared sometimes, and three participants believed that it should never be declared. In everyday practice, 24 participants (34.2%) said that they always declare conflicts of interest in their scientific works. Some other solutions were proposed by the participants (table 4). However, 41 (58.5% of cases) of them did not make any proposal.

| The participants’ proposals | Number of subjects |
|-----------------------------|--------------------|
| Respect for the deontological code | 3 |
| Legislation | 5 |
| Awareness and ethical values application (Patient’s interest, honesty, integrity, loyalty) | 9 |
| Teaching ethics and critical reading of articles | 5 |
| Finding other sources of funding | 5 |
| Limiting prescriptions | 1 |
| Limit gifts to free samples | 3 |
| No proposals | 41 |

**DISCUSSION**

The purpose of pharmaceutical companies is to persuade health care professionals that their product is the best, using various marketing strategies such as advertising, PRs, opinion leaders, and gifts distribution especially free samples. More than a quarter of the expenses of pharmaceutical companies are intended for the “detailed presentation” provided by the PRs (more than 10 billion USD on this form of marketing in 2004 in the United States) (6). PRs are hired to sell products. They have a personal financial interest because they receive a bonus based on sales made, in addition to their salary.

Healthcare professionals face many clinical problems, that they try to solve quickly and effectively. They often use unconscious decision-making shortcuts such as expert recommendations, colleague’s prescriptions, choosing the first treatment that comes to their mind, or available as a sample (7). They continue to rely on PRs to obtain drug data without verifying them (8,9). That is why we carried out this cross-sectional study to assess the influence of the PRs marketing strategies on medical prescription, and doctors’ abilities to face it.

Our results showed that there is an increased awareness of gifts’ role in conflicts of interest. Thirty-seven participants (52.8% of cases) believed that PR gifts induce an ethical dilemma. Sixty participants (85.7% of cases) thought that the PR’s priority was the promotion of the product rather than scientific interest. However, these beliefs did not change the daily practice, since most of the participants thought that gifts are useful (68.5%) and therefore we can continue to receive them. Besides, only 40 participants (66.6%) verified PRs information validity, most of them were specialists (p=0.03). Few participants (19 subjects or 27.1% of cases) thought that gifts can modify their medical prescription. However, there were significantly more participants (p=0.049) who thought that other colleagues would be more influenced (51 participants or 72.8%). This highlights the importance of the illusion of unique invulnerability. Factors that significantly facilitate the influence of gifts were age (p=0.002, OR=1.2) and the number of visits per month (p=0.015, OR=8.8).

The influence of the PRs is linked to several factors. The feeling of obligation and reciprocity is a basic human feeling. PRs “gifts” like free samples, pens, invitations to social or educational events, generate a positive response (10). Free food helps to create a friendly atmosphere, which will benefit to the company (10). In our series, thirty-seven participants (52.8% of cases) thought that gifts are the source of an ethical dilemma, but a small proportion admitted that these gifts can modify their prescription (19 participants or 27.1% of cases), and 14 subjects (20% of cases) would prescribe more products from the company distributing more gifts.
Small gifts would have a greater impact and help establish a friendly relationship between the delegate and the healthcare professionals. According to Katz, “Those who do not recognize the power of small gifts are the most likely to be influenced because they are not on their guard” (11).

Doctors who receive expensive gifts realize easily that the goal is to influence them. Small gifts, however, would be accepted without guilt (12). Expensive gifts are more effective than small gifts in changing the immediate behaviors while small gifts maintain the long-term change (11,12). According to our participants, expensive gifts would modify the medical prescription more than small gifts (63.1% for the financial support of international congresses and the funding of research). This highlights the success of the unconscious strategies used by pharmaceutical companies.

Free samples are a special kind of gift. Their objectives are the initiation of treatment, which can subsequently be sustained, the reduction of doctors’ uncertainty (13) and to recall of the product (13,14). Free samples are for many physicians the most important reason to receive PRs. It is often offered to patients who cannot afford these drugs (15). Kaiser showed that 92% of physicians agree to distribute free samples if the opportunity is presented and they are more likely to prescribe the drugs whose samples were distributed (16). For these reasons, in 2005, the US pharmaceutical companies spent on free samples more than all other marketing forms combined (17). This would explain the fact that 52.8% of our participants thought that gifts are the source of an ethical dilemma, and 68.5% believed that they are useful. We must however understand that free samples can alter prescribing choices. Patients may end up taking expensive and unnecessary drugs (18).

Misleading information is another strategy that aims to exaggerate the benefits and minimize the side effects of the product. It can be a distortion (inaccurate, exaggerated, or ambiguous information), an omission of relevant information, or a distraction by irrelevant ones (19). In our series, 60 participants (85.7% of cases) thought that the priority of the PR was the promotion of the product rather than scientific interest.

In the United States, pharmaceutical companies’ support for medical education increased from $ 310 million to $ 1.2 billion per year between 1998 and 2007. They paid more than 60% of its cost (20,21) because they know that prescribing habits are learned early during the curriculum and that there is no adequate ethical training that could oppose marketing strategies. In our series, the univariate study identified the group of students as being more likely to change their prescription because of gift receiving (p=0.031).

Many healthcare professionals continue to underestimate the effects of pharmaceutical promotion on their professional practice. They are, however, less confident in the ability of their colleagues to resist deceptive persuasion (22). In our series, 51 participants (72.8%) thought that it was the prescriptions of other colleagues that could be influenced (p=0.049).

Teaching conflicts of interest for medical students is almost non-existing in our universities. That could lead to serious health and economic issues. Only 55.7% of our participants thought that we must always declare conflicts of interest and there are only 34.2% who did it in everyday practice. Besides, 41 participants (58.5% of cases) did not propose solutions because they were not properly formed in ethics.

In our series, 78.6% did not agree to stop seeing the PRs because they are an important source of information on new therapies. However, this information was frequently distorted. Therefore, it would be better to count on more reliable sources, providing independent information. This was recommended in 2009 by the WHO which published a practical manual to better understand and manage pharmaceutical promotion (17).

To fight against conflicts of interest in the academic environment, several initiatives from North American and French student associations have been proposed (23-25). In Tunisia, a form for a public declaration of interest links, has been adopted by the ethics committee of the medical school of Tunis. Other concrete measures should be implemented quickly (25) such as: prohibiting any kind of gifts, replacing direct funding of academic activities by pharmaceutical companies, and prohibiting university physicians who have conflicts of interest from giving lectures for the benefit of laboratories (17).

The limits of our work were the small number of participants, which did not allow us to generalize the conclusions, and the heterogeneous population with several disciplines whose interactions are different with PRs. However, it is important to share these results with the academic officials, to consider appropriate preventive measures. The goal would be to establish a national policy defining clearly what is allowed and what is prohibited in the relationship between health professionals and pharmaceutical industry.

Declarations of interest: none

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