Int J Clin Pharm
DOI 10.1007/s11096-014-9968-z

SHORT RESEARCH REPORT

Patient characteristics among users of analgesic over-the-counter aspirin in a Danish pharmacy setting

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Received: 21 November 2013 / Accepted: 31 May 2014

Abstract *Background* Use of over-the-counter (OTC) high-dose acetylsalicylic acid (ASA) is a risk factor for experiencing gastric bleeding. However, more detailed knowledge on the characteristics of users of OTC ASA is needed. *Objective* To characterise users of OTC high-dose ASA in a Danish pharmacy setting. *Method* We conducted an interview based survey among users of OTC high-dose ASA. Questions were asked regarding: (1) demographic characteristics; (2) use patterns; (3) knowledge about adverse events; (4) risk factors for experiencing gastric bleeding; (5) reasons for choosing an ASA-containing medicine; and (6) whether their GP was informed on their use of high-dose ASA. *Results* One-hundred-seventeen interviews were completed. Nineteen percent and 37 % used high-dose ASA on a daily or weekly basis respectively. Sixty-eighth percent found high-dose ASA to be more effective than other analgesics. Fourty-seven percent had one or more risk factors for experiencing ulcer bleeding, most commonly age >60 years (32 %) and previous peptic ulcer (9 %). The most well-known adverse events were abdominal pain (32 %) and peptic ulcer (26 %). The most common source of information was friends and family (32 %). *Conclusion* A large proportion of users of high-dose ASA have risk factors for experiencing gastric bleeding. Health-care professionals needs to provide more information on potential adverse events.

Keywords Aspirin · Denmark · Drug toxicity · Gastric ulcer · Nonprescription drugs · Non-steroidal anti-inflammatory agents

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Impact of findings on practice statements

- There is a seemingly unmet patient need for information on potential adverse events related to the use of high-dose ASA.
- Pharmacists should focus on identifying the large proportion of users of high-dose ASA that have risk factors for experiencing ulcer bleeding.

Introduction

Gastrointestinal bleeding is a serious and potentially life-threatening situation, causing up to 2,500 annual hospital admissions in Denmark [1]. An important risk factor for

Published online: 12 June 2014

experiencing gastrointestinal bleeding is the use of non-steroidal anti-inflammatory drugs (NSAIDs), which increase the relative risk with a factor 4–7 [2]. NSAID-related ulcer-bleeding is found to account for an increasing proportion of bleeding episodes [3]. This is probably aided by the fact that both ibuprofen and acetylsalicylic acid (ASA) are available as over-the-counter (OTC) analgesics in Denmark as in many other countries. In one Danish study, one quarter of patients admitted with ulcer bleeding had used high-dose ASA, primarily as OTC (85 %) (from [3], personal communication).

Much attention has been given to the risk of gastric adverse events of low-dose ASA used in cardiology [2, 4]. A similar focus has not been given to users of high-dose ASA (≥500 mg), even though the gastroduodenal burden of ASA is known to be dose-dependent [5]. Furthermore, the absolute risk of experiencing ulcer bleeding is known to be influenced by the presence of other risk-factors, such as concomitant use of steroids, NSAID, selective serotonin reuptake inhibitors (SSRI), or having experienced previous ulcer or ulcer bleeding [2]. Whether users are aware of the increased risk of ulcer bleeding when using high-dose OTC ASA is unknown. We suspect a need for more elaborate patient information at pharmacies in conjunction with possible interventions towards inappropriate medication use. However, greater knowledge of the users of OTC ASA is necessary before specific pharmacy procedures can be established, e.g. the prevalence of risk factors, patient knowledge and reasons for choosing ASA over other pain-medications.

Aim of the study

We aimed to characterise OTC users of high-dose ASA in Danish pharmacies, with regards to demographic characteristics, use patterns, patient knowledge on potential adverse events, the prevalence of risk factors for experiencing gastrointestinal bleeding, and reasons for choosing ASA over other pain-medications.

Ethical approval

As the patients' contact information were erased upon completion of the questionnaire, all information was stored in an irreversibly anonymised fashion. An approval was therefore neither required from the Danish Data Protection Agency or an ethics committee.

Method

The study was conducted as a personal interview based survey among patients buying any medicine containing high-dose ASA (≥500 mg) at four Danish community pharmacies. The interviews were performed by telephone, guided by a pre-defined electronic questionnaire.

Acetylsalicylic acid in Denmark

High-dose ASA is in Denmark available in three different products: Aspirin® (500 mg ASA indicated to treat minor pains and rheumatic diseases), Treo® (500 mg ASA and 50 mg caffeine indicated to treat minor pains and migraine) and Kodimagnyl® (500 mg ASA and 10 mg codein indicated to treat minor pains). All three products are available as OTC, with OTC-sales comprising 97–98 % of all sales [6]. Aspirin is very rarely used compared to the combination products (≈1 % of the total sales [6]). In Denmark, persons under 18 years are not allowed to buy any oral pain-medication OTC.

Survey

The survey was conducted at four pharmacies in different geographical areas of Denmark (Nykøbing Mors, Copenhagen, Stege and Randers). At these pharmacies, participating pharmacists and pharmaconomists included all patients obtaining OTC high-dose ASA. Patients were excluded if they bought the medicine for someone else or had previously participated in the survey. If eligible, patients were invited to participate. Participants provided their telephone number and were subsequently contacted by a member of the study group (AKK), who performed the interviews.

The questionnaire contained six sections: (1) demographic characteristics of the patient (sex and age); (2) the use of the medicine (type and amount, reason for use, use pattern, and combinations with other analgesic); (3) patients' knowledge about potential adverse events (including drug–drug interactions, where he/she had obtained this knowledge and which adverse events the patient had experienced); (4) relevant co-morbidity (including concomitant use of selected medicines); (5) reasons for choosing an ASA-containing medicine (including reasons for not using paracetamol); and (6) whether the patients' regular GP knew about the use of the medicine.

Analysis

Data was analyzed using descriptive statistics. Analyses were carried out overall and for a predefined subgroup of patients with one or more risk factors for experiencing adverse events related to their use of high-dose ASA. These risk factors were defined as age ≥60 years, use of steroids,

others NSAIDs, low-dose ASA, other anti-thrombotics, or SSRIs and previous peptic ulcer, diabetes, previous blood clot or liver diseases [7]. All analyses were performed using SAS statistical software ver. 9.1 (SAS Institute, Cary, NC).

Results

One-hundred-seventeen interviews were completed. The participation rate was 44 %. Ninety-two (79 %) respondents were women and the mean age was 52 (range 18–87). The patients picked up a median of 60 tablets (interquartile range 50–100) by the time of inclusion.

The most common uses for high-dose ASA were headaches (70 %) and muscle aches (34 %). Eighteen percent used high-dose ASA on a daily basis. Overall, 47 % had one or more risk factors for experiencing gastric bleeding, most commonly age >60 years (32 %) and previous peptic ulcer (9 %) (Table 1).

Sixty-eighth percent preferred high-dose ASA as an analgesic since they found other analgesics to be less effective, while 17 % felt that it had a shorter onset of pain relief compared to other medicines. Nine percent had been recommended high-dose ASA by friends or family. When asked directly about use of paracetamol, 73 % answered that they found paracetamol to be less effective than high-dose ASA. Twenty-seven percent used paracetamol concomitantly with high-dose ASA.

Table 1 Characteristics of over-the-counter high-dose aspirin users

	n = 117
Male	25 (21 %)
Female	92 (79 %)
Age mean (range)	52 (18–87)
Reason for use	
Headaches	82 (70 %)
Migraine	22 (19 %)
Muscle aches	40 (34 %)
Osteoarthritis	12 (10 %)
Frequency of use	
Daily	22 (19 %)
Weekly	43 (37 %)
Monthly	36 (31 %)
<Monthly	16 (14 %)
Risk factors for upper gastrointestinal bleeding	
Age > 60 year	37 (32 %)
Previous ulcer	11 (9 %)
Use of NSAID	10 (9 %)
Use of low dose aspirin	5 (4 %)
Use of steroids	4 (3 %)
Use of SSRI	3 (3 %)

NSAID Non-steroidal anti-inflammatory drugs, *SSRI* Selective serotonin reuptake inhibitors

Thirty-seven percent had experienced one or more adverse events, described as heartburn (18 %), regurgitation (17 %), nausea (8 %) and stomach aches (18 %). Twelve percent of all persons interviewed used proton pump inhibitors. Among those with risk factors this proportion was 15 %.

Overall, 72 % had been in contact with their general practitioner (GP) within the last year. Within this group, 41 % responded that their GP knew of their use of high-dose ASA, while 6 % (n = 7) reported that their GP had suggested that they stopped using high-dose ASA. In the subgroup of patients having one or more risk factors (see above), 52 % reported that their GP knew of their use of high-dose ASA, while 11 % (n = 6) had been suggested to stop.

When asked what adverse events the patients knew were related to the use of high-dose ASA, patients most commonly mentioned abdominal pain (32 %), peptic ulcer (26 %), dyspepsia (15 %), medicine-induced headaches (7 %) and allergic reactions (5 %). The source of information on adverse events was most commonly friends and family (32 %), the pharmacy (21 %), patient package inserts (15 %) and the internet (9 %). Three percent (n = 4) reported having these information from a physician.

Discussion

Among a sample of 117 users of high-dose ASA, nearly half (47 %) had one or more risk factors for experiencing ulcer bleeding. More than half (55 %) used the medicine on a daily or weekly basis. Users had limited knowledge of potentially important adverse events related to the use of high-dose ASA.

The main strength of our study is the use of patient interviews to obtain information on drug utilization among real-life patients. The main limitation of our study is the relative low response rate (44 %), which might selectively have excluded the frailest patients if they e.g. had their medicine picked up by relatives or friends. Furthermore, the use of the patient as the only source of information holds certain implications to the interpretation: The number of GPs having suggested alternative pain medications or the number of patients having received information about potential adverse events might be underreported. However, the figures do reflect the current knowledge of the patient.

Serious gastrointestinal events related to high-dose ASA used for treatment of pain or cold is seldom described in randomized controlled trials (RCTs) [8]. However, patients

included in RCTs are generally healthy, and patients with serious co-morbid illnesses and hazardous co-therapies are excluded. In real-life patients, a broader spectrum of persons may use OTC ASA. Observational studies reporting on GI-safety of high-dose ASA indicate that its use is associated with an increased risk of major GI bleeding similar to other non-selective NSAIDs [2].

Only a few other studies have comparably described users of OTC high-dose ASA. OTC users have been found to differ from prescription users [9]. In line with our findings, a French study found contraindications for NSAID use in 50 % of OTC users [10].

Health-care providers need to be aware of regular use of ASA by their patients and to consider the presence of risk factors for experiencing gastrointestinal events. Often, the aim for health-care providers should be to make the patients stop using high-dose ASA. To this end, it is worth noting that the majority finds high-dose ASA to be more efficient than other analgesics, specifically paracetamol, and that a large proportion use paracetamol concomitantly with their high-dose ASA. This use pattern appears irrational based on evidence from current treatment guidelines, where paracetamol is recommended as first line treatment [11]. Among patients with risk factors, a way to convince patients might be more rigorous information on potentially serious adverse events.

In October 2013, new legislation came into force in Denmark: all OTC analgesics, including high-dose ASA, can now only be bought in packages of up to 20 tablets. While the main reason for this change is OTC paracetamol related suicides, it will hopefully also impact the utilization of high-dose ASA, as users now have to obtain a prescription if they wish to obtain larger amounts of tablets. Whether this legislation will be reflected as a change in the incidence rate of ulcer bleedings related to use of OTC NSAIDs remains to be seen.

Conclusion

In conclusion, many users of OTC high-dose ASA use it on a regular basis, almost half have risk factors for experiencing ulcer bleeding and the majority have insufficient knowledge regarding potential adverse events related to the use of high-dose ASA.

Acknowledgments The authors wish to thank the pharmacists and assistant pharmacists at the participating pharmacies for their aid in recruiting interview subjects for the study. Tora Hammar is acknowledged for valuable comments on the manuscript.

Funding No specific funding was obtained for this study.

Conflicts of interest The authors have no relevant conflicts, financial or otherwise, to declare.

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